

In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: October 12, 2021

HAROLD JACKSON as administrator of the Estate of STEPHANIE JACKSON,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

* PUBLISHED
* No. 16-1194V
* Special Master Nora Beth Dorsey
* Decision Denying Entitlement; Significant Aggravation; Influenza ("Flu") Vaccine; Ulcerative Colitis; Dementia.

Patrick J. Eskew, Scheuermann & Jones LLC, New Orleans, LA, for petitioner.
Christine M. Becer, U.S. Department of Justice, Washington, DC, for respondent.

DECISION

I. INTRODUCTION

On September 23, 2016, Harold Jackson ("petitioner") filed a petition, on behalf of Stephanie Jackson, for compensation under the National Vaccine Injury Compensation Program ("Vaccine Act" or "the Program"), 42 U.S.C. § 300aa-10 et seq. (2012).² Petitioner alleged that Ms. Jackson suffered from injuries, including exacerbation of ulcerative colitis, which resulted in

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

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

colon surgery and dementia, as the result of a Fluzone Quadrivalent influenza (“flu”) vaccination she received on September 26, 2013. Petition at 1 (ECF No. 1); Amended (“Am.”) Petition at 1 (ECF No. 36).

After carefully analyzing and weighing the evidence in accordance with the applicable legal standards, the undersigned finds that petitioner has not provided preponderant evidence that the flu vaccine Ms. Jackson received caused significant aggravation of her ulcerative colitis, and thus, petitioner has not satisfied the burden of proof under Loving v. Secretary of Health & Human Services, 86 Fed. Cl. 135, 142-44 (Fed. Cl. 2009) or Althen v. Secretary of Health & Human Services, 418 F.3d 1274, 1280 (Fed. Cir. 2005). Accordingly, petitioner is not entitled to compensation.

II. PROCEDURAL HISTORY

Petitioner filed his petition and medical records on behalf of Stephanie Jackson requesting compensation under the Vaccine Act on September 23, 2016. Petition; Petitioner’s Exhibits (“Pet. Exs.”) 1-5. On November 1, 2016, the special master presiding at the time scheduled an initial status conference and petitioner refiled medical records on November 2, 2016. Pet. Exs. 4-5.

Petitioner filed additional medical records on August 3 and 25, 2017. Pet. Exs. 6-10. On September 28, 2017, petitioner filed an expert report from Dr. John Cromwell. Pet. Ex. 11. Petitioner then filed an amended petition and a statement of completion in October and November 2017. Am. Petition; Statement of Completion, filed Nov. 10, 2017 (ECF No. 37). Respondent filed a responsive expert report from Dr. Andrew Warner on March 12, 2018. Respondent’s (“Resp.”) Exs. A-C.

Throughout 2018, petitioner filed medical records and two expert reports with accompanying medical literature from Dr. Cromwell and Dr. Thomas Krefft. Pet. Exs. 12-41. In March and April 2019, respondent filed two supplemental expert reports from Dr. Timothy Vartanian and Dr. Warner. Resp. Exs. D-F. Petitioner filed a responsive expert report from Dr. Cromwell on April 18, 2019. Pet. Ex. 42.

The special master held a status conference on May 15, 2019 and ordered petitioner to file additional expert reports from Drs. Cromwell and Krefft. See Order dated May 16, 2019, at 3 (ECF No. 57). Petitioner filed an expert report from Dr. Cromwell on September 24, 2019. Pet. Exs. 43-47. On November 26, 2019, respondent filed a status report indicating respondent would file no additional expert reports. Resp. Status Report (“Rept.”), filed Nov. 26, 2019 (ECF No. 61).

On January 2, 2020, petitioner filed a motion to substitute party and suggestion of death due to the passing of Ms. Jackson. Motion (“Mot.”) to Substitute Party and Suggestion of Death, filed Jan. 2, 2020 (ECF No. 63). The special master granted petitioner’s motion and the case caption changed to Harold Jackson as administrator of the Estate of Stephanie Jackson. Order Granting Mot. to Substitute Party dated Jan. 16, 2020 (ECF No. 65).

The case was reassigned to the undersigned on January 21, 2020. Order Reassigning Case dated Jan. 21, 2020 (ECF No. 66). On February 18, 2020, the parties requested a Rule 5 status conference. Joint Status Rept., filed Feb. 14, 2020 (ECF No. 68). The Rule 5 status conference was held on April 16, 2020, and the undersigned opined Dr. Krefft's theory that hypoxia occurred during surgery and caused short-term memory loss was "unpersuasive and lacking in foundational evidence." Rule 5 Order dated Apr. 16, 2020, at 1-2 (ECF No. 69). However, the undersigned stated that petitioner may be able to receive compensation based on Dr. Cromwell's theory that Ms. Jackson's ulcerative colitis was significantly aggravated by vaccination. Id. at 2. The undersigned encouraged the parties to engage in settlement negotiations. Id.

Petitioner filed medical records on June 12, 2020. Pet. Ex. 50. On June 17, 2020, respondent filed a status report stating respondent was not interested in settlement and requesting to file an expert report. Resp. Status Rept., filed June 17, 2020 (ECF No. 73). On August 17, 2020, respondent filed an expert report from Dr. Randy Longman. Resp. Exs. G-K. Petitioner filed a responsive expert report on September 8, 2020. Pet. Ex. 51.

The undersigned held a status conference on September 10, 2020 and the parties agreed to file a motion for a Ruling on the Record. Order dated Sept. 10, 2020 (ECF No. 77). In November 2020, petitioner filed medical records and a motion for Ruling on the Record. Pet. Exs. 52-57; Pet. Mot. for Ruling on the Record ("Pet. Mot."), filed Nov. 12, 2020 (ECF No. 83). Respondent filed a response to petitioner's motion on December 12, 2020. Resp. Response to Pet. Mot. ("Resp. Response"), filed Dec. 12, 2020 (ECF No. 84). Petitioner filed a reply on February 8, 2021. Pet. Reply to Resp. Response ("Pet. Reply"), filed Feb. 8, 2021 (ECF No. 87).

This matter is now ripe for adjudication.

III. ISSUES TO BE DECIDED

The parties dispute causation. Petitioner alleges that the flu vaccine administered on September 26, 2013, significantly aggravated Ms. Jackson's ulcerative colitis, which was in remission for three decades prior to vaccination. Pet. Mot. at 2. Petitioner alleges that Ms. Jackson's severe ulcerative colitis resulted in extensive surgery—a restorative proctocolectomy, which removed her colon and rectum. Id. Due to the surgery, petitioner asserts that Ms. Jackson developed cognitive impairment. Id. at 3. Petitioner therefore asserts the flu vaccination exacerbated Ms. Jackson's ulcerative colitis, which necessitated surgery, and the disease and resultant surgery caused her cognitive changes. Id. at 3-4.

Respondent disputes that the flu vaccine significantly aggravated Ms. Jackson's ulcerative colitis. Resp. Response at 1. Respondent further asserts petitioner is unable to satisfy his burden of proving causation under the three prongs of Althen or significant aggravation under

the six-factor test established in Loving. Id. at 5.³ Respondent also argues that petitioner has not established by preponderant evidence that Ms. Jackson’s surgery caused her to suffer dementia. Id. at 12.

IV. FACTUAL SUMMARY

A. Summary of Medical Records

On September 26, 2013, Ms. Jackson received a flu vaccine in her right deltoid. Pet. Ex. 2 at 1.⁴ Ms. Jackson was 62 years old at the time. Pet. Ex. 6 at 96.

On November 22, 2013, Ms. Jackson presented to Ochsner North Shore Gastroenterology (“North Shore Gastroenterology”) and was seen by Nurse Practitioner (“NP”) Elsa Treadway-Hahn. Pet. Ex. 10 at 4. Ms. Jackson complained of symptoms of bleeding for the last three-to-four weeks. Id. at 8. Ms. Jackson recalled that her last significant ulcerative colitis flare was in the 1990s.⁵ Id. Her “[f]lares [were] mildly triggered with certain foods or stress, but controlled when offending agent [was] removed.” Id. The problem was “gradually improving.” Id. Ms. Jackson was prescribed a suppository, mesalamine.⁶ Id. at 10. Ms. Treadway-Hahn

³ Because petitioner alleged significant aggravation the undersigned will analyze the evidence according to the six-factor test in Loving:

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

Loving, 86 Fed. Cl. at 144. The Loving factors four, five, and six constitute the three prong causation analysis set forth in Althen, as described more fully on page 27-28.

⁴ Fluzone Quadrivalent is an inactivated flu vaccine that does not contain any aluminum. U.S. Food & Drug Admin., Package Insert – Sanofi Pasteur 450/477 Fluzone® Quadrivalent, 19 (2014).

⁵ Medical records regarding Ms. Jackson’s treatment for ulcerative colitis were requested from the University of Alabama-Birmingham Hospital. According to petitioner, Ms. Jackson was seen there for ulcerative colitis around 1988, but this hospital only keeps patient records for 25 years, so petitioner reported that no records were available. Pet. Ex. 9 at ¶ 16.

⁶ Mesalamine is an active metabolite of sulfasalazine, used in the prophylaxis and treatment of inflammatory bowel disease and ulcerative proctitis; it is administered orally or rectally.

recommended continuing a daily probiotic, avoiding triggering foods, and scheduling a colonoscopy. *Id.* Ms. Jackson was diagnosed with ulcerative colitis confined to the rectum and rectal bleeding. *Id.* at 9.

On December 27, 2013, licensed practical nurse (“LPN”) Kacie Fourroux at North Shore Gastroenterology spoke on the phone with Ms. Jackson regarding a prescription of Cortenema⁷ because the suppository medicine was not working. Pet. Ex. 10 at 23-24. Ms. Fourroux recommended that Ms. Jackson schedule a colonoscopy; Ms. Jackson replied that she would consider it. *Id.* at 23.

On December 31, 2013, Ms. Jackson called North Shore Gastroenterology stating she had been feeling very tired and weak, and had bleeding with bowel movements. Pet. Ex. 10 at 26. Laboratory and stool studies were ordered and performed on January 7, 2014 by Dr. Malcom Andry. *Id.* at 30. Ms. Jackson’s stool studies were normal; she had an elevated white blood count (24.97; normal 3.90-12.70), and normal hemoglobin (15.2). *Id.* at 32, 45.

A computerized tomography (“CT”) was performed on January 8, 2014. Pet. Ex. 10 at 47-48. The study showed “extensive abnormal mucosal thickening and pericolic inflammatory fat stranding extending from the ascending colon to the rectosigmoid colon. Differential considerations for these findings include[d] *C. difficile* colitis/infectious colitis^{8]} and ulcerative colitis.” *Id.* at 48. She was again prescribed rectal suppositories. Pet. Ex. 6 at 90.

On January 14, 2014, Ms. Jackson called North Shore Gastroenterology reporting the medication did not help and she was feeling weaker every day. Pet. Ex. 10 at 64. She was advised on go to the emergency room (“ER”) at Ochsner Hospital. *Id.* at 64-63. She was admitted to the ER for rectal bleeding and ulcerative colitis. Pet. Ex. 6 at 93. The medical records note that the onset of symptoms was “since November 2013.” *Id.* at 96. In the ER, Dr. Edwin Forrest documented that Ms. Jackson’s last coloscopy was done in the mid-1990s, and she did “experience episodes of bloody stools in between the time of remission but not to this

Mesalamine, Dorland’s Online Med. Dictionary, <https://www.dorlandsonline.com/dorland/definition?id=30528&searchterm=mesalamine> (last visited Sept. 9, 2021).

⁷ Cortenema is the trademark for hydrocortisone, an anti-inflammatory cream. Cortenema, Dorland’s Online Med. Dictionary, <https://www.dorlandsonline.com/dorland/definition?id=11251&searchterm=Cortenema> (last visited June 17, 2021); Hydrocortisone, Dorland’s Online Med. Dictionary, <https://www.dorlandsonline.com/dorland/definition?id=23353> (last visited June 17, 2021).

