In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 19-477V
Filed: November 3, 2025

TIMOTHY RIESE, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Special Master Horner

Edward Kraus, Kraus Law Group, LLC, Chicago, IL, for petitioner.
Emilie Williams, U.S. Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

On April 1, 2019, petitioner, Timothy Riese, filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10, *et seq.* (2012),[2] alleging that he suffered ulcerative colitis and cavernous venous thrombosis as a result of the tetanus, diphtheria, and acellular pertussis ("Tdap") and Hepatitis A vaccines that he received on July 17, 2017. (ECF No. 1.) For the reasons set forth below, I conclude that petitioner is entitled to an award of compensation.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations,

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

[2] Within this decision, all citations to § 300aa will be the relevant sections of the Vaccine Act at 42 U.S.C. § 300aa-10, *et seq.*

including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B).

In many cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table. In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. § 300aa-13(a)(1)(B); § 300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005); *Hines v. Sec'y of Health & Human Servs.*, 940 F.2d 1518, 1525 (Fed. Cir. 1991).

In this case, petitioner has alleged that the Tdap and Hepatitis A vaccines caused him to suffer ulcerative colitis and cavernous venous thrombosis. Because the alleged injuries are not listed on the Vaccine Injury Table relative to the subject vaccines, petitioner must satisfy the above-described *Althen* test for establishing causation-in-fact.

The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. § 300aa-13(a)(1)(A); *see also Althen*, 418 F.3d at 1278-79; *Hines*, 940 F.2d at 1525. Under that standard, petitioner must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F.3d at 1279. She need not show that the vaccination was the sole cause but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition at issue and was a "but for" cause. *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999). Thus, petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury[.]" *Althen*, 418 F.3d at 1278 (quoting *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992)). Ultimately, petitioner must satisfy what has come to be known as the *Althen* test, which requires: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for

the injury; and (3) a showing of proximate temporal relationship between vaccination and injury. *Id*.

A petitioner may not receive a Vaccine Program award based solely on his or her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1). Medical records are generally viewed as particularly trustworthy evidence because they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. § 300aa-13(b)(1). A petitioner may rely upon circumstantial evidence. *See Althen*, 418 F.3d at 1280. Moreover, the *Althen* court noted that a petitioner need not necessarily supply evidence from medical literature supporting petitioner's causation contention, so long as the petitioner supplies the medical opinion of an expert. *Id*. at 1279-80. While scientific certainty is not required, that expert's opinion must be based on "sound and reliable" medical or scientific explanation. *Boatmon v. Sec'y of Health & Human Servs*., 941 F.3d 1351, 1359 (Fed. Cir. 2019).

Cases in the Vaccine Program are assigned to special masters who are responsible for "conducting all proceedings, including taking such evidence as may be appropriate, making the requisite findings of fact and conclusions of law, preparing a decision, and determining the amount of compensation, if any, to be awarded." Vaccine Rule 3(b)(1). Special masters must ensure each party has had a "full and fair opportunity" to develop the record but are empowered to determine the format for taking evidence based on the circumstances of each case, including having the discretion to decide cases without an evidentiary hearing. Vaccine Rule 3(b)(2); Vaccine Rule 8(a); Vaccine Rule 8(d). Special masters are not bound by common law or statutory rules of evidence but must consider all relevant and reliable evidence in keeping with fundamental fairness to both parties. Vaccine Rule 8(b)(1). 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." § 300aa-13(b)(1). The special master is required to consider the entirety of the evidentiary record, draw plausible inferences, and articulate a rational basis for the decision. *Winkler v. Sec'y of Health & Human Servs.*, 88 F.4th 958, 963 (Fed. Cir. 2023) (citing *Hines*, 940 F.2d at 1528).

II. Procedural History

Petitioner filed his petition on April 1, 2019, alleging that he suffered ulcerative colitis and cavernous venous thrombosis as a result of Tdap and Hepatitis A vaccines he received on July 17, 2017. (ECF No. 1.) This case was initially assigned to another special master. (ECF No. 4.) Between April and July of 2019, petitioner filed medical

records marked as Exhibits 1-32. (ECF Nos. 7-9, 12.) Thereafter, the case was reassigned to the undersigned. (ECF Nos. 13-14.)

On June 11, 2020, respondent filed his Rule 4 report, recommending against compensation. (ECF No. 24.) He argued, in pertinent part, that petitioner's treaters did not opine that his injuries were related to his vaccinations and that petitioner had not set forth a medical theory causally linking the subject vaccines to his alleged injuries. (*Id.* at 6.) In September of 2020, petitioner filed an expert report by gastroenterologist John Cromwell, M.D. (Ex. 39) and accompanying medical literature marked as Exhibits 41-47, as well as further medical records marked as Exhibits 33-38. (ECF Nos. 27-30.) In January of 2021, respondent filed a responsive expert report by gastroenterologist Randy Longman, M.D., along with accompanying medical literature. (ECF No. 33; Ex. A.) The parties engaged in another round of expert reports by Drs. Cromwell and Longman in March of 2021. (ECF Nos. 35-36; Exs. 48, C.)

I held a Rule 5 status conference on May 7, 2021. (ECF No. 37.) During the conference, I noted my understanding that there was no dispute regarding petitioner's ulcerative colitis diagnosis, that ulcerative colitis is an autoimmune condition, and that venous thromboembolism can be a further consequence of inflammatory bowel disease. (*Id.* at 1.) I explained that I was "very skeptical of the concept of nonspecific effects of vaccines as presented by Dr. Cromwell, both in general and as applied to ulcerative colitis." (*Id.* at 2.) However, I noted that Dr. Cromwell had successfully presented a similar causal theory in a prior Program case, albeit with regard to a different vaccine. (*Id.* at 1.) Finally, I indicated that both experts offered inadequate opinions regarding onset in this case. (*Id.* at 2.)

In response to the issues raised in my Rule 5 order, petitioner filed an expert report by immunologist and rheumatologist S. Sohail Ahmed, M.D., on July 15, 2021. (ECF No. 39; Ex. 49.) In October of 2021, petitioner filed medical literature marked as Exhibits 50-67. (ECF Nos. 43-45.) Respondent filed a supplemental expert report by Dr. Longman (Ex. D) and an expert report by immunologist John Bates, Ph.D. (Ex. E), along with accompanying medical literature, on November 15, 2021. (ECF Nos. 46-47.) Thereafter, petitioner filed a second supplemental expert report by Dr. Cromwell. (ECF Nos. 48-49; Exs. 68-70.) A three-day entitlement hearing was subsequently set to commence on September 11, 2024. (ECF No. 63.)

On April 28, 2023, petitioner filed a supplemental report by Dr. Ahmed. (ECF Nos. 58-59; Exs. 72-85.) In response, respondent filed a supplemental report by Dr. Bates on August 29, 2023. (ECF No. 64; Ex. G.) Between October of 2023 and January of 2024, the parties engaged in another round of experts reports by Drs. Ahmed and Bates. (ECF Nos. 65, 67, 72; Exs. 86-90, I.) Petitioner filed additional medical literature in July of 2024. (ECF No. 78; Ex. 92-95.)

In advance of the hearing, the parties filed their initial prehearing briefs on August 14, 2024. (ECF Nos. 81, 85.) They also filed a joint status report, stipulating to the following facts: petitioner received the subject Tdap and Hepatitis A vaccines on July

17, 2017; "[a]pproximately a week later, [petitioner] began to develop gastrointestinal symptoms that marked the onset of symptoms of [ulcerative colitis]"; petitioner was "properly diagnosed" with ulcerative colitis; and petitioner's venous thrombosis was a complication of his ulcerative colitis. (ECF No. 77, p. 1.) Just prior to the hearing, petitioner filed updated medical records. (ECF No. 87; Exs. 96-97.) A three-day entitlement hearing was held on September 11, 2024. (Transcript of Proceedings ("Tr."), at ECF No. 90.)

Accordingly, this case is now ripe for resolution.

III. Factual History

a. Medical Records

Prior to vaccination, petitioner was in relatively good health. (Ex. 2.) Petitioner presented for a routine physical examination on June 22, 2015. (*Id.* at 8-11.) Bloodwork completed that same day showed low hemoglobin level at 12.7L (reference range of 13.2-17.1 g/dL); however, mean corpuscular volume ("MCV") was normal at 85.2 fL (reference range of 80.0-100.0 fL) and high-sensitive C-reactive protein ("CRP") level was low at 0.4 mg/L (lower relative cardiovascular risk range of <1.0 mg/L). (*Id.* at 2-3.) Petitioner was reported to be "doing well otherwise." (*Id.* at 11.)

On July 17, 2017, petitioner presented to establish care with a new primary care physician without any apparent health concerns. (Ex. 4, p. 7.) A review of systems was negative for abdominal pain, nausea, vomiting, heartburn, constipation, diarrhea, excessive belching, and bloody stools, though petitioner reported fainting. (*Id.*) A physical examination of petitioner's abdomen was unremarkable with no tenderness. (*Id.* at 7-8.) Petitioner's bloodwork was similarly unremarkable. (Ex. 11.) It was during this encounter that petitioner received the subject Hepatitis A and Tdap vaccines.[3] (Ex. 4, p. 8.)

Petitioner presented to Mend Urgent Care on August 28, 2017, with complaints of intermittent diarrhea and constipation that was accompanied by blood and abdominal cramping. (Ex. 5, p. 1.) He reported that, about a month prior, he began noticing "bright red blood on the wipe" that eventually progressed to blood in the stool and floating in the toilet water. (*Id.*) He occasionally saw a "white frothy substance" in the stool as well. (*Id.*) He described two or more bowel movements per day, but stool was decreased in size and "at times slightly liquidy." (*Id.*) A physical examination revealed mild epigastric tenderness. (*Id.* at 2.) Petitioner was assessed with unspecified gastrointestinal hemorrhage and epigastric pain. (*Id.* at 3.) He was directed to drink plenty of fluids and follow up with his primary care physician for a referral to a gastrointestinal specialist. (*Id.*)

[3] It was also recommended that petitioner receive a vaccine for Japanese encephalitis, but there is no documentation of petitioner having received this vaccine. (Ex. 4, p. 8; Ex. 27, ¶ 3.)

Petitioner followed up with his primary care physician on September 7, 2017. (Ex. 4, pp. 5-6.) He reported that he had been experiencing progressively loose and bloody stools over the past six weeks, and his physical examination showed upper abdominal pain on palpation. (*Id.*) An examination of the rectum and prostate was unremarkable. (*Id.* at 6.) Petitioner was diagnosed with acute gastritis with bleeding, acute hemorrhagic gastritis, ulcerative (chronic) rectosigmoiditis with rectal bleeding, and rectal hemorrhage due to chronic ulcerative rectosigmoiditis. (*Id.*) He was ordered to adhere to a bland diet with small portions, begin a 4-day course of Protonix,[4] and undergo a CT scan of the abdomen without contrast. (*Id.*) Additionally, petitioner was referred to a gastroenterologist but advised to go to the emergency department "if bleeding increases suddenly." (*Id.*)

On September 21, 2017, before he was able to consult a specialist, petitioner presented to the emergency department with complaints of intermittent bloody stool for the past two months. (Ex. 3, pp. 1, 7.) He reported intermittent diarrhea, at least a small amount of blood with every bowel movement, intermittent dizziness, decreased appetite, and aggravated symptoms with eating. (*Id.* at 7.) Within the past week, petitioner reported that he had lost eight pounds. (*Id.*) His physical examination revealed soft, mild generalized tenderness to palpation of the abdomen but no rebound tenderness/guarding, McBurney's point[5] tenderness, or gross peritonitis. (*Id.* at 8.) Petitioner's abdomen was also non-distended and negative for Murphy sign,[6] and his bowel sounds were normal. (*Id.*) His rectal examination was similarly benign. (*Id.* at 8-9.) His blood work showed elevated globulin at 3.70 g/dl (reference range of 1.3-3.2 g/dl) and elevated total protein at 8.6 g/dl (reference range 6.1-8.1 g/dl), but decreased mean corpuscular hemoglobin at 28.4 pg (reference range of 29.0-33.0 pg) and decreased protime at 11.9 (reference range of 12.2-14.2). (*Id.* at 21-23.) It was noted that there were no signs of leukocytosis or anemia, based on petitioner's blood work. (*Id.* at 10.) Petitioner also underwent a CT scan of the abdomen and pelvis that revealed mildly thickened distal descending and sigmoid colon wall, which was

[4] Protonix is the trademark for preparations of pantoprazole sodium, which is an orally or intravenously administered proton pump inhibitor that is used in the treatment of erosiveesophagitis associated with gastroesophageal reflux disease, as well as pathologic hypersecretion associated with certain neoplastic conditions. *Protonix*, DOLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=41479 (last visited Oct. 14, 2025); *Pantoprazole Sodium*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=36645 (last visited Oct. 14, 2025).