⁸ *Clostridium difficile*, or *C. difficile*, is a bacteria species that is part of the normal colon flora in infants and some adults; it produces a toxin that can cause inflammation. Clostridium Difficile, Dorland’s Online Med. Dictionary, <https://www.dorlandsonline.com/dorland/definition?id=65630> (last visited July 7, 2021).

extent.” Id. at 97. Ms. Jackson was admitted to the hospital and a review of her diagnoses included “[a]cute hepatitis C.”⁹ Id. at 93.

A comprehensive exam performed on January 16, 2014 by Dr. Bryan DiBuono noted no focal sensory or motor neurologic deficits. Pet. Ex. 6 at 309. His impression was ulcerative colitis and an abnormal CT scan, and he recommended a colonoscopy. Id.

On January 17, 2014, Dr. DiBuono performed a colonoscopy. Pet. Ex. 6 at 44. Findings were “inflammation characterized by adherent blood, congestion (edema), erosions, erythema, friability, pseudopolyps and deep ulcerations [] found in a continuous and circumferential pattern from the anus to the hepatic flexure¹⁰. . . . This was severe and graded as Mayo Score 3 (severe, with spontaneous bleeding, ulcerations).” Id. at 44. The ascending colon and terminal ileum were normal. Id. at 437. A colorectal surgery consult was recommended. Id. at 45.

Ms. Jackson’s symptoms improved with aggressive treatment, however on January 26, 2014, Dr. DiBuono noted that her symptoms were worsening. Pet. Ex. 6 at 164. Endoscopic therapy was not recommended given Ms. Jackson’s “severe diffuse disease” and surgical intervention was thought to be likely. Id. at 165, 172.

Dr. Joshua Parks performed a restorative proctocolectomy with diverting ileostomy on January 31, 2014. Pet. Ex. 6 at 446. Preoperatively, Ms. Jackson’s oxygen saturation was normal, between 96-100%, and she was oriented and alert to time, person, place, and situation. Id. at 1912. During surgery, Ms. Jackson’s vital signs and oxygen status were monitored, and there were no problems noted. Id. at 1880-91. The surgery was without complication and Ms. Jackson was in stable condition. Id. at 448.

Ms. Jackson was stable postoperatively, from the date of surgery, through postoperative day six. See generally Pet. Ex. 6 at 196-246. There is no documentation to suggest that she had hypoxia. On postoperative day six, Ms. Jackson complained of abdominal pain and nausea, and she had episodes of rectal bleeding. Id. at 244, 259. An endoscopy performed showed “old blood noted at staple line,” but no active bleeding was seen. Id. at 264-65. Throughout her recovery period in the hospital, Ms. Jackson refused her meals, medications, and treatments. Id. at 110, 302-03, 305. Amanda Proulx, registered nurse (“RN”), documented, “[patient] is hindering some progressi[on] by refusing some medical treatments and modalities.” Id. at 305.

Ms. Jackson was discharged on February 12, 2014. Pet. Ex. 6 at 105. Her discharge notes stated she tolerated the proctocolectomy with diverting ileostomy well and had controlled postoperative rectal bleeding. Id. at 107. She was discharged home in stable condition. Id. Her discharge diagnoses were rectal bleeding, ulcerative colitis, anemia, and acute hepatitis C. Id. at 105.

⁹ The relevance of Ms. Jackson’s diagnosis of hepatitis C was not commented on by the experts.

¹⁰ Hepatic flexure is the bend in the large intestine at which the ascending colon becomes the transverse colon. Hepatic Flexure, Dorland’s Online Med. Dictionary, <https://www.dorlandonline.com/dorland/definition?id=76389> (last visited July 7, 2021).

On February 19, 2014, Ms. Jackson presented to Ochsner Hospital Emergency Department (“ED”) for fatigue, malaise, and a urinary tract infection. Pet. Ex. 6 at 14. Dr. Daniel Johnson noted a “gradual onset of fatigue since having part of her colon removed 1 week prior, secondary to having ulcerative colitis.” Id. at 16. Ms. Jackson was also reported to have had “some intermittent confusion episodes.” Id. Her neurological exam noted she was alert and oriented to person, place, and time. Id. at 17. A urinalysis revealed results consistent with a urinary tract infection. Pet. Ex. 10 at 73.

Ms. Jackson had a postoperative visit with Dr. Parks on February 25, 2014. Pet. Ex. 10 at 103. Dr. Parks noted Ms. Jackson was severely debilitated prior to surgery and was slowly recovering. Id.

On February 27, 2014, Ms. Jackson was admitted to Ochsner North Shore Medical Center for dehydration, abdominal pain, and distension. Pet. Ex. 10 at 105, 108. Dr. John Seymour diagnosed Ms. Jackson with dehydration and hypokalemia. Id. at 110. Petitioner told Ms. Jackson’s doctors she was not eating or drinking much at home. Id. Ms. Jackson was discharged from the hospital on March 2, 2014. Id. at 115. At discharge, it was noted that Ms. Jackson was experiencing confusion. Id. at 126.

Ms. Jackson had a hospital follow up with Dr. Sam Moghtader on March 19, 2014. Pet. Ex. 10 at 300. Ms. Jackson reported feeling better except for moderate fatigue and mild depression. Id. Dr. Moghtader reported appetite impairment. Id.

Ms. Jackson presented to Ochsner North Shore Neurology for memory loss on April 7, 2014. Pet. Ex. 10 at 320. Dr. Nisha P. Chhabria noted that since Ms. Jackson’s surgery in January, her family had noticed that she was confused and would repeat herself. Id. at 323-24. “She asks questions over and over again. She can’t remember details of things that have happened in the last month and a half.” Id. at 324. A review of a CT head scan showed “[m]ild brain atrophy with deep white matter ischemic changes otherwise negative head CT [] (the atrophy is mainly of the frontal lobes).” Id. at 325. Ms. Jackson was diagnosed with dementia, vitamin D insufficiency, and thiamine deficiency. Id. at 326.

In a follow up visit on April 29, 2014, Dr. Parks stated, “[patient’s] postoperative course has been complicated by issues of malnutrition, weakness, and return of strength as she was in fulminant colitis at the time of her surgery.” Pet. Ex. 10 at 363. “Her nutrition and strength have recovered well over the last month. She is having no pain, and denies [nausea or vomiting]. She continues to suffer and struggle with confusion and memory lapses.” Id.

Ms. Jackson had an ileostomy takedown and small bowel resection by Dr. Parks on May 6, 2014. Pet. Ex. 10 at 477. The surgery was uneventful, and she was discharged home the same day. Id. Dr. Parks stated she was doing well, but remained weak. Id. at 479.

On August 15, 2014, Ms. Jackson followed up with Dr. Chhabria for dementia. Pet. Ex. 10 at 717. At her last visit, she was encouraged to take vitamin B1 and D replacements. Id. Memory medication was suggested but she declined. Id. She felt that she was doing well, but

her husband thought otherwise. Id. Petitioner stated he set up and made sure she took her medications because otherwise she would not take them. Id.

Ms. Jackson had a flexible sigmoidoscopy performed by Dr. Parks on August 26, 2014. Pet. Ex. 10 at 731. Impression was “[p]atent ileal pouch-anal anastomosis. Localized mild inflammation was found at the anus secondary to proctitis ulcerative colitis.” Id. at 732. Dr. Parks diagnosed Ms. Jackson with chronic ulcerative proctitis. Pet. Ex. 6 at 40.

On February 11, 2015, Dr. Thomas Gann, a neurologist, diagnosed Ms. Jackson with frontal lobe dementia. Pet. Ex. 3 at 23. Ms. Jackson presented to Dr. Gann to file for disability. Id. at 26. Dr. Gann noted this was his first time seeing Ms. Jackson. Id. Dr. Gann stated that Ms. Jackson reported short-term memory issues that “sound to have begun a few years ago.” Id. at 23. He noted some personality changes, but no difficulties with executive function. Id. He documented her past medical history of inflammatory bowel disease, ulcerative colitis, blood transfusion, and hypertension. Id. at 23-24. On neurological exam, Dr. Gann noted “odd affect” and “recent and remote memory appear to be limited.” Id. at 26. A CT done in 2014 showed “mild brain atrophy with deep white matter ischemic changes,” but otherwise negative. Id.

Subsequently, on July 13, 2015, Ms. Jackson presented to Dr. Eileen Correa for a Neuropsychological Evaluation. Pet. Ex. 10 at 878. Dr. Correa stated Ms. Jackson was referred to her due to memory decline following surgery in 2014. Id. Dr. Correa reported that Ms. Jackson did not take any medications and had no family history of memory problems/dementia. Id. In a phone conversation with petitioner, petitioner told Dr. Correa that Ms. Jackson repeated herself, frequently asked what day and year it was, did not understand that she did not remember, forgot food in the microwave, might forget she left the stove on, and had gained 30 pounds in the past couple of years. Id.

The Neuropsychological Evaluation revealed impairment in immediate and delayed auditory/verbal and visual memory, temporal orientation, visuospatial perception, psychomotor speed, and mental flexibility, and variability in verbal fluency (low average and moderately impaired performances), with increased irritability and anger. Pet. Ex. 10 at 882. Dr. Correa opined that the pattern suggested mild frontal lobe dementia. Id.

On November 13, 2015, Ms. Jackson returned to see Dr. Gann. Pet. Ex. 3 at 84. He prescribed donepezil (Aricept) for dementia and reviewed her neuropsychological testing from Dr. Correa. Id. at 81, 84-85.

Ms. Jackson had a follow up with Dr. Gann on November 26, 2016 for frontal lobe dementia. Pet. Ex. 10 at 936. Dr. Gann filled out disability papers for Ms. Jackson and recommended a change in medication for her gastrointestinal issues. Id. He recommended she follow up with her primary care provider about the persistently low vitamin D. Id.

On October 15, 2019, Ms. Jackson was admitted to Ochsner Northshore Medical Center due to pneumonia, weakness, and acute liver failure. Pet. Ex. 50 at 1, 6. Unfortunately, during that admission, Ms. Jackson died from septic shock on October 19, 2019. Id. at 733; Pet. Ex. 49 at 1.

B. Affidavits

1. Affidavit of Petitioner

Petitioner is Ms. Jackson's husband. Pet. Ex. 9 at ¶ 1. Petitioner stated that Ms. Jackson had ulcerative colitis in the past, but the disease had been dormant and asymptomatic for over ten years prior to 2013. Id. at ¶ 4. He averred that a few days after her flu vaccination on September 26, 2013, he witnessed Ms. Jackson's ulcerative colitis flare up and noted that she attempted to treat her symptoms on her own. Id. at ¶¶ 5-7. Petitioner stated that after about three weeks of severe symptoms of abdominal pains, rectal bleeding, and diarrhea, Ms. Jackson attempted to get an appointment with a gastroenterologist. Id. at ¶¶ 9, 11. Petitioner averred that Ms. Jackson went to the ER at Ochsner Hospital North Shore on January 7, 2014.¹¹ Id. at ¶ 12. On January 31, 2014, Ms. Jackson had a restorative proctocolectomy and diverting ileostomy. Id. at ¶ 13. Immediately after the surgery and anesthesia, Ms. Jackson began exhibiting symptoms of memory loss and neurological deficits that did not exist prior to the surgery. Id. at ¶ 14.

2. Affidavit of Sheila Carter

Ms. Sheila Carter knew Ms. Jackson since 1995 and they spoke on a regular basis. Pet. Ex. 45 ¶¶ at 1-2. Prior to the flu vaccination on September 26, 2013, Ms. Carter affirmed Ms. Jackson did not experience any issues or symptoms related to ulcerative colitis or chronic bowel problems. Id. at ¶ 4. Ms. Carter stated prior to the flu vaccination, Ms. Jackson did not appear to experience any symptoms or issues related to cognitive impairment. Id. at ¶¶ 4-6.