[5] McBurney's point is located in the left lower quadrant of the abdomen – "about one third of the distance between the right anterior superior iliac spine and the umbilicus, corresponding with the normal position at the base of the appendix" – that is especially tender in patients with acute appendicitis. *McBurney point*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=99006 (last visited Oct. 14, 2025).

[6] Murphy sign is a maneuver performed during a physical examination of an abdomen that consists of interruption of the patient's deep inhalation when the physician's fingers are pressed deeply beneath the right costal arch, just below the hepatic margin. *Murphy sign*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=106381 (last visited Oct. 14, 2025). It is utilized to detect signs of gallbladder disease. *Id.*

nonspecific but could represent mild colitis from an inflammatory or infectious etiology. (*Id.* at 11, 42-43.) During this hospitalization, petitioner was treated with IV fluids but refused pain medication. (*Id.* at 10.) Petitioner's diagnosis at discharge was colitis, and he was advised to schedule an appointment with a specialist and to follow-up with his primary care provider. (*Id.* at 10-13.) In the interim, petitioner was prescribed Flagyl and ciprofloxacin to address a possible infectious etiology. (Ex. 3, p. 10.)

Later that same day, petitioner was seen by gastroenterologist Rahul Chhablani, M.D.. who diagnosed him with left lower quadrant abdominal pain of unknown etiology and colitis. (Ex. 7, pp. 4-6.) Regarding the abdominal pain, it was noted that petitioner's CT scan showed inflammation involving the left side of the colon, including the rectum, which made ischemic colitis less likely. (*Id.* at 6.) Dr. Chhablani prescribed antibiotics for empiric treatment of Clostridium difficile ("C. diff") toxin, and a colonoscopy with biopsy was ordered to exclude left-sided ulcerative colitis and inflammatory bowel disease. (*Id.*) He was prescribed a 2-week course of Flagyl for the colitis. (*Id.*)

Petitioner underwent a colonoscopy with biopsy on October 18, 2017. (Ex. 14.) The results showed new inflammation from the anus to the ascending colon, which was consistent with inflammatory bowel disease. (*Id.* at 1-2.) Petitioner returned to Dr. Chhablani on October 30, 2017, with complaints of persistent diarrhea with hematochezia, abdominal pain, and fatigue, which were not responding to treatment with prednisone. (Ex. 7, pp. 48-49.) He reported that he was experience 12-15 loose stools per day. (*Id.* at 49.) Dr. Chhablani determined that petitioner was appropriate for inpatient IV steroids; however, petitioner indicated that he wished to seek further care in Ohio where his family could provide additional support. (*Id.* at 51.) He was diagnosed with chronic pancolonic ulcerative colitis, based on the colonoscopy results, and advised to continue taking prednisone until he could be hospitalized in Ohio. (*Id.*; Ex. 15, p. 14.)

On November 1, 2017, petitioner presented to the emergency department of Ohio State University Wexner Medical Center. (Ex. 15, p. 14.) Since his colonoscopy two weeks prior, petitioner reported a 10-pound weight loss (a loss of 20 pounds total since onset) and 12-15 daily episodes of bloody diarrhea, as well as generalized weakness, nausea, and insomnia due to frequent bowel movements. (*Id.* at 3, 14.) On admission, petitioner's white blood count (WBC) was normal 13.15 K/uL, and his initial hypotension normalized after a fluid bolus. (*Id.* at 14.) However, his hemoglobin level was 12.2 g/dL, his hematocrit level was 36.5%, his erythrocyte sedimentation rate was 36, and his CRP level was 1.9, evidencing leukocytosis and normocytic anemia. (*Id.* at 14, 16; Ex. 6, p. 2.) On physical examination, petitioner's abdomen was soft and non-distended with tenderness in the right upper and lower quadrants. (Ex. 15, p. 16.) He was diagnosed with severe ulcerative colitis and admitted for IV steroids and further work up, though it was noted that there was a "[l]ow suspicion for infectious etiology." (*Id.* at 6-7, 16.) C. diff toxin and molecular stool panels were ordered, and petitioner

was treated with Solu-Medrol[7] and mesalamine.[8] (*Id.* at 16.) Throughout his hospitalization, petitioner's lab work showed consistently elevated WBC and low hemoglobin and hematocrit levels and mean platelet volume; however, by November 3, 2017, petitioner's anemia and leukocytosis was notably stabilized. (Ex. 6, pp. 22-35; Ex. 15, p. 27.) C. diff toxin and molecular stool panels were negative, and there was no evidence of active infection. (Ex. 6, p. 14; Ex. 15, p. 28.) Petitioner's leukocytosis was believed to be secondary to his treatment with high dose steroids, and his anemia were believed to be the result of losing blood with bowel movements. (Ex. 6, p. 14.) Petitioner underwent an x-ray of his abdomen, which was grossly negative. (*Id.* at 36; Ex. 15, p. 23.)

By November 2, 2017, petitioner's abdominal pain had radiated to his left upper and lower quadrant. (Ex. 15, pp. 23-24.) By the next day, petitioner was demonstrating signs of severe calorie malnutrition. (*Id.* at 24.) He continued to experience 12-15 bloody bowel movements per day, though his diarrhea was improving and his abdominal pain was well controlled with IV steroid treatment. (*Id.* at 24-25, 27-29.) Petitioner's physical examination showed mild tenderness to palpation in the abdomen. (*Id.* at 29-30.) On November 3, 2017, he presented for a gastroenterology follow up and the following was noted:

> He had a history of hemorrhoidal bleeding ~4 years ago and thought this was the cause. However, it persisted, along with lower abdominal pain and nocturnal diarrhea. No family history of [inflammatory bowel disease]. . . . [Petitioner] has never had any GI issues outside of recently. Says he enjoys all kinds of food, including spicy food and has a lot of raw veggies in his diet. Overall lives a healthy and active life. He was evaluated by a gastroenterologist in California and colonoscopy . . . demonstrated chronic colitis and proctitis. [Terminal ileum biopsy] was notably normal. . . . Despite the oral steroids [petitioner] continued to have bloody loose stools >10 times/24 hours and lower abdominal pain. His baseline weight was 135, but more recently has been about 110 lbs. He has been trying to eat well, but feels the pain limits his intake as well as losses from the diarrhea. . . .

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[7] Solu-Medrol is an intramuscularly or intravenously administered synthetic glucocorticoid derived from progesterone and used as an anti-inflammatory and immunosuppressant treatment in a wide variety of disorders. *Solu-Medrol*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=46174 (last visited Oct. 15, 2025); *Methylprednisolone sodium succinate*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=89219 (last visited Oct. 15, 2025); *Methylprednisolone*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=31014 (last visited Oct. 15, 2025).

[8] Mesalamine is an orally and rectally administered medication for the treatment of inflammatory bowel diseases and ulcerative proctitis. *Mesalamine*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=30528 (last visited Oct. 15, 2025); *see also Apriso*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=3863 (last visited Oct. 15, 2025) (trademark for the preparation of mesalamine).

> Has been receiving IV steroids for 2 days (today is day 3). Reports significant improvement after just a few doses, including less lower abdominal pain and bowel movements that are not purely liquid.

(*Id.* at 30.) Morphological findings were consistent with ulcerative colitis. (*Id.* at 31.) An MRE was ordered to exclude evidence of small bowel involvement. (*Id.* at 32.) The results of the study showed a long segment of continuous circumferential wall thickening/hyperenhancement and adjacent mesenteric stranding that was suggestive of inflammatory bowel disease, such as ulcerative colitis, as well as mild distention of the proximal ascending colon with smooth tapering towards the transverse colon and no evidence of perforation or intra-abdominal loculated fluid collections. (Ex. 6, pp. 38-39.) In completing the bowel prep in anticipation of the MRE, petitioner noted some regression in his clinical course, including abdominal pain and bloody diarrhea. (Ex. 15, pp. 36, 38, 46.) By November 5, 2017, petitioner's anemia had stabilized, but his leukocytosis persisted, although there was still "[n]o evidence of active infection or need for antibiotics at this time." (*Id.* at 40.) His abdomen was notably non-tender to palpation. (*Id.*) However, petitioner's course fluctuated through his hospitalization. (*Id.* at 45, 50, 54-56, 58, 61-62.) Eventually petitioner's symptoms improved on IV steroids, and he was transitioned to oral steroids on November 10, 2017. (*Id.* at 64-65.) After another day of monitoring, petitioner was discharged on November 11, 2017. (*Id.* at 7-12.) He was prescribed prednisone with a scheduled taper and mesalamine, as well as Canasa suppositories to be taken if his symptoms progressed, and he was directed to follow up with his primary care physician and a local gastroenterologist. (*Id.* at 9.)

On January 3, 2018, petitioner followed up with gastroenterologist, David S. Schulman, M.D. (Ex. 1, p. 10.) By this time, petitioner had tapered his prednisone from 40 mg to 10 mg daily and was asymptomatic with 1-3 formed, non-bloody bowel movements per day. (*Id.*) However, he continued to complain of weight loss and abdominal pain. (*Id.* at 11.) On physical examination, petitioner appeared thin, but there was no tenderness in his abdomen. (*Id.*) Petitioner was directed to liberalize his diet as he had only regained 6 pounds. (*Id.* at 12.) Because petitioner's fecal calprotectin level was normal, he was directed to continue tapering prednisone. (*Id.* at 3, 7, 12.) During a follow up appointment with his primary care physician on February 8, 2018, petitioner reported that he was doing well with 2 formed, non-bloody bowel movements per day after discontinuing prednisone. (*Id.* at 7.) However, he continued to complain of "occasional vague nonlocalized abdominal discomfort which is questionably positional" and mild fatigue. (*Id.* at 7-8.) Although he was directed to continue taking mesalamine, petitioner's ulcerative colitis was noted to be in clinical remission by February of 2018. (*Id.* at 8.) Petitioner's blood work showed mild anemia with a hemoglobin level at 13.0 g/L (reference range of 13.2-17.1 g/L) and a hematocrit level at 37.6% (reference range of 38.5-50.0%). (*Id.* at 2, 4.)

Petitioner returned to Dr. Schulman on April 11, 2018, reporting improved energy and weight gain. (Ex. 1, p. 4.) Although he reported occasional, mild right lower quadrant discomfort, there was no tenderness noted on abdominal examination during this encounter. (*Id.* at 4-5.) Petitioner indicated that he was "anxious to get off of

medication." (*Id.* at 4.) Because petitioner had only experienced a single flare of ulcerative colitis, his physician decided to slowly taper the mesalamine. (*Id.* at 5.) On May 31, 2018, petitioner presented to a new primary care physician with complaints of a "warm sensation" over the right shin that was thought to be "[p]ossibly related to compression of the nerve intermittently from prolonged sitting versus radiculopathy venous other." (Ex. 10, pp. 4-7.) His ulcerative colitis was noted to be stable. (*Id.* at 4-5.)

On June 6, 2018, petitioner presented to the emergency department at Providence Tarzana Medical Center with complaints of headache for the past week. (Ex. 17, p. 7.) It was reported that "he was speaking gibberish and not making sense." (*Id.* at 16.) Petitioner's blood work revealed no evidence of infection and only mild anemia. (*Id.* at 17.) A CT scan of his head was abnormal with "slight hyperdensity extending into the sulci suspicious for subarachnoid and/or subdural hemorrhage." (*Id.* at 12, 17-18.) Petitioner's differential diagnoses included tension headache, migraine, and intracranial process. (*Id.* at 18.) He was placed on Heparin drip and admitted for further work up. (*Id.* at 27-28.) An MRI of the brain showed left temporal lobe edema and venous congestion, which was believed to be due to acute near total occlusion and thrombosis of the left transverse sinus, sigmoid sinus, and jugular vein. (*Id.* at 37.) It was further noted that some of petitioner's smaller cortical venous branches of the left temporal lobe were thrombosed, causing significant left-sided temporal lobe venous congestion. (*Id.*) Petitioner also underwent a CT angiogram of the head and neck, which showed acute occlusion of the left transverse, sigmoid, and jugular vein, extending down to C3-C4 level, and the "appearance of filling defect worrisome for a partial thrombus . . . within the distal superior sagittal sinus near the confluence of sinuses." (*Id.* at 37-38.) Upon review of petitioner's test results, the attending neurologist diagnosed "acute cerebral venous thrombosis occlusion of the left transverse, sigmoid, and jugular vein extending down to C3C4." (*Id.* at 30.) Petitioner's treater also questioned whether the warm sensation in petitioner's leg, reported on May 31, 2018, was indicative of deep venous thromboses. (*Id.*) He was started on anticoagulation therapy and his prednisone prescription was switched to a three-day course of IV steroids, which he tolerated well. (*Id.* at 13, 30, 78, 85, 89.) He was also treated with mesalamine and Coumadin.[9] (*Id.* at 86, 89.) Despite petitioner's clinical improvement, repeat imagining revealed no major improvement. (*Id.* at 23, 59, 85.) Petitioner was discharged in stable condition on July 11, 2018, with a diagnosis of acute cerebral venous thrombosis of unknown etiology and acute ulcerative colitis flare. (*Id.* at 22-24.) On discharge, petitioner was prescribed a prednisone taper and continued anticoagulation. (*Id.* at 23.) He was directed to follow up with a gastroenterologist, neurologist, and hematologist, as well as his primary care physician. (*Id.*)

[9] Coumadin is "administered orally, intravenously, or intramuscularly in the treatment and prophylaxis of thromboembolic disorders." *Coumadin*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=11414 (last visited Aug. 28, 2024); *Warfarin sodium*, DORLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=118753 (last visited Aug. 28, 2024).

Petitioner returned to Dr. Schulman for a follow-evaluation of his ulcerative colitis. (Ex. 9, p. 8.) Dr. Schulman noted petitioner's recent hospitalization and noted this his thrombosis was "most likely related to hypercoagulability from his colitis." (*Id.*) Although his ulcerative colitis was noted to be "minimally symptomatic," Dr. Schulman planned to taper petitioner's prednisone slowly to prevent any further flare while he underwent anticoagulation therapy. (*Id.*) He was also continued on budesonide[10] and mesalamine. (*Id.*) Petitioner then presented to his primary care physician on July 16, 2018, and reported that he was "feeling better," despite suffering from continued mild headaches. (Ex. 10, pp. 8-12.) Regarding petitioner's cavernous sinus thrombosis, the following is noted: "unclear etiology. Steroids? UC?" (*Id.* at 10.) Petitioner presented to hematologist Christopher Ho, M.D., on July 23, 2018. (Ex. 8, pp. 1-3.) Dr. Ho diagnosed cavernous sinus thrombosis, which had improved with Coumadin. (*Id.* at 3.) He noted that petitioner's evaluation for inherited thrombophilia was normal for prothrombin gene mutation and factor V leiden, and that his examination for antiphospholipid syndrome was also normal, though lupus anticoagulant was still pending at this time. (*Id.*) The plan was to continue Coumadin for at least another six months. (*Id.*)

On August 29, 2018, petitioner returned to his primary care physician with complaints of worsening headaches with pain slightly radiating from the posterior left neck and some photophobia without significant nausea or focal deficits. (Ex. 10, p. 13.) Petitioner's neurologic examination was unremarkable, and it was suggested that his headaches were "possibly consistent with tension headaches with mild migraine related symptoms." (*Id.* at 14.) Petitioner reported that he was working to increase his anticoagulation treatment, and a repeat MRI venogram of the head was ordered. (*Id.* at 13-14.) On September 10, 2018, petitioner underwent the repeated MRI venogram, which revealed "minimal flow within the left transverse and sigmoid sinus and very little flow seen in the left jugular vein." (Ex. 16, pp. 6-7.)

Petitioner presented to neurologist Doris Cardenas, M.D., on September 13, 2018, reporting continued mild headaches. (Ex. 16, p. 1.) Dr. Cardenas noted that petitioner experienced an ulcerative colitis flare in June of 2018, characterized by bleeding and pain, that lead to "two distinct episodes of aphasia that brought him to the ER. A[n] MRI B[r]ain demonstrated T2/FLAIR hyperintense lesions of the left temporal lobe. CTA head and neck was negative. MRV demonstrated an extensive sinus thrombosis on the left." (*Id.* at 1-2.) While on Coumadin, petitioner had not experienced a return of aphasia, though he still suffered from mild headache. (*Id.* at 2.) Dr. Cardenas emphasized the need to keep petitioner's ulcerative colitis under control as further episodes "will likely lead to further worsening of his hypercoagulable state." (*Id.* at 1.)

On October 10, 2018, petitioner returned to Dr. Schulman, reporting that he was doing well after tapering off prednisone. (Ex. 9, p. 2.) It was noted that petitioner's

[10] Budesonide is an anti-inflammatory glucocorticoid that is used in the treatment of asthma, inflammatory nasal conditions, ulcerative colitis, and Crohn's disease. *Budesonide*, DOLAND'S MEDICAL DICTIONARY ONLINE, https://www.dorlandsonline.com/dorland/definition?id=7201 (last visited Oct. 16, 2025).

neurologist determined his cavernous venous thrombosis was "unchanged" on Coumadin. (*Id.*) His physical examination was normal, and a repeat fecal calprotectin test was unremarkable. (*Id.* at 1, 3.) Petitioner's ulcerative colitis was against assessed as "in clinical remission," but he was directed to continue taking mesalamine. (*Id.* at 3.)

Since 2018, petitioner has suffered from multiple flares of ulcerative colitis. These episodes were consistent with his prior episodes, including abdominal pain, bloody stools, anemia, diarrhea, fatigue, and weight loss, and required treatment with intravenous and oral steroids and, at times, hospitalization and blood transfusions. (Ex. 18, pp. 3-5; Ex. 31, pp. 17-19; Ex. 36, pp. 12-14; Ex. 37, pp. 32-35; Ex. 97, pp. 3, 15.) Additionally, petitioner required intravenous iron infusions to treat his iron deficiency anemia. (Ex. 35, pp. 18-20.) Petitioner's cavernous venous thrombosis also persisted, causing headaches and requiring long-term anticoagulation. (Ex. 31, pp. 17-19; Ex. 34, pp. 6-8.)

On August 26, 2024, petitioner presented to gastroenterologist Benedict Garrett, M.D., for an evaluation of a perianal fistula or abscess. (Ex. 97, pp. 3-5.) Dr. Garrett opined that the new development of perineal abscess, coupled with petitioner's history, was "now more suggestive of Crohn's [disease] rather than ulcerative colitis." (*Id.* at 5.) If oral steroids were not effective, Dr. Garrett noted that petitioner may need to be treated with Remicade or hospitalized for treatment with IV steroids. (*Id.*) Two days later, petitioner presented to surgical oncologist Philippe Quilici, M.D. (Ex. 96, p. 5.) He was assessed with a perineal abscess, which was drained in office. (*Id.* at 7.)

b. Testimony

Petitioner authored one affidavit in this case. (Ex. 27.) In his affidavit, petitioner attests to his excellent health prior to vaccination. (Ex. 27, ¶ 2.) He describes working a physically demanding job as a camera operator, leading an active lifestyle, and travelling frequently. (*Id.* ¶ 2.) He states that he received the subject vaccines during a routine physical examination on July 17, 2017. (*Id.* ¶ 3.) However, within six days of receiving the vaccines, petitioner states that he "began to feel ill." (*Id.* ¶ 4.) He describes a pin prick sensation and tingling in his arms, hands, legs, and feet, as well as blood in his stool. (*Id.*) By July 25, 2017, petitioner was also feeling nauseous and, within about a week thereafter, he began experiencing cramping and abdominal pain. (*Id.* ¶ 5.) Petitioner states that, by the end of August 2017, his constant symptoms, including "many episodes of diarrhea with blood every day," were interfering with his employment. (*Id.* ¶ 6.)

He further states,

> [A]lmost two years after receiving the tdap and hepatitis A vaccines, I cannot overstate how my life had changed. I am physically diminished in many ways from my pre-[ulcerative colitis] self. I have lost a good deal of weight and do not look or feel healthy. I now suffer form anemia which contributes to my fatigue and lack of energy. Since my stroke I suffer from daily

> headaches. I do not have the same energy level I need to work or run my business at full capacity. I am a camera operator, and even carrying my equipment has become exhausting. Underwater camera operating was my favorite part of my business and I have not been able to do that since my stroke. I cannot do any of the physical activities I have enjoyed all of my adult life like marathon running or scuba diving. I am having to adjust to a new understanding of myself as chronically ill. In additional to the physical toll this has taken on me, there is a psychological toll as well with the knowledge that at any moment I could begin another [ulcerative colitis] flare. I know that I will be dependent on costly medications that leave me fatigued and with headaches, and I am facing the very real likelihood of suffering another stroke from hypercoagulability caused by active [ulcerative colitis]. I also face the numerous known health risks of prolonged high dose steroid treatment. Additionally, my doctors have mentioned that if my [ulcerative colitis] continues to get worse, I may need to go on biologic infusions or even have part of my colon removed.

(Ex. 27, ¶ 20.)

IV. Expert Opinions

a. Petitioner's experts

i. Gastroenterologist John Cromwell, M.D., FACS, FASCRS[11]

Dr. Cromwell authored three expert reports on behalf of petitioner in this case. (Exs. 39, 48, 68.) He also provided expert testimony at the hearing. (Tr. 6-60, 234-35.) Dr. Cromwell opines that petitioner's Tdap and Hepatitis A vaccines more likely than not caused his ulcerative colitis. (Ex. 48, p .2.)

Dr. Cromwell explains that it is "widely accepted" that ulcerative colitis is autoimmune in nature, stressing the role of an "overly exuberant" T-cell response, but also noting a role for adaptive immunity. (Ex. 39, pp. 3-4; Tr. 47-48, 50-52.) He opines that onset of ulcerative colitis is explained by a combination of genetic susceptibility, environmental factors (which are not causative per se), and triggering events, such as infections, stress, or vaccination. (Tr. 47-51.) However, despite having initially put forth

[11] In 1994, Dr. Cromwell received his medical degree from the University of Minnesota Medical School, where he stayed to complete a surgical infectious disease fellowship in 1997, a research fellowship in 2000, a residency and internship in general surgery in 2002, and a colon and rectal surgery fellowship in 2003. (Ex. 40, p. 1.) He maintains an active medical license in Iowa, and he is board certified in general surgery, as well as colon and rectal surgery. (*Id.* at 3; Ex. 39, p. 1.) Dr. Cromwell currently works at the University of Iowa as Director of the Division of Gastrointestinal, Minimally Invasive, and Bariatric Surgery; Associate Chief Medical Officer and Director of Surgical Quality and Safety; a clinical professor; faculty in the graduate program in informatics; and a member of the Iowa Informatics Initiative. (Ex. 40, p. 2.) He has a background in transplant immunology research dealing with both innate and adaptive immunity in humans and primates. (Ex. 39, p. 1.) Additionally, he has authored 27 peer-reviewed papers. (Ex. 40, pp. 5-7.) Dr. Cromwell was proffered as an expert in gastroenterology without objection. (Tr. 12-13.)

a theory of causation, Dr. Cromwell deferred to petitioner's other expert, Dr. Ahmed, with respect to petitioner's theory of causation and confirmed that he agrees with Dr. Ahmed's theory.[12] (*Id.* at 52-53.)

According to Dr. Cromwell, petitioner was in his usual state of good health when he received the subject vaccinations on July 17, 2017. He then experienced the onset of new and worsening bloody diarrhea about one week later. (Ex. 39, p. 4; Tr. 16-20, 45.) Symptoms later progressed to include abdominal pain/tenderness, nausea, and poor appetite, by September 7, 2017. (Ex. 39, p. 4.) The first objective evidence of colitis was a September 21, 2017 CT scan that showed mildly thickened descending and sigmoid colon. (*Id.*; Tr. 22 (discussing Ex. 3, p. 11).) Ulcerative colitis was confirmed upon colonoscopy performed on October 18, 2017, which showed inflammation from the anus to the first part of the large intestine, noted by that time to be severe. (Ex. 39, p. 4; Tr. 25-26 (discussing Ex. 14).) However, Dr. Cromwell notes it would not be considered fulminant. (Tr. 235.) Petitioner's ulcerative colitis was recalcitrant to prednisone and he later suffered a cavernous sinus thrombosis, which Dr. Cromwell attributes to his ulcerative colitis, explaining that inflammatory mediators in the bloodstream from ulcerative colitis increases the risk of thrombosis. (*Id.* at 28-31.)