3. Affidavit of Miah Jackson

Mr. Miah Jackson knew Ms. Jackson since 1990 and they spoke on a regular basis. Pet. Ex. 46 at ¶¶ 1-2. Prior to the flu vaccination on September 26, 2013, Mr. Miah Jackson affirmed Ms. Jackson did not experience any issues or symptoms related to ulcerative colitis or chronic bowel problems. Id. at ¶ 4. Mr. Miah Jackson also stated prior to the flu vaccination, Ms. Jackson did not appear to experience any symptoms or issues related to cognitive impairment. Id. at ¶¶ 4-6.

4. Affidavit of Fay Lopez

Ms. Fay Lopez is Ms. Jackson's mother. Pet. Ex. 47 at ¶ 1. They spoke on a regular basis. Id. at ¶ 2. Prior to the flu vaccination on September 26, 2013, Ms. Lopez affirmed Ms. Jackson did not experience any issues or symptoms related to ulcerative colitis or chronic bowel problems. Id. at ¶ 4. Ms. Lopez stated prior to the flu vaccination, Ms. Jackson did not appear to experience any symptoms or issues related to cognitive impairment. Id. at ¶¶ 4-6.

¹¹ Based on the medical records, Ms. Jackson had blood work drawn on January 7, 2014, but she was not admitted to the ER until January 14, 2014. See Pet. Ex. 10 at 38.

C. Expert Reports

1. Petitioner – Dr. John W. Cromwell¹²

a. Background and Qualifications

Dr. Cromwell is board-certified in both General Surgery and Colon and Rectal Surgery and serves as the Director of gastrointestinal, minimally invasive, and bariatric surgery at the University of Iowa, where he is also a clinical professor of surgery. Pet. Ex. 11 at 1-2. He is the Associate Chief Medical Officer and Director of Surgical Quality & Safety at University of Iowa Healthcare. Id. at 2. He received his B.S. in chemistry from Nebraska Wesleyan University, and his M.D. from the University of Minnesota Medical School. Pet. Ex. 15 at 1. He also performed his residency in general surgery and a fellowship in surgical infectious disease at the University of Minnesota Hospitals and Clinics. Id. He has published numerous peer reviewed papers and authored several books and book chapters. Id. at 5-7.

b. Opinion

i. Loving Prongs 1, 2, & 3: Condition Before and After Vaccination and Significant Aggravation

Prior to vaccination, Dr. Cromwell noted that Ms. Jackson was employed full time as a registered nurse in a hospital. Pet. Ex. 43 at 2. According to the affidavit submitted by petitioner, Ms. Jackson had neither symptomatic ulcerative colitis nor symptomatic neurological impairment prior to vaccination. Id. Dr. Cromwell stated that prior to her surgical treatment, there are no medical records demonstrating that Ms. Jackson had signs or symptoms of dementia. Id. at 3. He referenced notes by Dr. Chhabria and Dr. Gann, which he asserted documented no cognitive issues prior to her surgery. Id.¹³

Dr. Cromwell opined Ms. Jackson’s condition was significantly aggravated by the flu vaccine. Pet. Ex. 43 at 1. He asserted that Ms. Jackson was employed full time as a registered nurse in a hospital prior to vaccination and had not had symptoms of ulcerative colitis for many years prior to the 2013 vaccination. Id. at 5. Then, according to Dr. Cromwell, within a week or two after vaccination, she began “having a major, life disrupting re-occurrence of ulcerative colitis.” Id. Dr. Cromwell believed that the post-vaccination changes in Ms. Jackson’s ulcerative colitis condition constituted a significant aggravation. Id. at 1.

¹² Petitioner filed six expert reports authored by Dr. Cromwell. Pet. Exs. 11, 12, 16, 42, 43, 51.

¹³ This may be incorrect. On February 11, 2015, Dr. Gann documented short-term memory issues that “sound to have begun a few years ago.” Pet. Ex. 3 at 23. Additionally, on April 7, 2014, Dr. Chhabria reviewed a CT head scan that showed, “[m]ild brain atrophy with deep white matter ischemic changes otherwise negative head CT [] (the atrophy is mainly of the frontal lobes).” Pet. Ex. 10 at 325. Dr. Cromwell stated, “[t]he presence of mild brain atrophy on CT imaging could be evidence of a chronic condition.” Pet. Ex. 12 at 2.

ii. **Althen Prong 1/Loving Prong 4: Is There a Medical Theory Causally Connecting a Significant Worsened Condition to the Vaccination?**

Dr. Cromwell explained that ulcerative colitis is an autoimmune condition, “in which pro- and anti-inflammatory mediators within the intestinal mucosa become imbalanced” and cause inflammation. Pet. Ex. 11 at 5. He stated that ulcerative colitis involves “a complex T-cell mediated mechanism, . . . specifically an ‘overly exuberant response’ from T[h]2 cells.”¹⁴ Id. (citing Pet. Ex. 53 at 8).¹⁵ He further asserted that this immune response is susceptible to modulation, as evidenced by the major therapies used to treat moderate to severe ulcerative colitis. Id. at 5-6 (citing Pet. Ex. 54).¹⁶ Dr. Cromwell opined that while the exact mechanisms of non-specific immunomodulation¹⁷ from vaccines is controversial, the presence of such immunomodulation, both favorable and unfavorable, is well documented. Id. at 6 (citing Pet. Ex. 19).¹⁸ Therefore, he posited that non-specific immunomodulation¹⁹ is “a plausible mechanism for vaccine-induced conversion to severe [ulcerative colitis].” Id. at 6.

As an example of his theory of non-specific immunomodulation, Dr. Cromwell stated that “inactivated vaccines such as DTP [(‘Diphtheria, Tetanus, Pertussis’)], the combined DTP-

¹⁴ T cells, or lymphocytes, are “cells primarily responsible for cell-mediated immunity.” T Lymphocytes, Dorland’s Online Med. Dictionary, <https://www.dorlandsonline.com/dorland/definition?id=87562> (last visited Aug. 4, 2021). “When activated by antigens, T lymphocytes proliferate and differentiate into T memory cells and the various types of regulatory and effector T cells.” Id. Adaptive, not innate, immunity is “mediated by B and T lymphocytes following exposure to a specific antigen.” Illustrated Dictionary of Immunology 18 (3d ed. 2009). Th2 cells are a “T cell subset based on cytokine production and effector functions. Th2 cells synthesize interleukin-4 (IL4), IL5, IL6, IL9, IL10, and IL13. Their main function is to induce antibody synthesis by B cells.” Illustrated Dictionary of Immunology 693 (3d ed. 2009). “Th2 cells are principally responsible for host defense exclusive of phagocytes.” Id.

¹⁵ Bernard Khor et al., Genetics and Pathogenesis of Inflammatory Bowel Disease, 474 *Nature* 307 (2011).

¹⁶ Asher Kornbluth & David B. Sachar, Ulcerative Colitis Practice Guidelines in Adults: American College of Gastroenterology, Practice Parameters Committee, 105 *Am. J. Gastroenterology* 501 (2010).

¹⁷ Immunomodulation is the adjustment of the immune response to a desired level. Immunomodulation, Dorland’s Online Med. Dictionary, <https://www.dorlandsonline.com/dorland/definition?id=24906> (last visited Aug. 4, 2021).

¹⁸ Kristoffer J. Jensen et al., Unravelling the Nature of Non-Specific Effects of Vaccines—A Challenge for Innate Immunologists, 28 *Seminars Immunology* 377 (2016).

¹⁹ Dr. Cromwell also referred to this as “upward modulation of the immune response.” Pet. Ex. 43 at 7.

HBV-HIB vaccine, hepatitis B [(‘hep B’)] vaccine, and inactivated polio [(‘IPV’)] vaccine have been epidemiologically linked to detrimental effects in recipients.” Pet. Ex. 11 at 6. He stated that the Fluzone vaccine is also an inactivated vaccine. Id.

In support of his opinion that inactivated vaccines cause detrimental effects, Dr. Cromwell cited a review article by Jensen et al. Pet. Ex. 19. The authors state that the concept of non-specific effects of vaccines is a controversial subject. Id. at 2. Generally, the concept is based on epidemiological studies which have reported that some live attenuated vaccines, like BCG²⁰ and measles vaccines, have beneficial effects shown to reduce “all-cause mortality” in a given population. Id. However, Jensen et al. state that inactivated vaccines (DTP, hep B, IPV), which protect against specific infections, may increase susceptibility to other infections. Id. As such, they “have been associated with an increase in all-cause mortality in settings with herd-immunity to the targeted diseases.” Id.

Jensen et al. describe two mechanisms proposed to explain the concept of non-specific effects, cross reactivity of T-lymphocytes (heterologous immunity) and trained immunity. Pet. Ex. 19 at 2. The authors discuss these mechanisms in the context of how vaccines improve resistance to other infections, as seen with BCG and measles vaccines, by boosting the “innate immune responses to other pathogens.” Id. However, the article does not appear to address mechanisms whereby vaccines may cause deleterious effects. Moreover, the Jensen et al. authors did not extend the findings applicable to DTP, hep B, and IPV to the flu vaccine.²¹ Nor did the authors extend the concept of non-specific effects to include autoimmune diseases. There is nothing in the article to suggest that a non-specific effect of a flu vaccine would exacerbate underlying ulcerative colitis or any other autoimmune illness. In short, nothing in the article extends the concept of non-specific effects of vaccines to the facts and circumstances here.

In another article cited by Dr. Cromwell, by Shann,²² the concept of non-specific effects of vaccines is described as the manner by which “vaccines alter the subsequent response to unrelated infections,” in that they may increase mortality from other infections. Pet. Ex. 20 at 5. As such, the concept does not appear to be relevant when the subsequent illness at issue does not involve an infectious pathogen.

²⁰ The BCG, Bacille Calmette-Guérin, vaccine “is used for routine vaccination of children only in regions where there is a high incidence of tuberculosis. In the United States it is recommended only for immunization of high-risk individuals. BCG vaccine is also administered intravesically in the treatment of carcinoma of the bladder.” BCG Vaccine, Dorland’s Online Med. Dictionary, <https://www.dorlandonline.com/dorland/definition?id=116498> (last visited Sept. 9, 2021).

²¹ To the extent that Dr. Cromwell cited Jensen et al. to suggest that the deleterious effect of inactivated vaccines is due to the alum adjuvant, it is not relevant, as there is no evidence here to suggest that the flu vaccine given to Ms. Jackson contained alum. See Pet. Ex. 19 at 3.

²² Frank Shann, The Non-Specific Effects of Vaccines, 95 Archives Disease Childhood 663 (2010).

Dr. Cromwell conceded that “the development or exacerbation of [ulcerative colitis] has not been documented in pre-or post-market trials of Fluzone.” Pet. Ex. 11 at 7. He attributed this to the fact that it would be a rare event. *Id.* Dr. Cromwell stated ulcerative colitis following vaccination is rare but does occur. Pet. Ex. 12 at 1. He cited Naurla et al.,²³ which reviewed the current literature pertaining to the efficacy and safety of seasonal flu vaccinations in inflammatory bowel disease patients receiving immunosuppressive therapy. Pet. Ex. 14. Naurla et al. reported two cases of potential flares of inflammatory bowel disease after flu vaccination. *Id.* at 3-4. The first case involved a 39-year-old woman with well-controlled (on medication) ulcerative colitis who experienced abdominal pain and frequent bowel movements three days after vaccination. *Id.* The second case described a 52-year-old woman with ulcerative colitis who had been in remission; however, within hours of receiving a flu vaccination, she experienced a severe exacerbation of her disease. *Id.* at 4. Her exacerbation could not be controlled and ultimately required surgical treatment. *Id.* That patient also subsequently recalled having a milder flare following a previous flu vaccination. *Id.* Of note, the authors noted that “the overall quality of these data is poor.” *Id.* at 3.

While Dr. Cromwell agreed that there are no reports of ulcerative colitis or exacerbation of the condition in pre- or post-marketing trials, he cited four cases²⁴ from the Vaccine Adverse Event Reporting System (“VAERS”)²⁵ of ulcerative colitis following the flu vaccine. Pet. Ex. 43 at 9 (citing Pet. Ex. 44). The first VAERS report (526248) documented a 61-year-old man whose onset of ulcerative colitis was 82 days after vaccination. Pet. Ex. 44 at 2. The second case (414602) was a 37-year-old man who reported an ulcerative colitis flare and asthma exacerbation 10 days after vaccination. *Id.* at 4. Third (305504), was a young man in his twenties who received several vaccinations,²⁶ including the flu vaccine, and tested positive for *C. difficile* infection 24 hours later. *Id.* at 6-7. He was diagnosed with “Infectious Colitis secondary to *C. diff.*” *Id.* at 7. Fourth, are the VAERS reports (354990 & 3582176) for the 52-year-old woman described above in the Naurla et al. article. *Id.* at 9-10, 13; see also Pet. Ex. 14 at 4.

Lastly, Dr. Cromwell cited another Vaccine Program case, where he was an expert for the petitioner, in support of his mechanistic theory. See Morgan v. Sec’y of Health & Hum. Servs., No. 13-529V, 2015 WL 9694667 (Fed. Cl. Spec. Mstr. Dec. 10, 2015). However, in Morgan, the vaccine at issue was human papillomavirus vaccine (“HPV”), not the flu vaccine.

²³ Neeraj Narula et al., Should My Patient with Inflammatory Bowel Disease on Immunosuppressive Therapy Be Vaccinated Against Influenza Virus, 24 Canadian J. Gastroenterology 121 (2010).

²⁴ Dr. Cromwell’s report stated that there are seven VAERS reports, however, he filed two VAERS reports that were duplicate of other VAERS reports and one report related to the human papillomavirus vaccine. Therefore, there were only four VAERS patients who submitted reports related to the flu vaccine.

²⁵ Each VAERS report states that the submission of a report “does not mean that . . . the vaccine caused or contributed to the adverse event.” See Pet. Ex. 44.

²⁶ This patient also received vaccines for anthrax, hep A, hep B, and smallpox.

iii. **Althen Prong 2/Loving Prong 5: Is There a Logical Sequence of Cause and Effect Showing That the Vaccination Significantly Aggravated Ms. Jackson's Condition?**

Dr. Cromwell opined it is more likely than not that the vaccination was responsible for exacerbating Ms. Jackson's pre-existing condition via non-specific immunomodulatory effects. Pet. Ex. 11 at 4. He opined that it is likely that a non-specific immune effect of the flu vaccine led to upward modulation of the immune response, which manifested as the development of severe ulcerative colitis. Id. at 6.

According to Dr. Cromwell, the flu vaccine that Ms. Jackson received falls into the class of inactivated vaccines that "may have detrimental non-specific effects," which he equated to the concept described in Jensen et al. Pet. Ex. 11 at 6; Pet. Ex. 19 at 3. Therefore, Dr. Cromwell argued that Ms. Jackson's condition following vaccination constituted a significant aggravation compared to her condition prior to vaccination. Pet. Ex. 11 at 6. He concluded, "it is most likely that this deterioration would not have occurred in the absence" of flu the vaccination. Pet. Ex. 16 at 2.

Dr. Cromwell stated that based on Ms. Jackson's history of greater than twenty-five years of quiescent disease, she was extremely unlikely to require surgical therapy in the absence of some inciting factor. Pet. Ex. 16 at 2. He believed that the administration of the flu vaccine with its accompanying non-specific immunomodulatory effects likely served as that inciting factor. Id.

Further, Dr. Cromwell opined that Ms. Jackson had a "benign phenotype of ulcerative colitis that remained quiescent for decades" until receiving the flu vaccine on September 26, 2013. Pet. Ex. 11 at 4. He explained that ulcerative colitis is an autoimmune disease that causes inflammation in the lining of the large intestine (colon). Id. The severity of the disease falls along a continuum that may range from very mild with virtually no clinical signs or symptoms of disease to severe that can be lethal without treatment. Id. at 4-5. According to Dr. Cromwell, benign phenotypes of ulcerative colitis are well known and constitute 16.3% of North American patients based on a 2016 study. Id. at 5 (citing Pet. Ex. 17 at 3).²⁷ Patients with this phenotype of disease are characterized by requiring neither aggressive medical treatment nor surgical management. Pet. Ex. 17 at 1. Ms. Jackson spent approximately 10-20 years of her life following diagnosis requiring no medical therapy. Pet. Ex. 11 at 5. Therefore, Dr. Cromwell opined, "[w]ith such longstanding diagnosis not requiring medical therapy, she qualifies as having exhibited [] a benign phenotype of [ulcerative colitis]." Id.

In support of his opinion that Ms. Jackson had a benign phenotype of ulcerative colitis, he cited a paper by Koplov et al. Pet. Ex. 17. The goal of the paper was to establish genetic

²⁷ Uri Kopylov et al., Genetic Predictors of Benign Course of Ulcerative Colitis—A North American Inflammatory Bowel Disease Genetics Consortium Study, 22 *Inflammatory Bowel Diseases* 2311 (2016).

predictors for those patients whose clinical courses were more benign than others. Id. at 1. However, patients, like Ms. Jackson, who did not have complete clinical data about past treatment were excluded from the study. Id. at 2. Further, the authors were unable to establish criteria or predictors of a benign course. Id. at 3. Disease classification depended on the extent of anatomical involvement. Id. Without baseline knowledge regarding Ms. Jackson’s prior colonoscopy findings, it is unlikely that the Koplov authors would have classified her as having a benign phenotype.

Similarly, Satsangi et al.²⁸ described the Montreal Working Group’s experience attempting to classify inflammatory bowel disease. Pet. Ex. 18 at 1. They observed that, “[t]he major drawback of the . . . classification system was clearly identified to be instability of disease extent over time, once again underlining the dynamic nature of inflammatory bowel disease.” Id. at 2.

In addition to his opinions about ulcerative colitis, Dr. Cromwell also opined that Ms. Jackson developed permanent cognitive impairment as a result of her surgical therapy. Pet. Ex. 11 at 4. Dr. Cromwell asserted that Ms. Jackson had no documented evidence of cognitive dysfunction prior to undergoing surgery on January 31, 2014. Id. at 7. He opined that she began developing profound confusion and memory loss immediately following surgery. Id. Therefore, Dr. Cromwell concluded that postoperative cognitive dysfunction was the most likely cause of her neurological disease. Id. at 7-8.

In support of this opinion, Dr. Cromwell cited Grape et al.,²⁹ which reports that postoperative cognitive dysfunction “is probably the most frequent type of postoperative cognitive impairment.” Pet. Ex. 52 at 1. It usually resolves within days to weeks, but may become a permanent disorder. Id. Postoperative cognitive dysfunction is more common following major surgery. Id. at 2. The largest study³⁰ evaluating the incidence of postoperative cognitive dysfunction “assessed the cognition of 1218 patients over 60 years of age after major non-cardiac surgery and found [postoperative cognitive dysfunction] in 26% of patients at 1 week after surgery and in 10% at 3 months after surgery.” Id.

Regarding Ms. Jackson’s postoperative cognitive dysfunction, Dr. Cromwell opined that she had no other cause for her sudden onset of cognitive dysfunction following surgery. Pet. Ex. 11 at 8. “Given the incidence of patients affected by this condition following surgery, it must be presumed that this is the cause in the absence of other documented reasons for new onset of cognitive dysfunction.” Id. at 9. He agreed that “[t]he presence of mild brain atrophy on CT

²⁸ J. Satsangi et al., The Montreal Classification of Inflammatory Bowel Disease: Controversies, Consensus, and Implications, 55 Gut 749 (2006).

²⁹ S. Grape et al., Postoperative Cognitive Dysfunction, 2 Trends in Anaesthesia Critical Care 98 (2012).

³⁰ J.T. Moller et al., Long-Term Postoperative Cognitive Dysfunction in the Elderly ISPOCD1 Study. ISPOCD Investigators. International Study of Post-Operative Cognitive Dysfunction, 351 Lancet 857e61 (1998). This study was not filed into evidence.

imaging could be evidence of a chronic condition,” however, he opined this was “irrelevant to the fact that she suffered from new deficits stemming from surgery and/or complications of the ulcerative colitis.” Pet. Ex. 12 at 2. He asserted that the CT findings, in the absence of signs or symptoms of dementia, would suggest very early or subclinical dementia, and the long-term significance of this finding to Ms. Jackson is unknown. Pet. Ex. 16 at 6. Further, Dr. Cromwell opined that the diagnosis of dementia does not exclude the development of other acute neurological conditions, such as delirium related to surgical treatment. Id.

In summary, Dr. Cromwell stated that the complications of the exacerbation of Ms. Jackson’s ulcerative colitis either, “1. Caused a new neurological state . . . or 2. Caused an acute exacerbation/acceleration of a previously unrecognized, asymptomatic underlying dementia.” Pet. Ex. 12 at 2. Regardless, Dr. Cromwell opined Ms. Jackson “suffered neurological damages as a direct result of the reactivation of ulcerative colitis caused by the [flu] vaccination.” Id.

iv. Althen Prong 3/Loving Prong 6: What Is a Proximate Temporal Relationship Between the Vaccination and the Significant Aggravation?

Dr. Cromwell opined that Ms. Jackson’s ulcerative colitis had a temporal association consistent with non-specific immune effects of vaccination. Pet. Ex. 11 at 6. He asserted that up to six months following vaccination, recipients are susceptible to non-specific immune effects. Id. at 5-6 (citing Pet. Ex. 20 at 2). The Shann article, cited by Dr. Cromwell, states, “[t]he non-specific effects of vaccines are generally stronger in girls; they appear to be maximal in the first 6 months after immunization.” Pet. Ex. 20 at 2. He stated that Ms. Jackson’s onset of severe ulcerative colitis was in that timeframe. Pet. Ex. 11 at 6.

Dr. Cromwell relied on petitioner’s affidavit regarding the onset of Ms. Jackson’s ulcerative colitis flare. Pet. Ex. 43 at 9-10. Dr. Cromwell cited petitioner’s affidavit which averred that Ms. Jackson’s flare began “a few days following the administration of the Fluzone vaccine . . . get[ting] increasingly worse for approximately two to three weeks after.” Id. (citing Pet. Ex. 9 at ¶¶ 5-7).

2. Petitioner – Dr. Thomas Krefft³¹

a. Background and Qualifications

Dr. Krefft is a physician who has been board-certified in neurology since 1988. Pet. Ex. 26 at 1-2. He received his B.S. in math from Tulane University in 1973 and received his M.D. from Louisiana State University School of Medicine in 1980. Pet. Ex. 27 at 1. Dr. Krefft completed his residency in neurology at University of California Los Angeles and completed a fellowship in behavioral neurology at the Mayo Clinic in Jacksonville, Florida. Id. For the past 16 years, Dr. Krefft has subspecialized as a behavioral neurologist, specializing in the diagnosis and treatment of cognitive disorders, including memory disorders (of any cause) and dementia.

³¹ Petitioner filed one expert report authored by Dr. Krefft. Pet. Ex. 26.

Pet. Ex. 26 at 2. He has treated over 5,000 patients with memory and other cognitive disorders. Id.

b. Opinion

Dr. Krefft opined that, “more likely than not, [Ms.] Jackson sustained a hypoxic encephalopathy, manifested by a disabling permanent short-term memory impairment, due to the January 31 surgery that was necessitated by the exacerbation of her [ulcerative colitis] caused by the Fluzone vaccine.” Pet. Ex. 26 at 17. Dr. Krefft did not opine as to the theory of vaccine causation.