By August of 2024, petitioner had developed a perianal fistula or abscess. (Tr. 31-34.) Such a finding could be consistent with Crohn's disease (*Id.* at 35-36); however, petitioner's overall history is not indicative of Crohn's disease and that finding alone is insufficient to diagnose Crohn's disease. It can also be consistent with ulcerative colitis. (*Id.* at 35-38.) While ulcerative colitis can progress to Crohn's disease, most patients with a perineal abscess will maintain their ulcerative colitis diagnosis. (*Id.* at 39-40.) If petitioner did have Crohn's disease, then Dr. Cromwell would be unsure if the same immunologic theory would apply. (*Id.* at 59-60.)

Although respondent had raised the possibility that a prior abnormal hemoglobin level from June of 2015 could indicate pre-existing asymptomatic ulcerative colitis, Dr. Cromwell disagrees with such an assertion for several reasons. While the hemoglobin was low on that date (12.7 g/dL versus a reference of 13.2 g/dL), the MCV was normal, which would not be expected for the type of anemia posited by respondent. (Ex. 68, pp. 1-2; Tr. 42-44.) Additionally, CRP was not elevated at that time, which is expected in chronic inflammatory diseases, such as ulcerative colitis. (Ex. 68, p. 2.) Instead, petitioner's low hemoglobin on that date is more likely attributable to the fact that the test was the result of a fasting sample, which is well known to affect hemoglobin levels. (*Id.*; Tr. 43.) Moreover, petitioner had no other indicator of inflammatory bowel disease

[12] A substantial portion of Dr. Cromwell's expert presentation focused on his theory regarding non-specific negative effects of vaccines. (Exs. 39, 48.) In their respective reports, respondent's experts responded to Dr. Cromwell's theories; however, petitioner abandoned this theory in favor of Dr. Ahmed's molecular mimicry theory. (ECF No. 85, p. 13 & n.2.) Although I have reviewed all expert reports in this case, I find that Dr. Cromwell's non-specific vaccine reactions theory does not change the outcome of this case. Accordingly, for the sake of brevity, I have not summarized the expert presentations regarding this proposed theory.

at that time and he had a normal hemoglobin level when next tested in July of 2017, shortly before onset of his symptoms. (Tr. 44-46.)

Regarding respondent's position that the gradient pattern of inflammation in petitioner's colon is inconsistent with molecular mimicry, Dr. Cromwell disagrees. In addition to the points raised by Dr. Ahmed, he opines that respondent has not factored in the bacterial component within the large intestine, explaining that "there's a difference in the bacterial flora and the density of the bacterial flora going from the right side to the left side of the colon" and, thus, the "interplay between cytotoxicity of an antibody plus the other factors that are involved in – in driving mucosal damage could explain that gradient pattern." (Tr. 234-35.)

Ultimately, Dr. Cromwell opines that a logical sequence of cause-and-effect implicating petitioner's vaccinations as a cause of his condition is supported because he had no prior demonstratable evidence of inflammatory bowel disease, developed alterations in bowel habits and gastrointestinal bleeding about a week after vaccination, and then later developed evidence of severe, recalcitrant ulcerative colitis. Moreover, no other trigger or environmental factor explains petitioner's condition. (Tr. 57-58.) In particular, petitioner was not suffering any infection at the time of onset. (*Id.* at 58.) Dr. Cromwell opines that onset of symptoms of ulcerative colitis occurring within one to two weeks of an environmental trigger supports a causal inference. (*Id.* at 57-58.)

ii. Immunologist/rheumatologist S. Sohail Ahmed, M.D., M.B.A.[13]

Dr. Ahmed authored three expert reports on behalf of petitioner in this case. (Exs. 49, 71, 86.) He also provided expert testimony at the hearing. (Tr. 61-156, 226-32.) Dr. Ahmed narrowed petitioner's claim, opining that petitioner's ulcerative colitis[14] was caused by his Hepatitis A vaccine, but indicating that he cannot opine that the Tdap vaccine more likely than not contributed. (*Id.* at 80-81.) He contends that molecular mimicry causally connects the Hepatitis A vaccine with the development of ulcerative colitis. (Ex. 49, pp. 4-5.)

Molecular mimicry is a mechanistic process that begins with initiation of antibody response by a non-self-protein possessing a peptide region that mimics a self-epitope. (Ex. 49, p. 4 (citing Janet M. Davies, *Molecular Mimicry: Can Epitope Mimicry Induce*

[13] Dr. Ahmed received his medical degree from the University of Texas Medical School in 1998; however, prior to graduating with his medical degree, he completed a National Institute of Health ("NIH") research fellowship in Maryland and a research fellowship training in immunology at MD Anderson Cancer Center in Texas. (Ex. 91, pp. 1-2; Ex. 49, p. 2.) Following graduation, Dr. Ahmed completed postdoctoral training in advanced vaccinology. (Ex. 91, p. 2; Ex. 49, p. 2.) He maintains an active medical license in Massachusetts, and he is board certified in rheumatology and internal medicine. (Ex. 91, p. 5.) Dr. Ahmed's clinical training includes general medicine, cardiology, oncology, and rheumatology, as well as academic investigation. (Ex. 49, p. 2.) He has published a total of 30 articles, reviews, letters, editorials, and textbook chapters. (Ex. 91, pp. 5-6.) Dr. Ahmed was proffered as an expert in both rheumatology and immunology without objection. (Tr. 77)

[14] Dr. Ahmed was not willing to opine that his theory of causation would explain the development of Crohn's disease. (Tr. 96-97.)

Autoimmune Disease?, 75 IMMUNOLOGY & CELL BIOLOGY 113 (1997) (Ex. 56)).) "If a virus has a stretch of amino acids identical to a self-epitope, an autoimmune response may result." (*Id.* (citing Michael B. A. Oldstone, *Molecular Mimicry and Immune-Mediated Diseases*, 12 FASEB J. 1255 (1998) (Ex. 54)).) Dr. Ahmed explains that an article by Kovvali and Das discusses the role for molecular mimicry in the pathogenesis of ulcerative colitis. (*Id.* at 5 (citing Gopala Kovvali & Kiron M. Das, *Molecular Mimicry May Contribute to Pathogenesis of Ulcerative Colitis*, 579 FEBS LETTERS 2261 (2005) (Ex. 50)); Tr. 87-89.) Specifically, the authors searched bacterial genomes for homologous sequences to the human TM isoform 5 (hTM5) and identified a sensory protein from *Bacillus cereus*, as well as a hypothetical protein from cyanobacteria *Nostoc punctiforme*. (Ex. 49, p. 5.) Dr. Ahmed opines that, because infectious agents that display self-like peptides are "source material" for vaccines, it is "not surprising that molecular mimicry can occur and lead to autoimmunity that, in individuals carrying HLA susceptible genes, can progress to autoimmune disease." (*Id.* at 4-5; Tr. 86-87.) In that regard, Dr. Ahmed contends that "in silico/bioinformatic homologies provide a foundation for plausibility." (Ex. 49, p. 5.)

Dr. Ahmed explains that studies dating back to 1959 have found high-grade hemagglutinating antibodies to a colon antigen in children with ulcerative colitis that reacted with colonic epithelial cells. (Ex. 71, p. 5 (citing Ove Broberger & Peter Perlmann, *Autoantibodies in Human Ulcerative Colitis*, 110 J. EXPERIMENTAL MED. 657 (1959) (Ex. 75); Ove Broberger & Peter Perlmann, *Demonstration of an Epithelial Antigen in Colon by Means of Fluorescent Antibodies from Children with Ulcerative Colitis*, 115 J. EXPERIMENTAL MED. 13 (1962) (Ex. 76)).) These findings were subsequently confirmed by other investigators. (*Id.* (citing Claudio Fiocchi et al., *High Prevalence of Antibodies to Intestinal Epithelial Antigens in Patients with Inflammatory Bowel Disease and Their Relatives*, 110 ANNALS INTERNAL MED. 786 (1989) (Ex. 77)).) Specifically, and more recently, antibodies to human tropomyosin "have been convincingly demonstrated in patients with ulcerative colitis (and not in normal subjects or unrelated disease controls for inflammatory bowel disease)." (*Id.* at 2, 5 (citing Kiron M. Das & Manisa Bajpai, *Tropomyosin in Human Diseases: Ulcerative Colitis*, *in* 664 TROPOMYOSIN 177 (Peter Gunning ed., 2008) (Ex. 72)).) He cites a study by Das et al., which found that blood taken from 95% of ulcerative colitis patients responded positively to tropomyosin. (*Id.* at 5 (citing Kiron M. Das et al., *Autoimmunity to Cytoskeletal Protein Tropomyosin: A Clue to the Pathogenic Mechanism for Ulcerative Colitis*, 150 J. IMMUNOLOGY 2487 (1993) (Ex. 78)).) Tropomyosin isoform 1 and tropomyosin isoform 5 have been subsequently identified as primarily involved in the pathogenesis of ulcerative colitis "with immunoglobulin, particularly IgG1, synthesized *in vivo* by lamina propria mononuclear cells (LMPC) against tropomyosins and leading to antibody-dependent cell-mediated cytolysis (ADCC)." (*Id.* (footnotes omitted) (citing Livia Biancone et al., *Production of Immunoglobulin G and G1 Antibodies to Cytoskeletal Protein by Lamin Propria Cells in Ulcerative Colitis*, 109 GASTROENTEROLOGY 3 (1995) (Ex. 79); Xin Geng et al., *Tropomyosin Isoforms in Intestinal Mucosa: Production of Autoantibodies to Tropomyosin Isoforms in Ulcerative Colitis*, 114 GASTROENTEROLOGY 912 (1998) (Ex. 80)); Ex. 86, p. 1 (citing Kiron M. Das et al., *Antibody-Dependent Cell-Mediated Cytotoxicity in Serum Samples from Patients with Ulcerative Colitis: A*

Relationship to Disease Activity and Response to Total Colectomy, 77 AM J. MED. 791 (1984) (Ex. 89); I.O. Auer et al., *Ulcerative Colitis Specific Cytotoxic IgG-Autoantibodies Against Colonic Epithelial Cancer Cells*, 29 GUT 1639 (1988) (Ex. 90)).)

According to Dr. Ahmed, these studies confirm that tropomyosin is an established auto-antigen for ulcerative colitis, that antibodies against tropomyosin cause destruction of colonic epithelial cells vis-à-vis direct cytotoxic damage, and that anti-tropomyosin antibodies are therefore pathogenic of ulcerative colitis and not merely an epiphenomenon or secondary phenomenon. (Tr. 87-94, 98-99.) Describing a diagram by Das et al., Dr. Ahmed summarizes the disease process as follows:

> [T]ropomyosin is presented to T-cells through expression with a major histocompatibility complex, so it's the protein that the peptide has to fit into to be recognized by the T-cells. The T-cells are then stimulated by the tropomyosin-producing cytokines.
>
> They upregulate the expression of tropomyosin and epithelial cells of the colon, and these stimulated T-cells produce factors that stimulate the B-cells that cause the production of tropomyosin-specific antibodies, and these antibodies may induce disease by triggering antibody-dependent cellular cytotoxicity and complement-mediated lysis.

(Tr. 97-98 (discussing Das & Bajpai, *supra*, at Ex. 72, p. 183, fig.2).)

Dr. Ahmed has conducted a BLAST[15] analysis of the inactivated Hepatitis A protein in the subject vaccine against human tropomyosin. (Ex. 71, pp. 4, 7-10; Tr. 119-22.) He demonstrates eight potential molecular mimics between Hepatitis A antigens in the Hepatitis A vaccine at issue and peptides contained in the human tropomyosin. (Ex. 71, pp. 2, 4, 7-10; Tr. 122-23.) Two of the eight mimics are in immunodominant antigen domains for Hepatitis A virus and "to which strong reactivity (antibody generation) has been demonstrated using sera of patients recovering from [Hepatitis A virus]," suggesting that these mimics in the Hepatitis A vaccine generate strong immune responses. (Ex. 71, pp. 2, 4, 7-11; Tr. 123-24, 126-27.) Dr. Ahmed opines that these strong immune responses to the Hepatitis A vaccine mimics would, more likely than not,

[15] BLAST searches are performed by using BLAST Global Alignment from the NIH "BLAST" website to identify similarity between sequences – in this case, between full-length Hepatitis A sequences contained in the subject Hepatitis A vaccine and tropomyosin. (Ex. 71, p. 6.) "[T]he minimum peptide length for MHC-restricted T cell responses is generally 12-15 amino acids for MHC class II (antibody-mediated immunity)." (*Id.* (citing Bernard Hemmer et al., *Minimal Peptide Length Requirements for CD4+ T Cell Clones – Implications for Molecular Mimicry and T Cell Survival*, 12 INT'L IMMUNOLOGY 375 (2000) (Ex. 84)).) Protein sequences are then aligned ("Query" and "Subject") and amino acids that are "IDENTICAL" (i.e., represented by respective amino acid symbol) or those that are a "POSITIVE MATCH" (i.e., represented by "+" and meaning not identical, but considered "conserved substitutions" based on similar charge/structure) are identified. (*Id.*) Dr. Ahmed explains that he limited his report to protein sequences with a high% of IDENTICAL amino acids, at the expense of not detecting high% of POSITIVE MATCH amino acids that could also facilitate mimicry, thus underrepresenting the total number of Hepatitis A vaccine mimics that could be capable of cross-reactivity with human tropomyosin. (*Id.*)

cross-react with human tropomyosin. (Ex. 71, pp. 2, 11.) He testified that his results demonstrate "not just any peptide. It's a peptide that's mapping to the area that your body, your immune system recognizes would make antibodies, and, therefore, cross reactivity would be more likely than not." (Tr. 124.) These two mimics demonstrate 28% and 33% identical amino acids, respectively.[16] (Ex. 71, p. 11.) Dr. Ahmed opines, based on experimental autoimmune encephalomyelitis (EAE) modeling, that this degree of homology is capable of causing autoimmune disease. (Tr. 129-37.)

Dr. Ahmed further cites the package insert for the Hepatitis A vaccine. (Ex. 49, pp. 5-6.) The package insert for the Hepatitis A vaccine that petitioner received includes information concerning a surveillance study of 28,375 adult recipients over the course of 60 days that determined that diarrhea/gastroenteritis is a vaccine-related adverse event. (*Id.* (citing VAQTA® (Hepatitis A Vaccines, Inactivated) Suspension for Intramuscular Injection: Initial U.S. Approval: 1996 [hereinafter Hepatitis A vaccine package insert] (Ex. 66)); Tr. 110-11.) Though acknowledging that diarrhea and gastroenteritis is not the same as ulcerative colitis, Dr. Ahmed opines that these observations still fit with the other available evidence.[17] (Tr. 111-12.) And, although respondent is critical of this study because these findings pertained only to "non-serious events," Dr. Ahmed indicates that ulcerative colitis would not fit the definition of a "serious event" as used in vaccine clinical trials. (Ex. 71, p. 2; Tr. 110-13.) Additionally, Dr. Ahmed has collected seven VAERS reports[18] in which ulcerative colitis was reported in connection with the Hepatitis A vaccine. (Ex. 49, p. 6 (citing The Vaccine Adverse Event Reporting System (VAERS) Data Search Results [hereinafter Hepatitis A VAERS reports] (Ex. 67)); Tr. 113-19.) He found an additional report of a "flare of ulcerative colitis" that developed one day after Hepatitis A vaccination in a 55-year-old patient with preexisting ulcerative colitis. (Ex. 49, p. 7.) Dr. Ahmed opines that this report demonstrates "vaccine 'antigen challenge'" and provides evidence that the Hepatitis A vaccine can trigger pathways relevant for ulcerative colitis. (*Id.*) He elaborates that this

[16] The six remaining peptides he identified are contained in antibody-recognized antigen domains of Hepatitis A virus. (Ex. 71, p. 11.) Thus, Dr. Ahmed asserts that any of the eight homologies he identified could trigger antibodies after Hepatitis A vaccination and likely cross-react with human tropomyosin, which is a known antigen in ulcerative colitis pathogenesis. (*Id.* at 2, 11.)

[17] The lack of any indication within the Tdap vaccine package insert that the vaccine causes gastrointestinal symptoms is the primary reason Dr. Ahmed narrowed his opinion to focus on the Hepatitis A vaccine. (Tr. 80-82.) He further emphasizes that both the absence of "diarrhea/gastroenteritis" in the Tdap package insert and the lack of VAERS reports associating ulcerative colitis with the Tdap vaccine bolsters the relevance of this evidence with regards to the proposed association between the Hepatitis A vaccine and ulcerative colitis. (Ex. 71, pp. 2-3.)

[18] The Vaccine Adverse Event Reporting System ("VAERS") is a national early warning system to detect possible safety problems in U.S.-licensed vaccines. (Ex. 49, p. 6.) Dr. Ahmed explains that VAERS is a passive safety monitoring system that accepts and analyzes reports of adverse events (possible side effects) after a person has received a vaccine. (*Id.*; Tr. 113-14.) He further explains that healthcare professionals are required to report certain adverse events to VAERS and that the vast majority of VAERS reports are submitted by people who are directly involved in the management of the patient's care, while vaccine manufacturers are required to report all adverse events that come to their attention and utilize the VAERS information in making conclusions about vaccine safety. (Ex. 49, p. 6; Tr. 114-15.)

report could reflect a "boost" in Hepatitis A virus mimics to the ongoing autoimmune response in a genetically susceptible patients with established ulcerative colitis. (Ex. 71, p. 3.) Dr. Ahmed acknowledges there is no epidemiology to support a causal relationship between the vaccination and ulcerative colitis, but suggests that this should not be viewed as surprising. Dr. Ahmed indicates that the vaccine development process is very sensitive to autoimmune conditions and that the Hepatitis A vaccine would not have come to market if a relevant signal had been detected. (Tr. 85-86, 105-07.) He posits that a signal is only likely to be detected following a mass vaccination campaign, such as the 1970's swine flu vaccination campaign that first demonstrated an association between flu vaccines and GBS. (*Id.* at 107-08.)

Regarding petitioner's own clinical course, Dr. Ahmed opines that there is no evidence of abnormalities prior to vaccination that would reflect inflammation (e.g., white blood cell count, platelet counts, and differential), anemia (e.g., lowered hemoglobin from chronic blood loss from the gut),[19] metabolic abnormalities, or kidney dysfunction. (Ex. 49, p. 7 (citing Ex. 4, pp. 2-3).) Thus, Dr. Ahmed opines that petitioner did not suffer from an undiagnosed, asymptomatic ulcerative colitis prior to vaccination. (Ex. 71, p. 4.) However, within 7 days following administration of the Hepatitis A vaccine, petitioner developed bloody stools, and "[t]here is no other explanation for his development of bloody diarrhea." (Ex. 49, p. 7.) Although respondent suggested that only pan-colitis would be consistent with Dr. Ahmed's theory, Dr. Ahmed disagrees. He opines that autoantibodies can affect tissue in selective ways and that tropomyosin may be expressed on a gradient within the colon. (Tr. 226-28.)

Dr. Ahmed opines that a 7-day onset is a medically acceptable timeframe to infer vaccine causation. (Ex. 49, pp. 7-8.) He explains that the Hepatitis A vaccine that petitioner received is adjuvanted with aluminum (alum), which is a potent immunopotentiator that enhances the adaptive immune response by both forming a deposit at the administration site from which an antigen is slowly de-absorbed and released, extending the duration of B- and T-cell activation, and by preferentially inducing cytokine IL-4 through aluminum exposed macrophages. (*Id.* (citing Claire-Anne Siegrist, *Vaccine Immunology*, *in* STANLEY A. PLOTKIN ET AL., PLOTKIN'S VACCINES (7th ed. 2017) (Ex. 60)).) He notes that antibodies are detectable in the blood within a few days after vaccination. (*Id.* at 8 (citing Siegrist, *supra*, at Ex. 60).) Immune stimulation would be even stronger with an alum adjuvanted vaccine, resulting in a "more rapid" immune response. (*Id.*) Dr. Ahmed opines that "2 days after vaccination with an aluminum adjuvanted hepatitis A vaccine, . . . [petitioner] would have mounted a potent immune response that in the following 5 days would have led to immune pathology of the colonic mucosa/tissue and the symptoms of bloody diarrhea." (*Id.*) He cites a study of vaccination-induced EAE, demonstrating onset of clinical disease within 7-15 days post vaccination. (Ex. 86, p. 2 (citing Jonathan P.C. Hasselmann et al.,

[19] Regarding petitioner's low hemoglobin levels in June of 2015, Dr. Ahmed opines that the causes of low hemoglobin "can be sporadic, diet-related, or due to physiological changes in response to kidney disease, cancer, and diseases of the gastrointestinal tract," and petitioner's levels on the date of vaccination were normal and remained normal until 3 months following onset of clinically apparent gastrointestinal issues. (Ex. 71, p. 4.)

Consistent Induction of Chronic Experimental Autoimmune Encephalomyelitis in C57BL/6 Mice for the Longitudinal Study of Pathology and Repair, 284 J. NEUROSCI. METHODS 71 (2017) (Ex. 87); *Mouse Models of Multiple Sclerosis (MS) – Experimental Autoimmune Encephalomyelitis (EAE)*, REDOXIS, www.redoxis.com [hereinafter EAE Model Description] (Ex. 88)).)

b. Respondent's experts

i. Gastroenterologist Randy Longman, M.D., Ph.D.[20]

Dr. Longman authored three expert reports on behalf of respondent in this case. (Exs. A, C, D.) He also provided expert testimony at the hearing. (Tr. 157-96.) He opines that petitioner's vaccinations were not a cause of petitioner's ulcerative colitis.

While the cause of ulcerative colitis remains unknown, Dr. Longman agrees that scientific research has identified both environmental and genetic factors as contributing to disease. (Ex. D, p. 2; Tr. 173-74.) However, he does not agree that an autoantigen has been identified and, therefore, he prefers the term "hyper-inflammatory disease" to autoimmune disease in the "strict" sense. (Tr. 177.) He acknowledges the literature pertaining to tropomyosin antibodies, as cited by Dr. Ahmed, but opines that the pathologic role of those antibodies is not yet determined. (*Id.* at 193.)

Dr. Longman characterizes ulcerative colitis as a "process," rather than an acute event. (Tr. 175.) He opines that serological markers of inflammation can predate symptoms of ulcerative colitis by years. (Ex. D, p. 2; Tr. 165-66 (discussing Daniel Bergemalm et al., *Systemic Inflammation in Preclinical Ulcerative Colitis*, 161 GASTROENTEROLOGY 1526 (2021) (Ex. D, Tab 1)).) However, although he explains that some patients develop ulcerative colitis over years, there is great variance in symptom presentation and some patients develop symptoms "much more quicky," "on the order of weeks to months." (Tr. 177-78.) Additionally, despite opining that the overall development of ulcerative colitis is a long, insidious process, he agrees that symptom onset can be caused by "watershed events." (*Id.* at 164-65.)

Dr. Longman asserts that petitioner's clinical course "is consistent with the insidious and progressive onset associated with the natural history of [ulcerative colitis]."

[20] Dr. Longman received his Ph.D. in immunology from the Rockefeller University in 2006 and his medical degree from Weill Cornell Medical College in 2007, before going on to complete an internship and residency in internal medicine, as well as a fellowship in gastroenterology, at New York-Presbyterian Hospital/Columbia University Medical Center. (Ex. J, pp. 1-2; Ex. A, p. 1.) Dr. Longman completed a postdoctoral research fellowship at New York University/Skirball Institute of Biomolecular Medicine in 2014. (Ex. J, p. 2.) He maintains an active medical license in New York, and he is board certified in internal medicine and gastroenterology. (*Id.* at 3; Ex. A, p. 1.) He currently works as an associate professor of medicine and serves as the director of the Jill Roberts Center for IBD at Weill Cornell Medicine. (Ex. J, pp. 2-3; Ex. A, p. 1.) Additionally, Dr. Longman is an assistant attending physician at New York-Presbyterian Hospital/Weill Cornell. (Ex. J, p. 2.) He has authored 44 peer-reviewed articles, 13 reviews, 2 book chapters, and 3 case reports. (*Id.* at 21-26.) Dr. Longman was proffered as an expert in gastroenterology without objection. (Tr. 161-62.)