Dr. Krefft performed a neurological consultation, including taking a history, and performing a complete neurological examination of Ms. Jackson on October 9, 2018. Pet. Ex. 26. His report and opinions are based on his review of the records and his examination.

He opined that Ms. Jackson’s sudden onset of short-term memory impairment was caused by hypoxic encephalopathy during her January 31, 2014 surgery. Pet. Ex. 26 at 13, 15-16. He further opined that prior to her surgery, Ms. Jackson had no short-term memory impairment. Id. at 13.

Dr. Krefft argued it is unclear whether Ms. Jackson had dementia. Pet. Ex. 26 at 14. The American Geriatric Society defines dementia syndrome as the “chronic acquired decline in memory and in at least one other cognitive function (eg, language, visual-spatial, executive) sufficient to affect daily life.” Pet. Ex. 31 at 1.³² In support of his opinion, Dr. Krefft cited Santacruz and Swagerty,³³ who state, “the diagnosis of dementia begins with the clinical recognition of a progressive decline in memory, a decrease in the patient’s ability to perform activities of daily living, psychiatric problems, personality changes[,] and problem behaviors.” Pet. Ex. 35 at 2.

Also in support of his opinion as to dementia, Dr. Krefft cited Galvin and Sadowsky,³⁴ who state, “[m]aking a diagnosis of dementia in the early stages can be a clinical challenge. The insidious and variable emergence of dementia symptoms makes recognition of the syndrome problematic.” Pet. Ex. 32 at 3. Dr. Krefft stated that Ms. Jackson’s onset of memory impairment was neither slow, nor progressive, and therefore he believed that she suffered from memory impairment, not dementia. Pet. Ex. 26 at 13-14.

Further, Dr. Krefft disputed that Ms. Jackson had frontal lobe dementia. Pet. Ex. 26 at 14. Dr. Krefft opined that Ms. Jackson’s physicians discerned she had cognitive impairment,

³² American Geriatrics Society, A Guide to Dementia Diagnosis and Treatment (2013).

³³ Karen S. Santacruz & Daniel Swagerty, Early Diagnosis of Dementia, 63 Am. Fam. Physician 703 (2001).

³⁴ James E. Galvin & Carl H. Sadowsky, Practical Guidelines for the Recognition and Diagnosis of Dementia, 25 J. Am. Board Family Med. 367 (2012).

“but, they all misdiagnosed the reason for it. [Ms.] Jackson does not have, and never has had, dementia in the historical context; and, she does not, and never has had, a frontal lobe disorder of any type.” Id.

Instead of dementia, Dr. Krefft believed that Ms. Jackson’s sudden onset of short-term memory impairment was due to hypoxia (decreased oxygenation) that occurred during her surgery on January 31, 2014. Pet. Ex. 26 at 15. He cited Korth and Shin,³⁵ who define hypoxic brain injury as “a diffuse brain injury as a result of hypoxia or reduction of oxygen. . . . These events are typically caused by respiratory failure such as pulmonary disease, suffocation, complications of anesthesia or drug use.” Pet. Ex. 38 at 1. Dr. Krefft opined that hypoxia is a known and accepted risk during surgery when general anesthesia is administered. Pet. Ex. 26 at 15.

Citing additional medical literature, Dr. Krefft stated that hypoxia can damage the hippocampus, an area of the brain necessary for forming new memories. Id. (citing Pet. Ex. 37 at 1).³⁶ “Memory impairments are common in hypoxic-ischemic brain injury especially in disturbances in immediate recall and working memory. Delayed recall is frequently impaired.” Pet. Ex. 38 at 3. Dr. Krefft opined Ms. Jackson’s “clinical history and exam are typical of [h]ypoxic [e]ncephalopathy.”³⁷ Id. at 15-16.

In regard to Ms. Jackson’s CT scan in 2014 that showed “[m]ild brain atrophy with deep white matter ischemic changes otherwise negative head CT,” Dr. Krefft stated the CT results were misleading. Pet. Ex. 26 at 17; Pet. Ex. 10 at 325. Ms. Jackson was described as dehydrated multiple times in the medical record. He opined that dehydration can cause the brain to shrink and appear atrophic on brain imaging. Pet. Ex. 26 at 17. Dr. Krefft cited to Streitburger et al.³⁸ who reported “[a] significant decrease of GM (gray matter) and WM (white matter) volume associated with dehydration” was found in the results of their study. Id. (citing Pet. Ex. 40 at 1). Kempton et al.³⁹ had similar findings showing that dehydration causes shrinkage of brain tissue. Pet. Ex. 41 at 1. Therefore, Dr. Krefft opined Ms. Jackson’s brain atrophy was not related to

³⁵ Sarah Ann Korth & Mi Ran Shin, Hypoxic Brain Injury, PM&R Knowledge NOW, <https://now.aapmr.org/hypoxic-brain-injury/> (last updated Sept. 1, 2017).

³⁶ Dimitri Agamanolis, Cerebral Ischemia and Stroke, in Neuropathology (Am. Acad. Neurology ed. 2008).

³⁷ Dr. Krefft did not provide any citations to the medical records or opinions of Ms. Jackson’s treating physicians to illustrate how Ms. Jackson’s clinical history was “typical of hypoxic encephalopathy.”

³⁸ Daniel-Paolo Streitburger et al., Investigating Structural Brain Changes of Dehydration Using Voxel-Based Morphometry, 7 PLOS One e44195 (2012).

³⁹ Matthew Kempton et al., Dehydration Affects Brain Structure and Function in Healthy Adolescents, 32 Hum. Brain Mapping 1 (2010).

dementia, which “does not depend in any way on the findings of testing,” but instead she was dehydrated. Pet. Ex. 26 at 17.

3. Respondent – Dr. Andrew S. Warner⁴⁰

a. Background and Qualifications

Dr. Warner is a board-certified gastroenterologist who has had a clinical practice for over 26 years. Resp. Ex. A at 1; Resp. Ex. F at 1. Dr. Warner received his B.A. from Skidmore College and his M.D. from University of Health Sciences/The Chicago Medical School. Resp. Ex. B at 1. He performed his residency in medicine at Mt. Auburn Hospital and a fellowship in gastroenterology at the Lahey Clinic. Id. He is the Chairman of the Division of Gastroenterology and the Founding Director of the Inflammatory Bowel Disease Center at Lahey Hospital and Medical Center. Resp. Ex. A at 1; Resp. Ex. F at 1. He is also an Associate Clinical Professor of Medicine at Tufts University School of Medicine. Resp. Ex. A at 1. He has authored a number of journal articles and participated in numerous presentations and clinical trials. Resp. Ex. B at 7-11.

b. Opinion

It is Dr. Warner’s opinion “that the [flu] vaccine did not cause Ms. Jackson to have an ulcerative colitis flare and that surgery did not cause her to develop frontal lobe dementia.” Resp. Ex. A at 2. Dr. Warner opined there is no evidence to support the claim that the flu vaccine can cause an ulcerative colitis flare. Id. In fact, the American College of Gastroenterology recommends that all ulcerative colitis patients be administered the flu vaccine. Id. (citing Resp. Ex. C at 3);⁴¹ Resp. Ex. F at 2. Dr. Warner opined that Dr. Cromwell does not offer any scientific evidence to support the claim that vaccination exacerbated Ms. Jackson’s ulcerative colitis “via non-specific immunomodulatory effects.” Resp. Ex. A at 2; Resp. Ex. F at 2. Dr. Warner stated, “[n]on-specific immunomodulatory effects are not a mechanism of action. By definition non-specific means it is non-specific; a clear and detailed immunomodulatory pathway by which the [flu] vaccine triggered a [ulcerative colitis] flare has not been described.” Resp. Ex. F at 1-2.

According to Dr. Warner, the typical clinical course for patients with ulcerative colitis is to episodically have flares of their disease, and this can be seen even in patients who have been in remission for many years. Resp. Ex. A at 2. The causes of ulcerative colitis, and the reasons that ulcerative colitis may flare are not known. Resp. Ex. F at 2. Because of this, patients and their families typically associate the development of ulcerative colitis, or a flare of ulcerative colitis, to some event immediately preceding the flare. Id. Therefore, Dr. Warner opined it is not surprising that Ms. Jackson and her family may have associated her ulcerative colitis flare with receiving a vaccination. Id. He stated, “[g]iven that administering the [flu] vaccine to

⁴⁰ Respondent filed two expert reports from Dr. Warner. Resp. Exs. A, F.

⁴¹ Francis A. Farraye et al., ACG Clinical Guideline: Preventive Care in Inflammatory Bowel Disease, 112 Am. J. Gastroenterology 241 (2017).

[ulcerative colitis] patients is standard-of-care . . . one would expect to have countless reports of this phenomenon.” Id.

In regard to Ms. Jackson’s cognitive decline, Dr. Warner disagreed with Dr. Cromwell’s assessment of postoperative cognitive dysfunction. Resp. Ex. A at 2. He stated that postoperative cognitive disorder is a clinical diagnosis for which there is no test. Id. Also, he noted that the neurologists who examined and treated Ms. Jackson diagnosed her with frontal lobe dementia and not postoperative cognitive change. Id. Dr. Warner opined that Ms. Jackson’s head CT scan is most consistent with chronic changes and not an acute process. Id. Therefore, he believed that Ms. Jackson’s prolonged illness and surgery most likely unmasked frontal lobe dementia that was present prior to her ulcerative colitis flare. Id.

4. Respondent – Dr. Timothy Vartanian⁴²

a. Background and Qualifications

Dr. Vartanian is a board-certified neurologist who subspecializes in the care of people with inflammatory demyelinating diseases. Resp. Ex. D at 1. He completed his Ph.D. degree in biochemistry and molecular biology at the University of Chicago Division of Biological Sciences and his M.D. degree at the University of Chicago Pritzker School of Medicine. Id. Dr. Vartanian completed an internal medicine internship at the Brigham and Women’s Hospital in 1989, and his neurology residency at the Massachusetts General Hospital in 1992. Id. Dr. Vartanian taught as Instructor, Assistant Professor, and Associate Professor at Harvard Medical School from 1992 to 2009. Id. He currently is a Professor of Neurology and Neuroscience at Weill Cornell Medical College of Cornell University. Id. He stated his primary clinical practice is with patients with autoimmune demyelinating disease. Id.

b. Opinion

Dr. Vartanian opined regarding the neurological issues related to Ms. Jackson’s cognitive impairment. Resp. Ex. D at 7. While petitioner’s neurology expert, Dr. Krefft, argued that Ms. Jackson’s memory disorder was due to hypoxic encephalopathy, which allegedly occurred during her January 31, 2014 surgery, Dr. Vartanian opined that Ms. Jackson’s memory impairment pre-existed her flu shot and surgery. Id. at 7-8. Additionally, he opined that there is no record of compromised cardio-pulmonary function during surgery and Ms. Jackson’s physicians document the surgery itself had no complications. Id. at 7.

Ms. Jackson’s CT scan on April 7, 2014 revealed atrophy localized to primarily the frontal lobes and deep white matter ischemic changes. Resp. Ex. D at 8 (citing Pet. Ex. 10 at 325). Dr. Vartanian opined that selective atrophy of the frontal lobes is not a consequence of hypoxia-ischemia, as proposed by Dr. Krefft, but rather a manifestation of various forms of dementia. Id. Dr. Vartanian explained that the deep white matter ischemic changes seen on CT are typical of cerebrovascular disease—and not typical of global hypoxia-ischemia. Id. While global hypoxia-ischemia can cause selective injury to the hippocampus, there was no report of

⁴² Respondent filed one expert report from Dr. Vartanian. Resp. Ex. D.

sustained hypoxia-ischemia during surgery. Id. He therefore concluded Ms. Jackson’s dementia was pre-existing. Id.