(Ex. A, p. 4 (citing Inger Camilla 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) (Ex. A, Tab 1)); Ex. D, p. 3 (citing Solberg et al., *supra*, at Ex. A, Tab 1)); Ex. C, p. 2.) He explains that it is common for ulcerative colitis to present with progression from loose bowel movements to more frequent and bloody bowel movements over the course of 2-3 months. (Ex. A, p. 4.) Dr. Longman agrees that petitioner's cavernous sinus thrombosis is sequela of his ulcerative colitis. (*Id.* at 3-4; Ex. D, p. 3; Tr. 172-73.) He also agrees that petitioner's later presentation, though potentially concerning for Crohn's disease, is not diagnostic of Crohn's disease. (Tr. 167-68.) He agrees that petitioner's diagnosis remains ulcerative colitis to date. (*Id.* at 169.)

Although Dr. Longman had raised the issue of longstanding inflammatory markers predating symptom onset in ulcerative colitis (Tr. 179-80), he confirmed during cross examination that onset of petitioner's condition was in July of 2017 and that "I have no evidence to suggest that he had ulcerative colitis prior to 2017." (*Id.* at 189-90.) Rather, the inflammatory markers represent only a predisposition to developing ulcerative colitis. (*Id.* at 189.) However, while he agrees that the timing of symptom onset in this case aligns with the time frame for activation of innate and early adaptive immunity, Dr. Longman does not agree that the timing of onset supports vaccine causation. (Ex. D, pp. 3-4.) Dr. Longman states, "if one were to assume that a cross-reactive response via molecular mimicry also occurred, it is not clear to me that this timing would be sufficient to allow for colonic inflammation and symptoms within this time period or with the specific restriction to the descending colon." (*Id.* at 3.)

Dr. Longman also disagrees with Dr. Ahmed's theory. (Ex. D, p. 2; Tr. 182-83.) In particular, he opines that the tropomyosin antibodies identified by Dr. Ahmed are more likely to be a consequence, rather than a cause, of epithelial cell death. (Tr. 183-84.) Regarding Dr. Ahmed's citation to a post-marketing study, he explains that the relevant package insert documented only post-vaccination "diarrhea/gastroenteritis," which is overly broad and notably "non-serious." (Ex. D, p. 2.) He further explains that the conditions mentioned in the package insert likely reflect a completely different pathophysiology than the ulcerative colitis suffered by petitioner. (*Id.*) Regarding the VAERS reports, Dr. Longman opines that "more information would be needed to assert any reasonable or even probable causation." (*Id.* at 1-2.) Additionally, Dr. Longman opines that if Dr. Ahmed's molecular mimicry theory were correct, then petitioner should have experienced a more uniform pan-colitis. (*Id.* at 3; Tr. 194-95.) However, petitioner's clinical course began with colitis and progressed to ascending colitis while sparing parts of the right colon and secum. (Tr. 194-95.)

Ultimately, Dr. Longman opines that petitioner's course of ulcerative colitis has been consistent with the natural history of the condition. (Ex. A, p. 5; Ex. C, p. 2; Ex. D, p. 3.) Noting that petitioner was in the age group with the highest incidences of disease onset, he opines that there is no logical sequence of cause and effect that would support a role for petitioner's vaccinations as a cause of his condition. (Ex. A, pp. 4-5 (citing Natalie A. Molodecky et al., *Increasing Incidence and Prevalence of the*

Inflammatory Bowel Diseases with Time, Based on Systemic Review, 142 GASTROENTEROLOGY 46 (2012) (Ex. A, Tab 3)); Tr. 186.)

ii. Immunologist John Bates, Ph.D., for respondent[21]

Dr. Bates authored three expert reports on behalf of respondent in this case. (Exs. E, G, I.) He also provided expert testimony at the hearing. (Tr. 197-225.) Dr. Bates describes ulcerative colitis as a chronic inflammatory bowel disease involving mucosal inflammation of the colon, for which the etiology is unclear. (Ex. E, pp. 4, 8 (citing Mahesh Gajendran et al., *A Comprehensive Review and Update on Ulcerative Colitis*, 65 DISEASE-A-MONTH 100851 (2019) (Ex. E, Tab 2)).) However, he contends that it is unlikely that the subject vaccines played a role in petitioner's illness. (*Id.* at 9.) He notes that petitioner's medical records show that he had a low hemoglobin level in June of 2015, suggesting that he may have suffered from an undiagnosed, mild ulcerative colitis nearly two years prior to vaccination. (*Id.* at 8-9 (citing Ex. 2, p. 2).) He further notes that blood in the stool may sometimes be hard to detect, and there are no stool occult blood test results available from around the time that he had low hemoglobin levels. (*Id.* at 8.)

Dr. Bates notes that homologies between viral and bacterial sequences and human genes are common and points to the IOM's statement that many homologies exist between exogenous agents and self-antigens but are not associated with biologically relevant autoimmune phenomena or actual human disease. (Ex. E, p. 6 (citing ADVERSE EFFECTS OF VACCINES: EVIDENCE AND CAUSALITY (Kathleen Stratton et al. eds., 2012) [hereinafter 2012 IOM Report] (Ex. 57)); Ex. G, p. 1.) Within his reports, Dr. Bates questions the relevance of tropomyosin in the pathogenesis of ulcerative colitis as the disease is limited to the colon but tropomyosin is expressed in other tissues throughout the body. (Ex. G, p. 3 (citing Zafar K. Mirza et al., *Localization of Specific Human Tropomyosin Isoforms in the Intestine and Extraintestinal Organs*, 12 INFLAMMATORY BOWEL DISEASES 1036 (2006) (Ex. G, Tab 2)).) Although Dr. Bates concedes that "[s]everal reports of tropomyosin-specific antibodies in the sera of individuals with [ulcerative colitis] have been published, and it is possible that these antibodies contribute to the pathology of [ulcerative colitis]," he contends that "the presence of antibodies which bind to tropomyosin in individuals with ulcerative colitis . . . does not demonstrate a causative role for antibodies in the illness." (*Id.* at 1, 3 (emphasis omitted).) During the hearing, however, Dr. Bates ultimately concedes that

[21] Dr. Bates received his Ph.D. in microbiology from the University of Alabama at Birmingham in 2005, before going on to complete a postdoctoral fellowship in the Department of Microbiology and Immunology at Wake Forest University School of Medicine in 2010, followed by another postdoctoral fellowship at the Vanderbilt Vaccine Center in 2014. (Ex. K, p. 1; Ex. E, p. 1.) Dr. Bates currently works as an associate professor in the Department of Cell and Molecular Biology and the Department of Medicine at the University of Mississippi Medical Center. (Ex. K, p. 2.) He is a member of the American Association of Immunologists, the International Society for Vaccines, and the American Society for Microbiology. (*Id.*; Ex. E, p. 1.) He has published over 30 publications and served as an ad hoc member of four different NIH study sections related to vaccines and immunology. (Ex. K, pp. 3-5; Ex. E, p. 1.) Dr. Bates was proffered as an expert in immunology without objection. (Tr. 200.)

the Das and Mott studies cited by Dr. Ahmed demonstrate that tropomyosin antibodies destroy epithelial cells and that they are pathologic. (Tr. 206, 215-18, 221-22.) Thereafter, he maintains only that it is yet to be established whether the antibodies are the initiator of disease. (*Id.* at 206, 215-18.)

Dr. Bates explains that pathology in ulcerative colitis is believed to be the result of barrier dysfunction in the gut whereby damage to the tissue and entry of microbes from lumen in the gut into the tissue stimulates an immune response that causes colitis. (Ex. G, p. 3; Tr. 205-08.) However, none of Dr. Ahmed's citations address barrier dysfunction. (Ex. G, pp. 1-2.) Regarding the paper by Auer et al., Dr. Bates suggests that the antibodies identified were likely stimulated following barrier dysfunction and injury to the gut, rather than causal. (Ex. I, p. 1.) He notes that a review article Kobayashi et al. includes the most updated, albeit incomplete, understanding of ulcerative colitis pathology, and there is no mention of autoantibodies or B cells. (Ex. G, p. 2 (citing (citing Taku Kobayashi et al., *Ulcerative Colitis*, 6 NATURES REVS.: DISEASE PRIMERS 1 (2020) (Ex. G, Tab 1)).) Dr. Bates concludes, "I simply can't see how the theory is possible. Additionally, subcutaneous vaccinations are typically not effective at stimulating mucosal immune responses, so it's not clear that these vaccine specific B cells would migrate to the gut in the first place." (*Id.* at 3.)

Dr. Bates disputes the relevance of the Hepatitis A vaccine package insert (Ex. 66) and the Hepatitis A VAERS reports (Ex. 67). (Ex. E, p. 7.) Regarding the package insert, Dr. Bates explains that the study did not observe any serious adverse events related to vaccination and that observations of non-serious adverse events are difficult to interpret in this context as the rate of occurrence in an unvaccinated population is unknown. (*Id.*) Similarly, with regard to the Hepatitis A VAERS reports, Dr. Bates explains that there is no information concerning how frequently these events occur in the vaccinated population, much less how frequently these events occur among those who are not vaccination against Hepatitis A. (*Id.*) Additionally, Dr. Ahmed identified only two VAERS reports of ulcerative colitis attributed to the Hepatitis A vaccine that petitioner received. (*Id.*) With regard to the VAERS report that details a flare experienced by a 55-year-old patient, Dr. Bates suggests that the flare could have been stress-related or coincidental. (*Id.*; Ex. G, p. 2.) Especially given the limitation of VAERS reports – namely, that VAERS reports alone cannot be used to determine vaccine causation; that VAERS reports may include incomplete, inaccurate, coincidental or unverified information; and that the number of reports alone cannot be used to reach any determination about the existence, severity, frequency, or rates of adverse events following vaccination – the cited Hepatitis A VAERS reports cannot be used to causally connect petitioner's vaccination to his ulcerative colitis. (Ex. E, p. 7 (citing Hepatitis A VAERS reports, *supra*, at Ex. 67, p. 3); Ex. G, p. 2.)

With regard to timing, Dr. Bates acknowledges that the normal immune response to vaccination "is certainly well underway six days following immunization" and that IgM and low levels of IgG appear in the blood within a few days of vaccination. (Ex. E, pp. 7-8; Tr. 223-25.) However, he disputes that the degree of immunopathology required to produce bloody stools could be stimulated in a 6-day time frame. (Ex. E, pp. 7-8; Ex. G,

p. 2; Tr. 215.) He argues that the two-dose series of Hepatitis A vaccinations suggests that petitioner's vaccination, which was presumably only the first dose, did not "elicit a 'potent immune response.'" (Ex. E, p. 8 (citing CTRS. FOR DISEASE CONTROL & PREVENTION, EPIDEMIOLOGY AND PREVENTION OF VACCINE-PREVENTABLE DISEASE app. A at 20 (Elisha Hall et al. eds., 14th ed. 2021) (Ex. E, Tab 6)); Tr. 202.) Although recognizing that there are significant differences between EAE in mice and colitis in humans, Dr. Bates points to a mouse model that provides "reasonable comparison." (Ex. E, p. 8 (citing Michael K. Racke, *Experimental Autoimmune Encephalomyelitis (EAE)*, 14 CURRENT PROTOCOLS NEUROSCI. 9.7.1 (2001) (Ex. E, Tab 8)).) In this study, mice were immunized with a peptide formulation in adjuvant and disease manifested within 10-15 days following immunization. (*Id.* (citing Racke, *supra*, at Ex. E, Tab 8).) In a variation of this protocol, lymphocytes were activated *in vitro* and mice were injected with the activated lymphocytes, resulting in disease onset 8 days after cell transfer. (*Id.* (citing Racke, *supra*, at Ex. E, Tab 8).) Dr. Bates opines that the latter 8-day time frame "provides a better estimate of the minimum time required for lymphocytes to induce pathology after they have been activated," as the time required to activate the cells is not included in the timeline. (*Id.* (emphasis omitted).) However, it takes time for lymphocytes to be activated in the draining lymph nodes, for the antigen-specific population of cells to then expand, and for those cells to then recirculate into the tissue where disease occurs. (*Id.*)

Dr. Bates disputes the relevance of the mouse study by Hasselmann et al., as cited by Dr. Ahmed, because that study involves a T-cell-mediated injury, while Dr. Ahmed's proposed mechanism is antibody-mediated, and involved conditions that are not comparable to a single vaccination. (Ex. I, pp. 1-2; Tr. 204.) Dr. Bates also disputes Dr. Ahmed's proposed scenario, by which IgG1, synthesized *in vivo* by lamina propria mononuclear cells, leads to antibody-dependent cell-mediated cytolysis, as "not compatible" with the time frame for onset following an intramuscular immunization. (Ex. G, pp. 2-3.) Thus, because the basic steps in the Dr. Ahmed's theory for how petitioner's vaccine could have caused his ulcerative colitis are not the same as those seen in EAE, Dr. Bates further opines that a 6-day onset is not a medically acceptable time frame to support vaccine causation in this case. (Ex. E, p. 8; Tr. 203-04, 215.) Ultimately, Dr. Bates opines that immunization can stimulate autoimmunity after ten days at the earliest. (Tr. 204-05.)

V. Discussion

a. Diagnosis

Where the identity and nature of the vaccine-related injury is in dispute, the Federal Circuit has concluded that it is "appropriate for the special master to first determine what injury, if any, [is] supported by the evidence presented in the record before applying the *Althen* test to determine causation." *Lombardi v. Sec'y of Health & Human Servs.*, 656 F.3d 1343, 1352-53 (Fed. Cir. 2011). In that regard, some question was raised as to whether petitioner's later medical records, which documented the development of an abscess or fistula, suggested that petitioner's correct diagnosis may

be Crohn's disease, rather than ulcerative colitis. This is potentially significant because, although the gastroenterology experts indicated that the two conditions exist on a spectrum of inflammatory bowel diseases (Tr. 14-16, 169), petitioner's immunology expert, Dr. Ahmed, explained that petitioner's theory of causation was advanced with respect to ulcerative colitis and does not necessarily extend to Crohn's disease (*Id.* at 96-97). Importantly, however, respondent's gastroenterology expert ultimately agreed with petitioner's expert that there is insufficient evidence to disturb the diagnosis of ulcerative colitis as diagnosed by the treating physicians. (*Id.* at 167-69.)

Accordingly, the evidence preponderantly establishes that petitioner suffers from ulcerative colitis, rather than Crohn's disease.

b. *Althen* prong one

Under *Althen* prong one, petitioner must provide a "reputable medical theory," showing that the subject vaccine can cause the type of injury alleged. *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355-56 (Fed. Cir. 2006) (quoting *Pafford v. Sec'y of Health & Human Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *mot. for rev. denied*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006)). Such a theory need only be "legally probable, not medically or scientifically certain." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioner may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *See Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1325-26 (Fed. Cir. 2006)). However, "[a] petitioner must provide a 'reputable medical or scientific explanation' for [the proposed causal] theory. While it does not require medical or scientific certainty, it must still be 'sound and reliable.'" *Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019) (citation omitted) (first quoting *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1322 (Fed. Cir. 2010); then quoting *Knudsen*, 35 F.3d at 548-49).

As with many cases in the Program, petitioner's theory involves molecular mimicry. Molecular mimicry is a concept whereby a susceptible host encounters a foreign antigen that has sufficient similarity ("homology") with components of host tissue such that the immune system "cross-reacts," producing antibodies that attack the host tissue instead of the foreign antigen to ultimately cause disease or injury. Molecular mimicry "is a generally accepted scientific principle, [but] mere invocation of the scientific term does not carry a petitioner's burden in a Program case." *Deshler v. Sec'y of Health & Human Servs*., No. 16-1070V, 2020 WL 4593162, at *20 (Fed. Cl. Spec. Mstr. July 1, 2020) (citing *Forrest v. Sec'y of Health & Human Servs.*, No. 14-1046V, 2019 WL 925495, at *3 (Fed. Cl. Spec. Mstr. Jan. 28, 2019)). Importantly then, although respondent's gastroenterologist questioned whether ulcerative colitis is an autoimmune condition (Tr. 177, 194-95), literature filed in this case does support petitioner's assertion that ulcerative colitis is an autoimmune condition for which molecular mimicry is a likely mechanism. (Kovvali & Das, *supra*, at Ex. 50, pp. 2-3.)

Prior cases have explained that when assessing theories based on molecular mimicry in light of petitioner's preponderant burden of proof, "[t]he line must be drawn somewhere between speculation and certainty." *Brayboy v. Sec'y of Health & Human Servs.*, No. 15-183V, 2021 WL 4453146, at *19 (Fed. Cl. Spec. Mstr. Aug. 30, 2021). In particular, "the finding of sequence homology does not necessarily mean the similarity has significance to the immune system." *Tullio v. Sec'y of Health & Human Servs.*, No. 15-51V, 2019 WL 7580149, at *15 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), ***aff'd***, 149 Fed. Cl. 448 (2020); *see also Caredio ex rel. D.C. v. Sec'y of Health & Human Servs.*, No. 17-0079V, 2021 WL 4100294, at *31 (Fed. Cl. Spec. Mstr. July 30, 2021) ("[D]emonstration of homology alone is not enough to establish a preponderant causation theory." (emphasis omitted) (citing *Schultz v. Sec'y of Health & Human Servs.*, No. 16-539V, 2020 WL 1039161, at *22 n.24 (Fed. Cl. Spec. Mstr. Jan. 24, 2020))), *mot. for rev. denied*, No. 17-79V, 2021 WL 6058835 (Fed. Cl. Dec. 3, 2021). Thus, for example, in *Brayboy*, an omnibus proceeding addressing autoimmune premature ovarian insufficiency, the special master found it sufficient that the petitioners "identified cross-reaction between components of the vaccine and proteins in the body that are directly responsible for the health and productivity of the organ at issue" and further expressed that requiring additional steps, or insisting on direct, testable evidence would impermissibly heighten petitioner's burden of proof.[22] 2021 WL 4453146, at *19.

The question of whether vaccines can cause ulcerative colitis via molecular mimicry was most recently addressed in *Cerrone v. Secretary of Health & Human Services*. In that case, the petitioner alleged that either the HPV, influenza, or Hepatitis A vaccines caused his ulcerative colitis. No. 17-1158V, 2023 WL 3816718, at *1 (Fed. Cl. Spec. Mstr. June 1, 2023), *mot. for rev. denied*, 168 Fed. Cl. 745 (2023), ***aff'd***, 146 F.4th 1113 (Fed. Cir. 2025). The *Cerrone* special master concluded, however, that petitioner had not demonstrated that ulcerative colitis can be caused by vaccination and, in particular, that petitioner's assertion of molecular mimicry "did not rise above plausibility" and "was not bulwarked by studies or other evidence showing that mimicry in this context was likely disease-causing or at least contributory." *Id*. at *27. Specifically, petitioner's expert "could not identify what specific components of any of the relevant vaccines might be at the center of such a process." *Id*. Ultimately, the Federal Circuit found no error in the *Cerrone* special master's analysis, stressing that the overall weight of evidence presented under *Althen* prong one must in totality

[22] In prior cases, the following four criteria have been described as the manner by which molecular mimicry can be demonstrated to scientific certainty: (1) similarity between a host epitope and an epitope of an environmental agent; (2) detection of antibodies or T-cells that cross-react with both epitopes in patients; (3) an epidemiologic link between exposure and development of the disease; and (4) reproduction of such autoimmunity in an animal model. *See, e.g.*, *Meyers v. Sec'y of Health & Human Servs.*, No. 19-272V, 2025 WL 2754664, at *22 (Fed. Cl. Spec. Mstr. Aug. 22, 2025); *Datte v. Sec'y of Health & Human Servs.*, No. 18-2V, 2025 WL 1565894, at *15 (Fed. Cl. Spec. Mstr. May 9, 2025); *Gross v. Sec'y of Health & Human Servs.*, No. 17-1075V, 2022 WL 9669651, at *36 (Fed. Cl. Spec. Mstr. Sept. 22, 2022). This provides some insight into the types of evidence that may be available, but, of course, petitioner need not demonstrate these four specific points. *See Gross*, 2022 WL 9669651, at *36 ("[F]ulfillment of these criteria would require scientific certainty, which is a bar too high."); *Knudsen*, 35 F.3d at 548-49.

establish that the vaccine at issue can more likely than not cause the condition alleged. 146 F.4th 1113, 1122 (Fed. Cir. 2025). However, the record of this case is very different from the record in *Cerrone*.[23]

Whereas the *Cerrone* petitioner was unable to identify what vaccine components would have been central to the disease process at issue, this petitioner has so demonstrated. Specifically, Dr. Ahmed presented "BLAST" search results that showed homology between multiple antigen peptides within the Hepatitis A vaccine and tropomyosin proteins (discussed further below). (Ex. 71, pp. 5-11; Tr. 119-37.) Dr. Ahmed has opined that the disease-causing potential of the homology he has found using BLAST is evidenced by animal model studies showing that the degree of homology identified is sufficient to result in autoimmune disease. (Tr. 123-26, 135-39 (discussing Anand M. Gautam et al., *Minimum Structural Requirements for Peptide Presentation by Major Histocompatibility Complex Class II Molecules: Implications in Induction of Autoimmunity*, 91 PROC. NAT'L ACAD. SCI. USA 767 (1994) (Ex. 93)).) Though they note that homology alone is not predictive of disease, respondent's experts do not dispute the utility of BLAST searches generally or the reliability Dr. Ahmed's own BLAST results. Nor do they otherwise dispute that the degree of homology presented by Dr. Ahmed has disease-causing potential. Accordingly, while BLAST results have significant limitations, the reliability and utility of the results generated by Dr. Ahmed in this case are not meaningfully challenged.[24] Moreover, Dr. Ahmed has further cited literature demonstrating that two of the homologous peptides he has located within the

[23] Also of note, although *Cerrone* did involve the Hepatitis A vaccine, as is at issue in this case, it was only one among multiple vaccinations potentially involved in that case and the special master's analysis suggests that the petitioner's molecular mimicry theory sought primarily to substantiate a causal role for the HPV vaccine. 2023 WL 3816718, at *26-27. In contrast to *Cerrone*, one prior petitioner has been found entitled to compensation for vaccine-caused ulcerative colitis relative to the HPV vaccine. *Morgan v. Sec'y of Health & Human Servs*., No. 13-529V, 2015 WL 9694667 (Fed. Cl. Spec. Mstr. Dec. 10, 2015). Other petitioners have been denied compensation for allegedly vaccine-caused ulcerative colitis; however, these cases did not involve the Hepatitis A vaccine. *Jackson v. Sec'y of Health & Human Servs*., No. 16-1194V, 2021 WL 5231984 (Fed. Cl. Spec. Mstr. Oct. 12, 2021) (rejecting Dr. Cromwell's theory that the flu vaccine can significantly aggravate ulcerative colitis); *see also Gapen v. Sec'y of Health & Human Servs*., No. 19-422V, 2022 WL 1711616 (Fed. Cl. Spec. Mstr. May 5, 2022) (rejecting claim that PCV-13 vaccine significantly aggravated ulcerative colitis).

[24] The use of BLAST searches is well known in the Program. It has been previously criticized. *E.g.*, *Forrest*, 2019 WL 925495, at *4-5; *A.T. v. Sec'y of Health & Human Servs*., No. 16-393V, 2021 WL 6495241, at *24-25 (Fed. Cl. Spec. Mstr. Dec. 17, 2021). However, it has also been credited in some cases as contributing to the overall conclusion that petitioners have met their burden of proof under *Althen*. *E.M. v. Sec'y of Health & Human Servs*., No. 14-753V, 2021 WL 3477837, at *36-39 (Fed. Cl. Spec. Mstr. July 9, 2021); *White v. Sec'y of Health & Human Servs.*, No. 15-1521V, 2019 WL 7563239, at *24 (Fed. Cl. Spec. Mstr. Dec. 19, 2019). A significant limitation of BLAST searches is that the results showing homology are not in themselves predictive of meaningful molecular mimics, having a high likelihood of showing matches that result merely from chance. *J.C. v. Sec'y of Health & Human Servs*., No. 17-69V, 2024 WL 3412625, at *18-19 (Fed. Cl. Spec. Mstr. May 16, 2024). Therefore, I have previously concluded that "the evidentiary value of these search results is limited and turns on whether the other evidence of record likewise supports a causal relationship between the vaccination and the type of injury at issue. . . . Without more, BLAST search results do not meet petitioner's preponderant burden of proof under *Althen* prong one." *Id*. at *19.