Based on his review of the records, Dr. Vartanian stated that Ms. Jackson’s surgery went smoothly. Resp. Ex. D at 9. Postoperatively, Ms. Jackson was noted to be alert and oriented. Id. It was not until February 19, 2014, that Ms. Jackson was noted to be confused. Id. According to Dr. Vartanian, if Ms. Jackson had sustained a “hypoxic ischemic insult at the time of surgery,” it would have been evident at the time of the insult. Id.

Further, Dr. Vartanian opined that Ms. Jackson had a very complicated postoperative course marked by abscess, infections, hyponatremia, hypokalemia, hypomagnesemia, and thiamine deficiency. Resp. Ex. D at 8. Additionally, she had persistent poor intake of food and liquids. Id. Dr. Vartanian opined that any one of these metabolic or toxic insults would be sufficient to explain Ms. Jackson’s poor cognitive function in the setting of pre-existing atrophy. Id. Taken together they constitute a significant toxic/metabolic insult that would compromise the function of even a normal central nervous system. Id.

In summary, Dr. Vartanian concluded that Ms. Jackson had pre-existing frontal lobe atrophy of unknown etiology and deep white matter cerebrovascular disease complicated by numerous toxic and metabolic insults, in addition to poor nutrition that persisted throughout her postoperative course, sufficient to compromise her cognition. Resp. Ex. D at 8-9.

5. Respondent – Dr. Randy S. Longman⁴³

a. Background and Qualifications

Dr. Longman is a gastroenterologist with clinical expertise in the treatment of patients with inflammatory bowel disease. Resp. Ex. G at 1. He is an Associate Professor of Medicine and serves as the Director of the Jill Roberts Center for inflammatory bowel disease at Weill Cornell Medicine. Id. He has been in clinical practice since 2013 and has provided direct care to over 2,000 patients with inflammatory and non-inflammatory diseases of the intestine. Id. Dr. Longman received his M.D. from Weill Cornell Medical College and completed internal medicine and gastroenterology training at Columbia University Medical Center. Id. He is board certified in both internal medicine and gastroenterology and has a Ph.D. in immunology from The Rockefeller University. Id. He completed a post-doctoral fellowship in immunology at New York University and has published over 26 peer reviewed publications detailing the role for the microbiome and immune cell function in inflammatory disease. Id.

b. Opinion

i. Althen Prong 1/Loving Prong 4: Is There a Medical Theory Causally Connecting a Significant Worsened Condition to the Vaccination?

⁴³ Respondent filed one expert report from Dr. Longman. Resp. Ex. G.

Dr. Longman disputed Dr. Cromwell's theory that "non-specific immune effects" of vaccines can cause an ulcerative colitis flare. Resp. Ex. G at 3. Dr. Longman stated that Dr. Cromwell's concept, and his reference to the Jensen et al. article, is premised on live vaccines such as BCG, smallpox, and the oral polio vaccines. Id. While Jensen et al. stated that "[i]nactivated vaccines may have detrimental non-specific effects," they also specifically acknowledged that "there are no reports of a sustained imprinting effect of the inactivated vaccines DTP vaccine, [hep] B vaccine or IPV on innate immunity." Pet. Ex. 19 at 3, 5. Thus, Dr. Longman opined the Jensen et al. data do not substantiate any mechanistic effect of inactivated vaccines that can reasonably be extrapolated to the flu vaccine or to Ms. Jackson's case. Resp. Ex. G at 4.

Dr. Cromwell also cited Narula et al., which stated patients with ulcerative colitis are commonly given immunosuppressive therapy. Resp. Ex. G. at 4 (citing Pet. Ex. 14 at 1). The article reviewed the safety and efficacy of administering the flu vaccination to patients undergoing immunosuppressive therapy. Pet. Ex. 14 at 1. Narula et al. addressed two case reports of ulcerative colitis reactivation after flu vaccination, but noted the poor quality of the data. Id. at 3. Dr. Longman stated the Narula article referenced by Dr. Cromwell does not substantiate a mechanistic theory. Resp. Ex. G at 4. He also opined that neither of the studies cited by Narula et al. support the idea that "over-activation of the immune system causes a poor outcome." Id.

Dr. Longman explained that ulcerative colitis is a chronic inflammatory disease of the intestine and a subtype of inflammatory bowel disease. Resp. Ex. G at 3. Although there is no medical cure for ulcerative colitis, inflammation can be managed by various medicines. Id. The natural history of ulcerative colitis is variable and may reflect a wide clinical spectrum. Id. While some patients progress quickly to severe disease during their initial presentation, the majority of patients respond to medical therapy. Id. Presentation with extensive colitis and high inflammatory markers is associated with increased risk of colectomy. Id. (citing Resp. Ex. I at 4).⁴⁴ While the majority of patients with relapsing disease do well, 20% of patients with proctitis or left-sided disease may progress to extensive colitis. Resp. Ex. I at 10.

Inadequate control with medicine is a major reason for flares as histologic or microscopic inflammation precedes symptomatic detection. Resp. Ex. G at 3. Dr. Longman cited the American College of Gastroenterology guidelines to illustrate management and recommended treatment of ulcerative colitis. Id. These guidelines recommend treating patients with ulcerative colitis to achieve mucosal healing (as determined by colonoscopy) or using fecal calprotectin⁴⁵

⁴⁴ Inger C. Solberg et al., Clinical Course During the First 10 Years of Ulcerative Colitis: Results from a Population-Based Inception Cohort (IBSEN Study), 44 *Scandinavian J. Gastroenterology* 431 (2009).

⁴⁵ Fecal calprotectin is a test used to identify a patient with inflammation of the intestines (such as celiac disease) and particularly inflammatory bowel disease (such as Crohn's disease and ulcerative colitis). Mosby's Manual of Diagnostic and Laboratory Tests 792 (6th ed. 2018).

as a surrogate for colonoscopy when colonoscopy is not feasible. Resp. Ex. K at 12.⁴⁶ The guidelines suggest “[s]creening and subsequent surveillance colonoscopy to assess for dysplasia in individuals with [ulcerative colitis] of extent greater than the rectum should start 8 years after diagnosis.” Id. at 22. “Routine visits to assess the state of [ulcerative colitis] are recommended to monitor for relapse and address health maintenance needs.” Id. at 12. Overall, approximately 20-30% of patients with ulcerative colitis will require surgery to remove the colon for medically refractory disease. Resp. Ex. G at 3 (citing Resp. Ex. K at 19).

ii. Althen Prong 2/Loving Prong 5: Is There a Logical Sequence of Cause and Effect Showing That the Vaccination Significantly Aggravated Ms. Jackson’s Condition?

Dr. Longman did not find any evidence to support a cause-and-effect relationship between the flu vaccine and Ms. Jackson’s flare of ulcerative colitis. Resp. Ex. G at 5. He stated that, although the triggers for flares are not always clear, they can frequently build up over time from inadequate or suboptimal therapeutic control. Id.

Strong evidence from the natural history of disease shows a frequent pattern of ulcerative colitis disease relapse. Resp. Ex. G at 5. While factors such as smoking cessation or intercurrent infection can be associated with flares, disease extension and flares are commonly associated with the underlying disease etiology. Id. Dr. Longman stated it is likely the Ms. Jackson’s disease was sub-optimally managed in that she did not have routine surveillance provided by colonoscopy or measurement of fecal calprotectin. Id. Dr. Longman also pointed to Ms. Jackson’s January 8, 2014 CT scan that revealed the likelihood of extra-intestinal inflammatory sacroiliitis associated with chronic inflammatory disease to evidence an alternative cause for her flare.⁴⁷ Id.

iii. Althen Prong 3/Loving Prong 6: What Is a Proximate Temporal Relationship Between the Vaccination and the Significant Aggravation?

Dr. Longman opined that the timing of Ms. Jackson’s ulcerative colitis likely reflected the natural history of sub-optimally managed ulcerative colitis. Resp. Ex. G at 5. He stated, “[i]t is clear, given the absence of routine gastroenterology care and surveillance colonoscopies, [Ms. Jackson] either did not know or did not adhere to the appropriate management of emerging ulcerative colitis.” Id. “As such, despite the absence of clinically significant symptoms, it is likely that her chronic underlying illness was not optimally managed.” Id. Dr. Longman opined

⁴⁶ David T. Rubin et al., ACG Clinical Guideline: Ulcerative Colitis in Adults, 114 Am. J. Gastroenterology 384 (2019).

⁴⁷ The study showed “extensive abnormal mucosal thickening and pericolic inflammatory fat stranding extending from the ascending colon to the rectosigmoid colon. Differential considerations for these findings include *C. difficile* colitis/infectious colitis and ulcerative colitis.” Pet. Ex. 10 at 48.

that the medical records reflect the progression of her underlying ulcerative colitis from over a four-month period from September 2013 to January 2014. Id. This timing is consistent with that expected from an underlying flare of ulcerative colitis. Id.

V. DISCUSSION

A. Standards for Adjudication—Causation

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

Petitioner’s burden of proof is by a preponderance of the evidence. § 13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec’y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec’y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, petitioner must prove that the vaccine was “not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury.” Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec’y of Health & Hum. Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); see also Pafford v. Sec’y of Health & Hum. Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). The received vaccine, however, need not be the predominant cause of the injury. Shyface, 165 F.3d at 1351. A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccinee’s injury is “due to factors unrelated to the administration of the vaccine.” § 13(a)(1)(B).

B. Causation Theory

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

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

The causation theory must relate to the injury alleged. Thus, petitioner must provide a reputable medical or scientific explanation for his theory, although the explanation need only be “legally probable, not medically or scientifically certain,” it must be “sound and reliable.” Boatmon v. Sec’y of Health & Hum. Servs., 941 F.3d 1351, 1360 (Fed. Cir. 2019); Knudsen v. Sec’y of Health & Hum. Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner cannot establish entitlement to compensation based solely on assertions. Rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 13(a)(1). In determining whether petitioner is entitled to compensation, the special master shall consider all material contained in the record, including “any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation.” § 13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties’ offered experts and rule in petitioner’s favor when the evidence weighs in his favor. See Moberly, 592 F.3d at 1325-26 (“Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence.”); Althen, 418 F.3d at 1280 (noting that “close calls” are resolved in petitioner’s favor).

1. Evaluation of Medical Record Evidence

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. § 11(c)(2). The special master is required to consider “all [] relevant medical and scientific evidence contained in the record,” including “any diagnosis, conclusion, medical judgment, or autopsy or coroner’s report which is contained in the record regarding the nature, causation, and aggravation of the petitioner’s illness, disability, injury, condition, or death,” as well as “the results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions.” § 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. See Burns v. Sec’y of Health & Hum. Servs., 3 F.3d 415, 417 (Fed. Cir. 1993) (noting it is within the special master’s discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such a determination is evidenced by a rational determination).

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. Lowrie v. Sec’y of Health & Hum. Servs., No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. Cucuras, 993 F.2d at 1528; see also Murphy v. Sec’y of Health & Hum. Servs., 23 Cl. Ct. 726, 733 (1991) (“It has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.” (citing United States v. U.S. Gypsum Co., 333 U.S. 364, 396 (1947))), aff’d, 968 F.2d 1226 (Fed. Cir. 1992).

However, there are situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. Campbell v. Sec’y of Health & Hum. Servs., 69 Fed. Cl. 775, 779 (2006) (“[L]ike

any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking.”); Lowrie, 2005 WL 6117475, at *19 (“Written records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent.” (quoting Murphy, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness’s credibility is needed when determining the weight that such testimony should be afforded. Andreu v. Sec’y of Health & Hum. Servs., 569 F.3d 1367, 1379 (Fed. Cir. 2009); Bradley v. Sec’y of Health & Hum. Servs., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

2. Evaluation of Expert Testimony

Another important aspect of the causation-in-fact case law under the Vaccine Act concerns the factors that a special master may consider in evaluating the reliability of expert testimony and other scientific evidence. In Daubert v. Merrell Dow Pharmaceutical, Inc., the Supreme Court listed certain factors that federal trial courts should utilize in evaluating proposed expert testimony concerning scientific issues. 509 U.S. 579 (1993). In Terran v. Secretary of Health & Hum. Services, the Federal Circuit ruled that it is appropriate for special masters to utilize the Daubert factors as a framework for evaluating the reliability of causation-in-fact theories presented in Program cases. 195 F.3d 1302, 1316 (Fed. Cir. 1999).

Daubert instructs fact-finders to consider:

(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). However, Boatmon noted, “[s]pecial masters may, but are not required to, analyze expert testimony according to Daubert.” Boatmon, 941 F.3d at 1359. In addition, 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 v. Sec’y of Health & Hum. Servs., 219 F.3d 1357, 1362 (Fed. Cir. 2000)). 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 v. Sec’y of Health & Hum. Servs., 88 Fed. Cl. 706, 743 (2009) (quoting Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146 (1997)).

A treating physician’s opinions are considered “quite probative,” as treating physicians are in the “best position” to evaluate the vaccinee’s condition. Capizzano, 440 F.3d at 1326. However, no treating physician’s views bind the special master, per se; rather, their views should be carefully considered and evaluated. § 13(b)(1); Snyder, 88 Fed. Cl. at 745 n.67. Each opinion from a treating physician should be weighed against other, contrary evidence present in the record—including conflicting opinions from other treating physicians. Hibbard v. Sec’y of

Health & Hum. Servs., 100 Fed. Cl. 742, 749 (Fed. Cl. 2011), aff'd, 698 F.3d 1355 (Fed. Cir. 2012); Caves v. Sec'y of Health & Hum. Servs., 100 Fed. Cl. 119, 136 (2011), aff'd, 463 F. App'x 932 (Fed. Cir. 2012); Veryzer v. Sec'y of Health & Hum. Servs., No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), mot. for rev. denied, 100 Fed. Cl. 344 (2011).

“Expert medical testimony which merely expresses the possibility—not the probability—of the occurrence of a compensable injury is insufficient, by itself, to substantiate the claim that such an injury occurred.” LaCour v. Sec'y of Health & Hum. Servs., No. 90-316V, 1991 WL 66579, at *5 (Fed. Cl. Spec. Mstr. Apr. 15, 1991); accord Burns v. Sec'y of Health & Hum. Servs., No. 90-953V, 1992 WL 365410, at *6 (Fed. Cl. Spec. Mstr. Nov. 6, 1992), aff'd, 3 F.3d 415. The Federal Circuit has likewise made clear that the mere possibility of a link between a vaccination and a petitioner's injury is not sufficient to satisfy the preponderance standard. Moberly, 592 F.3d at 1322 (emphasizing that “proof of a ‘plausible’ or ‘possible’ causal link between the vaccine and the injury” does not equate to proof of causation by a preponderance of the evidence); Waterman v. Sec'y of Health & Hum. Servs., 123 Fed. Cl. 564, 573-74 (2015) (denying petitioner's motion for review and noting that a possible causal link was not sufficient to meet the preponderance standard). While certainty is by no means required, a possible mechanism does not rise to the level of preponderance. Id.; see also De Bazan v. Sec'y of Health & Hum. Servs., 539 F.3d 1347, 1351 (Fed. Cir. 2008).

3. Consideration of Medical Literature

Both parties filed medical and scientific literature in this case, including some articles that do not weigh heavily on the outcome herein. The undersigned has reviewed and considered all of the medical literature submitted in this case, though the undersigned only discusses those articles that are most relevant to entitlement and/or are central to petitioner's case—just as the undersigned has not exhaustively discussed every individual medical record filed. 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 he does not explicitly reference such evidence in his decision.”); see also Paterek v. Sec'y of Health & Hum. Servs., 527 F. App'x 875, 884 (Fed. Cir. 2013) (“Finding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.”).

C. Standards for Adjudication—Significant Aggravation

Additional analysis is required to determine whether Ms. Jackson's vaccination significantly aggravated her pre-existing injury. The elements of an off-Table significant aggravation case are set forth in Loving. See W.C. v. Sec'y of Health & Hum. Servs., 704 F.3d 1352, 1357 (Fed. Cir. 2013) (holding that “the Loving case provides the correct framework for evaluating off-table significant aggravation claims”). The Loving court combined the Althen test, which defines off-Table causation cases, with a test from Whitecotton. See Whitecotton v. Sec'y of Health & Hum. Servs., 17 F.3d 374 (Fed. Cir. 1994), rev'd sub nom., Shalala v. Whitecotton, 514 U.S. 268 (1995) (concerning on-Table significant aggravation cases). The resultant test has six components, which are:

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

Loving, 86 Fed. Cl. at 144.

D. Analysis

1. Loving Prongs 1, 2, & 3: Condition Before and After Vaccination and Significant Aggravation

Ms. Jackson's pre-vaccination condition is difficult to ascertain due to the lack of medical records documenting the results of her last colonoscopy or other objective evidence of the extent and severity of her baseline ulcerative colitis. According to petitioner's affidavit, Ms. Jackson was diagnosed with ulcerative colitis in the 1980s, but she had not experienced any symptoms of ulcerative colitis for over ten years, nor was she taking any medications to manage her illness.

After vaccination, the first medical record evidence establishing Ms. Jackson was experiencing a flare of her ulcerative colitis was dated November 22, 2013, when Ms. Jackson presented to North Shore Gastroenterology and was seen by NP Elsa Treadway-Hahn. Ms. Jackson complained of symptoms of bleeding for the last three-to-four weeks. Additional records are consistent with the history taken at this visit, and establish that the onset of Ms. Jackson's symptoms of a flare of ulcerative colitis began November 2013. See Pet. Ex. 6 at 96, 100-01. Her condition did not improve with medication, and her clinical course progressively worsened, requiring her to undergo surgery on January 31, 2014. Ms. Jackson's deterioration is consistent with the Vaccine Act's definition of significant aggravation resulting in markedly greater disability, pain, or illness accompanied by substantial deterioration of health. § 33(4). Therefore, this leaves the question of whether that significant aggravation was vaccine-related.

2. Althen Prong 1/Loving Prong 4: Is There a Medical Theory Causally Connecting a Significant Worsened Condition to the Vaccination?

Under Althen Prong One/Loving Prong Four, petitioner must set forth a medical theory explaining how the received vaccine could have caused the sustained injury. Andreu, 569 F.3d at 1375; Pafford, 451 F.3d at 1355-56. Petitioner's theory of causation need not be medically or scientifically certain, but it must be informed by a "sound and reliable" medical or scientific explanation. Boatmon, 941 F.3d at 1359; see also Knudsen, 35 F.3d at 548; Veryzer v. Sec'y of Health & Hum. Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioner relies upon a medical opinion to support his theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen, 618 F.3d at 1347 ("The special master's

decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories.”); Perreira v. Sec’y of Health & Hum. Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an “expert opinion is no better than the soundness of the reasons supporting it” (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980))).

The undersigned finds that the petitioner has failed to prove by preponderant evidence that the proposed causal mechanism of immunomodulation is a sound and reliable theory for how the flu vaccine can cause a flare of ulcerative colitis for the following reasons.

First, petitioner’s theory of non-specific effects of vaccines/immunomodulation is not a mechanism of causation applicable to the facts and circumstances here. Instead, it is a framework based on epidemiologists’ observations about how vaccines may alter an “immune response to an unrelated (heterologous) organism.” Pet. Ex. 20 at 1. That is, what are the effects of vaccines on “mortality caused by infections other than the target disease[?]” Id. There are two general observations. One is that live vaccines (like measles) may decrease mortality from infections other than the target infection (the infection vaccinated against measles). The second observation is that inactivated vaccines (like DTP) may decrease deaths caused by the infections vaccinated against (diphtheria, tetanus, pertussis), but may increase deaths caused by other infections. Id.

The medical literature filed by the petitioner in support of the proposed theory does not extend the general concept of non-specific effects of vaccines to the context of autoimmune illnesses or inflammatory illnesses thought to be immune-mediated.

Second, the medical literature cited by petitioner does not support the posited mechanistic theory. Dr. Cromwell cited medical articles; however, these articles suggest that the idea of non-specific effects of vaccines as a causal theory is controversial. Jensen et al. state “vaccines are considered specific modulators of the immune system,” however, “besides the specific effects, vaccines also have immune-modulating effects that influence host defense to other diseases than the targeted pathogen, so-called ‘nonspecific effects’ [] of vaccines or ‘heterologous immunity.’” Pet. Ex. 19 at 2. The article continues, “[t]he concept of [non-specific effects] is still controversial . . . possibly because of the perceived lack of underlying immunological mechanisms.” Id.

In addition to being controversial, the idea espoused by Jensen et al. that inactivated vaccines have detrimental effects on all-cause mortality and morbidity is not a well-developed concept, especially as it relates to inactivated vaccines. The authors do not elaborate on detrimental effects of inactivated vaccines. Jensen et al. focus mainly on the BCG vaccine and how it may “train” innate immunity. The authors note that “at a more mechanistic level, many questions remain to be answered.” Pet. Ex. 19 at 6. The Jensen article does not describe how the flu vaccine could cause immunomodulation to occur. It does not describe how any non-specific effects of the flu vaccine could cause an ulcerative colitis flare or otherwise affect the colon.

The Shann article cited by Dr. Cromwell describes the idea that vaccines work in tandem with other vaccines to respond to future infections not necessarily vaccinated for. Pet. Ex. 20 at 1. The author describes this as the non-specific effects of vaccines or “heterologous immunity.”

Id. The non-specific effects “appear to be maximal in the first 6 months after immunization and are largely determined by the last vaccine administered.” Id. at 2. Shann states that inactivated vaccines that “may reduce mortality from the target disease, but increase mortality from other infections; for example, [DTP] vaccine may reduce mortality from diphtheria, tetanus and pertussis, but increase mortality from other infections.” Id. at 1. However, Shann does not reference the flu vaccine or ulcerative colitis. Thus, the author’s observations of non-specific effects of vaccines do not apply to the facts and circumstances of this case.

In summary, the articles cited by Dr. Cromwell do not support his mechanistic theory. Immunomodulation and the idea of non-specific effects of vaccines as discussed in the cited articles are concepts that may have broad ranging implications, but they have not been described or used to suggest that a flu vaccine can cause a relapse of an autoimmune disease like ulcerative colitis.

Third, respondent’s experts provide more persuasive opinions related to causation. Dr. Longman explained that the natural history of ulcerative colitis is variable and may reflect a wide clinical spectrum. While the majority of patients with relapsing disease do well, 20% of patients with proctitis or left-sided disease progress to extensive colitis. Resp. Ex. I at 10. Dr. Longman also suggested inadequate control with medicine is a major reason for flares as histologic or microscopic inflammation precedes symptomatic detection. Dr. Longman cited the American College of Gastroenterology guidelines that suggested “[r]outine visits to assess the state of [ulcerative colitis] are recommended to monitor for relapse and address health maintenance needs.” Id. at 12. Approximately 20-30% of patients with ulcerative colitis will require colectomy for medically refractory disease.

Lastly, Dr. Cromwell cited Morgan, where he was an expert and surgeon for the petitioner, in support of his mechanistic theory. 2015 WL 9694667. In Morgan, the petitioner contended that non-specific immunomodulator effects of Gardasil, an HPV vaccine, caused ulcerative colitis in petitioner, a genetically susceptible individual. Id. at *1. Petitioner received the HPV vaccine and that same night she began to have diarrhea. Id. at *2. Her symptoms worsened and approximately one year later, the petitioner underwent a laparoscopic proctocolectomy. Id. at *4. Dr. Cromwell stated that when he performed petitioner’s proctocolectomy, he did not see evidence of longstanding, severe ulcerative colitis in the appearance of the colon, and thus believed the HPV vaccine caused ulcerative colitis via non-specific immunomodulatory effects. Id. at *7. Overall, Dr. Cromwell’s theory proposed that “petitioner had a cytokine response that caused diarrhea within six hours after vaccination, which developed into full blown ulcerative colitis about a week later through the non-specific, adaptive immune response, within the time frame where he would expect a non-specific cross reactive immune response.” Id. at *8. The special master found that “given the current state of medical knowledge,” Dr. Cromwell “provided a reasonable scientific explanation of causation.” Id. at *12.

Special masters’ decisions are non-binding. Boatmon, 941 F.3d at 1358. “By extension, special masters are not required to distinguish non-binding decisions of other special masters. That is, in part, because ‘[c]ausation in fact under the Vaccine Act is . . . based on the circumstances of the particular case.’” Id. at 1358-59 (quoting Knudsen, 35 F.3d at 548). Here,

Ms. Jackson received the flu vaccine, not the HPV vaccine the petitioner in Morgan received. Moreover, based on the medical literature filed in the case, the undersigned's knowledge and experience in the Program, and the facts and circumstances of this case, Dr. Cromwell's theory does not persuasively translate from the HPV vaccine to the flu vaccine simply because the injury is similar.

For all of these reasons, the undersigned finds that petitioner has not provided preponderant evidence of a sound and reliable causal theory satisfying Althen Prong One/Loving Prong Four.

3. Althen Prong 2/Loving Prong 5: Is There a Logical Sequence of Cause and Effect Showing That the Vaccination Significantly Aggravated Ms. Jackson's Condition?

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

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee's treating physicians are entitled to some weight. Andreu, 569 F.3d at 1367; Capizzano, 440 F.3d at 1326 ("[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" (quoting Althen, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. Cucuras, 993 F.2d at 1528. The petitioner need not make a specific type of evidentiary showing, i.e., "epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Capizzano, 440 F.3d at 1325. Instead, petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. Id. at 1325-26.

In regard to a logical sequence of cause and effect, the undersigned finds petitioner failed to prove by preponderant evidence a logical sequence of cause and effect, failing to show that the flu vaccine caused Ms. Jackson's ulcerative colitis flare.

Ms. Jackson's treating physicians did not attribute her ulcerative colitis flare to the flu vaccination. Moreover, when Ms. Jackson was first seen for treatment of her ulcerative colitis, she reported that her flares were triggered by "certain foods or stress" and Ms. Jackson did not attribute or relate her flare to vaccination.

Ms. Jackson's clinical course is consistent with the natural course of the progression of the ulcerative colitis, and thus, there is no reason to implicate vaccination as a cause or contributing factor. Dr. Longman stated, "[s]trong evidence from the natural history of disease

shows a frequent pattern of ulcerative colitis disease relapse.” Resp. Ex. G at 5. He opined Ms. Jackson’s ulcerative colitis flare is consistent with her underlying disease etiology. It is likely that Ms. Jackson’s disease was sub-optimally managed in that she did not have routine surveillance provided by colonoscopy or measurement of fecal calprotectin. The American College of Gastroenterology Guidelines provide, “[n]onadherence to therapy is common in patients with [ulcerative colitis] and is associated with an increased risk of relapse.” Resp. Ex. K at 11. Dr. Longman stated overall that approximately 20-30% of patients with ulcerative colitis will require colectomy for medically refractory disease.

There are two cases, Locane and Sharpe, that illustrate the Circuit’s significant aggravation analysis with regard to the evolution of petitioner’s clinical course. Locane v. Sec’y of Health & Hum. Servs., 685 F.3d 1375 (Fed. Cir. 2012); Sharpe v. Sec’y of Health & Hum. Servs., 964 F.3d 1072 (Fed. Cir. 2020).

In Locane, petitioner alleged her Crohn’s disease, an inflammatory bowel disease, was significantly aggravated by the hep B vaccine—specifically the first and third vaccination doses. Locane, 685 F.3d at 1377-78. The special master determined that petitioner failed to show “by a preponderance of the evidence that she was entitled to compensation under the significant aggravation theory because the course of her disease was not affected by the vaccination.” Id. at 1378. The Federal Circuit found that the special master’s finding—that petitioner’s clinical course was not inconsistent with the disease generally and not affected by the vaccinations—was considered from “the relevant evidence of record, [drawn from] plausible inferences and articulated a rational basis for the decision,” therefore, the decision was not arbitrary or capricious. Id. at 1381-82. The Circuit continued stating that petitioner was “given ample opportunity to develop her significant aggravation claim but ‘failed to present persuasive evidence that separates [her] problems from an expected course of Crohn’s disease.’” Id. at 1382.

In Sharpe, petitioner alleged L.M. had a pre-existing “seizure disorder” and the administration of the several childhood vaccines at her six-month wellness check-up significantly aggravated L.M.’s pre-existing condition. Sharpe, 964 F.3d at 1076-77. The special master denied petitioner’s significant aggravation claim because L.M.’s genetic mutation, and not the vaccination, was the sole, substantial cause of L.M.’s significantly aggravated seizure disorder. Id. at 1080. The Circuit found the special master’s analysis “required [p]etitioner to prove the expected outcome for a child with a DYNC1H1 gene mutation and to show that L.M.’s current, post-vaccination condition was worse than that expected outcome.” Id. at 1081. The Circuit stated, “a court should consider all evidence in the record, including evidence of other possible sources of injury. There is, however, a fine line between a court properly considering evidence in the record . . . and improperly placing the burden on the petitioner to prove that her significantly aggravated condition was not caused by her gene mutation.” Id. at 1082. The Circuit distinguished the special master’s decision from Locane stating, “the [Locane] special master did not require the petitioner to prove that her significantly aggravated condition was not caused by her preexisting condition. Instead, the special master found that the petitioner’s condition ‘was not affected by the vaccination.’” Id.

The undersigned has not required petitioner to prove Ms. Jackson's post-vaccination condition was worse than the expected outcome. Instead, the undersigned notes that the evidence taken as a whole shows that Ms. Jackson's course was not inconsistent with the disease generally and petitioner's condition was not affected by the vaccination. This finding is consistent with Locane.

Dr. Cromwell cited the Narula et al. article that summarized two case reports of ulcerative colitis occurring after the flu vaccination. The first case report described a 39-year-old woman with ulcerative colitis well controlled on oral mesalamine, who experienced abdominal pain and frequent bowel movements three days after vaccination, but responded to steroid induction. The second case was a 52-year-old woman with ulcerative colitis who had been in remission without steroids for nine months; however, within hours of receiving a flu vaccination, the woman experienced a severe exacerbation of her disease that could not be controlled with steroids and immunosuppressive medications and she underwent a total colectomy within three months. Both of these cases demonstrated severe ulcerative colitis reactions within hours or days of the flu vaccine. Ms. Jackson's flare of ulcerative colitis was progressive over the four-month period from September 2013 to January 2014. Moreover, Narula et al. noted the poor quality of the data used to describe the case reports.

Further, the VAERS reports submitted by Dr. Cromwell do not support how the proposed mechanistic theory is applicable to Ms. Jackson's case. VAERS is a passive surveillance system. Tompkins v. Sec'y of Health & Hum. Servs., No. 10-261V, 2013 WL 3498652, at *9 (Fed. Cl. Spec. Mstr. June 21, 2013), mot. for rev. denied, 117 Fed. Cl. 713 (2014). In a number of decisions, special masters and judges have concluded that VAERS data is not reliable as the basis for a causation determination in Vaccine Act cases, based on difficulties inherent in the system's design. Id. The Court of Federal Claims has routinely upheld special master's concerns regarding the reliability of VAERS data. Analla v. Sec'y of Health & Hum. Servs., 70 Fed. Cl. 552, 558 (2006); see also Capizzano v. Sec'y of Health & Hum. Servs., 63 Fed. Cl. 227, 231 (2004), vacated & remanded sub nom., 440 F.3d 1317 (explaining VAERS data has limited value due to the manner in which it is collected, the lack of confirmation of the reported information, and the lack of any systemic analysis); Manville v. Sec'y of Health & Hum. Servs., 63 Fed. Cl. 482, 494 (2004) (noting VAERS reports can be filed by anyone, thus raising questions about the quantity and quality of the information gathered); Ryman v. Sec'y of Health & Hum. Servs., 65 Fed. Cl. 35, 40, 43 (2005) (discussing how VAERS reports may be biased toward pre-existing notions of adverse events).

Further, the facts in the VAERS case reports can be distinguished from those presented here. The first report documented a 61-year-old man who had ulcerative colitis onset eighty-two days post-vaccination. In contrast, Ms. Jackson's husband averred that her symptoms began within days after vaccination and progressed over a four-month period. The second case was a 37-year-old man who reported an ulcerative colitis flare and exacerbation of asthma 10 days after vaccination. These combined illnesses suggest a systemic illness different than that experienced by Ms. Jackson. Third, was a young man in his twenties who received several vaccinations, including the flu vaccine, and tested positive for *C. difficile* infection 24 hours later. The cause of his colitis was stated to be *C. difficile*, an infectious agent, not the flu vaccine. Fourth, was the 52-year-old woman described in the Narula article. She had symptoms the night of vaccination.

Thus, her onset was more immediate than Ms. Jackson's. Ms. Jackson did not seek treatment for her ulcerative colitis until approximately two months after vaccination, in comparison to the patient described in the Naurla article who appeared to have a more acute and severe presentation immediately following vaccination.

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

4. Althen Prong 3/Loving Prong 6: What Is a Proximate Temporal Relationship Between the Vaccination and the Significant Aggravation?

Althen Prong Three/Loving Prong Six requires petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. Althen, 418 F.3d at 1281. That term has been equated to mean a "medically acceptable temporal relationship." Id. The petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disease's etiology, it is medically acceptable to infer causation-in-fact." de Bazan, 539 F.3d at 1352. The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under Althen Prong One). Id.; Koehn v. Sec'y of Health & Hum. Servs., 773 F.3d 1239, 1243 (Fed. Cir. 2014); Shapiro v. Sec'y of Health & Hum. Servs., 101 Fed. Cl. 532, 542 (2011), recons. den'd after remand, 105 Fed. Cl. 353 (2012), aff'd mem., 503 F. App'x 952 (Fed. Cir. 2013).

According to petitioner's affidavit, Ms. Jackson experienced an onset of ulcerative colitis flare within a few days of vaccination. She first sought treatment on November 22, 2013, about two months after vaccination. At that time, she reported symptoms of bleeding for three or four weeks.

Dr. Cromwell asserts that non-specific immunomodulation occurs within a six-month time frame. Thus, Ms. Jackson's ulcerative colitis flare occurred within that time frame. However, a temporal association alone is insufficient to establish causation. See Moberly, 592 F.3d at 1323 ("[A] proximate temporal association alone does not suffice to show a causal link between the vaccination and the injury." (citing Grant v. Sec'y of Health & Hum. Servs., 956 F.2d 1144, 1148 (Fed. Cir. 1992)))

The undersigned will not reach the issue of what caused Ms. Jackson's cognitive decline as it is not necessary in light of petitioner's failure to establish that the flu vaccine caused significant aggravation of Ms. Jackson's ulcerative colitis.

VI. CONCLUSION

It is clear from the medical records that Ms. Jackson suffered as a result of her illnesses, and the undersigned extends her sympathy to petitioner for his loss. The undersigned's decision, however, cannot be decided based upon sympathy, but rather on the evidence and law.

Based on the record as a whole, medical records, affidavits, and the petitioner's expert opinions, the undersigned finds that petitioner has failed to prove causation or significant aggravation by preponderant evidence. Therefore, the case must be dismissed.

IT IS SO ORDERED.

s/Nora Beth Dorsey

Nora Beth Dorsey

Special Master