Hepatitis A vaccine are considered "immunodominant," meaning they are immune reactive and capable of antibody binding. (Ex. 71, p. 11 (citing Yury E. Khudyakov et al., *Antigenic Epitopes of the Hepatitis A Virus Polyprotein*, 260 VIROLOGY 260 (1999) (Ex. 85)).) Specifically, antibody binding at the site where Dr. Ahmed has identified homology has been confirmed in samples of sera drawn from human subjects infected with Hepatitis A virus. (Tr. 123-24.) Again, respondent's experts have not challenged this point.

Additionally, whereas the *Cerrone* petitioner "at most posited the possibility of some cross-reaction" affecting the epithelial cells of the gut, 2023 WL 3816718, at *27, Dr. Ahmed has demonstrated that the anti-tropomyosin antibodies implicated by this theory are pathogenic of ulcerative colitis. (Tr. 87-94, 97-99 (discussing Das & Bajpai, *supra*, at Ex. 72, p. 183, fig.2).) Indeed, during the hearing, Dr. Bates agreed on respondent's behalf that 90% of ulcerative colitis patients have these antibodies, that these antibodies have been shown to cause epithelial cell destruction, and that these antibodies are therefore pathogenic of ulcerative colitis. (*Id.* at 221-22.) Dr. Bates hypothesizes, however, that rather than being initiators of the disease process, the antibodies are propagated following some other injury to the colon that causes disruption to the barrier between the colon and the circulating immune system. (*Id.* at 205-07.) But Dr. Bates has not substantiated that this alternative hypothesis should be viewed as mutually exclusive of petitioner's theory. While Dr. Bates posited that an injury or disruption to the intestinal barrier of the colon may be a prerequisite to an antibody response, literature filed by respondent suggests that an abnormally permeable intestinal barrier may already be part of the underlying genetic susceptibility to the condition. (Khor et al., *supra*, at Ex. E, Tab 1, p. 3.) The gastroenterology experts otherwise agree that development of ulcerative colitis involves a combination of susceptibility and external factors. (Tr. 48-49, 173-74.) Moreover, Dr. Longman agreed on respondent's behalf that ulcerative colitis can be subject to "watershed events" that cause symptoms to appear. (*Id.* at 164-65, 176.) During the hearing, Dr. Ahmed stressed that the fact that the tropomyosin antibodies have specifically been shown to cause cytotoxic damage to colonic epithelial cells (a point that Dr. Bates initially disputed but ultimately conceded) refutes any notion that the antibodies are merely an epiphenomenon or secondary phenomenon of the disease process. (*Id.* at 93-94, 98-99.)

Given the above, I am persuaded that petitioner has presented preponderant evidence of a biologic mechanism which could explain how the Hepatitis A vaccine would cause (or trigger) ulcerative colitis. However, apart from petitioner's demonstration of this potential biologic mechanism, there is little else in the record that either refutes or meaningfully supports petitioner's theory of causation, leaving this a close question despite a fairly robust showing as to the pathologic effect of anti-tropomyosin antibodies. Dr. Ahmed acknowledges that no epidemiology is available to implicate the Hepatitis A vaccine as a cause of ulcerative colitis, but suggests that this should not be expected given that the vaccine development process is very sensitive to any signals of autoimmune disease. (Tr. 105-08.) Of course, petitioners are not obligated to present epidemiology to support their case. *Andreu*, 569 F.3d at 1378-79.

Moreover, respondent has not presented any epidemiology that would potentially undermine petitioner's theory by seeking to exonerate the Hepatitis A vaccine as a cause of ulcerative colitis.

Dr. Ahmed did note that a post-marketing study for the Hepatitis A vaccine at issue did observe diarrhea and gastroenteritis resulting in outpatient medical visits following vaccination that were determined to be adverse vaccine reactions. (Tr. 110-11 (discussing Hepatitis A vaccine package insert, *supra*, at Ex. 66, p. 9).) However, these are only nonspecific symptoms *potentially* consistent with ulcerative colitis. There is no evidence confirming that these subjects ultimately suffered ulcerative colitis.[25] Apart from the study discussed in the package insert, Dr. Ahmed merely points to individual case reports drawn by him from the VAERS database. (Ex. 49, pp. 6-7; Ex. 71, pp. 2-3; Tr. 116-18.) Case reports are some evidence potentially supportive of petitioner's claim, but they are not strong evidence of causation. *Paluck v. Sec'y of Health & Human Servs.*, 104 Fed. Cl. 457, 75 (2012) (noting that "case reports 'do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value,'" but "the fact that case reports can by their nature only present indicia of causation does not deprive them of all evidentiary value" (quoting *Campbell v. Sec'y of Health & Human Servs.*, 97 Fed. Cl. 650, 668 (2011))); *Crutchfield v. Sec'y of Health & Human Servs.*, No. 09-0039V, 2014 WL 1665227, at *19 (Fed. Cl. Spec. Mstr. Apr. 7, 2014) (noting that a "single case report of Disease X occurring after Factor Y . . . do not offer strong evidence that the temporal relationship is a causal one – temporal relationship could be pure random chance" (emphasis omitted)).

Finally, Dr. Bates noted that, if Dr. Ahmed's theory were correct, Hepatitis A infection should also be a cause of ulcerative colitis. (Tr. 215.) Thus, he finds it significant that Hepatitis A infection is not a known risk factor for ulcerative colitis. (*Id*.) This point is not persuasive for two reasons. First, parallels to wild infection are not necessarily strong evidence. *E.g.*, *Gaskin v. Sec'y of Health & Human Servs*., No. 21-835V, 2025 WL 786306, at *12 (Fed. Cl. Spec. Mstr. Feb. 11, 2025) (noting that the IOM concludes that evidence of parallels to natural infection, though some evidence, "is never sufficient" to either accept or reject a causal relationship). Ultimately, petitioners are not obligated to "demonstrate that a vaccine's infectious counterpart is a known-disease trigger." *Morrison v. Sec'y of Health & Human Servs.*, No. 18-386V, 2024 WL 3738934, at *18 (Fed. Cl. Spec. Mstr. July 18, 2024). Second, Dr. Bates merely testified that he does not know of any evidence that Hepatitis A infection causes ulcerative colitis. (Tr. 215.) He has not pointed to any literature purporting to examine the question or suggesting that Hepatitis A infection is not among the potential triggers of ulcerative colitis.

[25] Respondent's experts stress that the reported instances of diarrhea were determined to be "nonserious" adverse events, suggesting that ulcerative colitis could not be considered "nonserious." (Ex. D, p. 2.) However, the study at issue was only a 60-day surveillance study and, while medical charts were reviewed relative to the events, there is no indication that the subjects were followed to determine the ultimate course of their condition. In any event, according to Dr. Ahmed, vaccine safety studies follow a strict definition of "serious" adverse events that would not encompass ulcerative colitis. (Tr. 112-13.)

Ultimately, the medical literature of record reflects that ulcerative colitis is multifactorial, involving an interplay of genetics, environmental factors, the gut microbiota, and autoimmunity, including both innate and adaptive immune responses. (*E.g.*, Gajendran et al., *supra*, at Ex. E, Tab 2, p. 7.) Considering all of the above, I find that petitioner has presented a sound a reliable theory by which he has preponderantly shown that the Hepatitis A vaccine can be a but for cause and substantial contributing factor in the development of ulcerative colitis.

c. *Althen* prongs two and three

Under the first *Althen* prong, petitioner must present a general medical theory explaining that the vaccine in question "can" cause the type of injury in question. *Pafford*, 451 F.3d at 1355-56. However, under the second and third prongs, petitioner must also present evidence that the vaccine "did" cause petitioner's own injury. *Id*. The third prong asks whether the timing of injury in this specific case aligns with what would be expected under the general theory presented under *Althen* prong one. *Id.* at 1358. The second *Althen* prong requires preponderant proof of a logical sequence of cause and effect, which is usually supported by facts derived from petitioner's medical records.[26] *Althen*, 418 F.3d 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326; *Grant*, 956 F.2d at 1148. While the opinions of treating physicians are often favored, *Capizzano*, 440 F.3d at 1326, a petitioner may support a cause-in-fact claim through presentation of either medical records or an expert medical opinion. *See* § 300aa-13(a).

The Federal Circuit has cautioned that the second *Althen* prong "is not without meaning," but has also indicated that satisfaction of *Althen* prongs one and three is probative with respect to *Althen* prong two.[27] *Capizzano*, 440 F.3d at 1326-27.

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[26] Medical records are generally viewed as trustworthy evidence. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). These records are generally contemporaneous to the medical events and "contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium." *Id.* However, medical records and/or statements of a treating physician's views do not *per se* bind the special master. § 300aa-13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 745 n.67 (2009) (reasoning that "nothing . . . mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted").

[27] The *Capizzano* Court described the circumstances in which *Althen* prong two may be a stumbling block as follows:

> There may well be a circumstance where it is found that a vaccine *can* cause the injury at issue and where the injury was temporally proximate to the vaccination, but it is illogical to conclude that the injury was actually caused by the vaccine. A claimant could satisfy the first and third prongs without satisfying the second prong when medical records and medical opinions do not suggest that the vaccine caused the injury, or where the probability

Nonetheless, temporal association alone is not enough to satisfy petitioner's burden of proof. *See*, *e.g.*, *Veryzer v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 344, 356 (2011) (explaining that "a temporal relationship alone will not demonstrate the requisite causal link and that petitioner must posit a medical theory causally connecting [the] vaccine and injury"), *aff'd per curiam sub nom. Veryzer v. United States*, 475 F. App'x 765 (Fed. Cir. 2012); *A.Y. v. Sec'y of Health & Human Servs.*, 152 Fed. Cl. 588, 595 (2021); *Forrest v. Sec'y of Health & Human Servs.*, No. 10-032V, 2017 WL 4053241, at *18 (Fed. Cl. Spec. Mstr. Aug. 10, 2017); *Cozart v. Sec'y of Health & Human Servs.*, No. 00-590V, 2015 WL 6746616, at *18 (Fed. Cl. Spec. Mstr. Oct. 15, 2015), *mot. for rev. denied*, 126 Fed. Cl. 488 (2016); *Crosby v. Sec'y of Health & Human Servs.*, No. 08-799V, 2012 WL 13036266, at *37 (Fed. Cl. Spec. Mstr. June 20, 2012).

In this case, there is no dispute that petitioner suffered ulcerative colitis or that the first symptoms of his condition arose post-vaccination. However, none of petitioner's treating physicians recorded any medical opinion either favoring or disfavoring vaccine causation. Accordingly, having concluded that the Hepatitis A vaccine can causally contribute to the development of ulcerative colitis, assessing whether petitioner's Hepatitis A vaccine "did" cause his ulcerative colitis is a question of weighing the competing expert opinions. Petitioner's two experts, a gastroenterologist and an immunologist, have opined that petitioner's vaccine did cause his condition, explaining that the timing is appropriate and asserting that the proposed causal chain is "logical." (Ex. 39, p. 4; Ex. 49, pp. 7-8.) In response, respondent's two experts dispute both points. Apart from his experts' differing views on general causation, respondent's opposition as to specific causation stems primarily from four points raised by his experts, all relating to the pattern and timing of onset. Respondent has not suggested that any other potential cause of ulcerative colitis is at issue. Indeed, Dr. Longman repeatedly noted that petitioner's ulcerative colitis simply followed the natural course of the condition. (Ex. A, p. 5; Ex. C, p. 2; Ex. D, p. 3.)

First, Dr. Longman has raised the issue that development of ulcerative colitis is "a process" and that there is some evidence to suggest that petitioner's ulcerative colitis may have predated his vaccination by some two years. (Tr. 175-76.) However, this is not ultimately persuasive. To the extent Dr. Bates had relied on petitioner's low hemoglobin in June of 2015 as evidence of preexisting ulcerative colitis (Ex. E, p. 8), Dr. Longman explained during the hearing that this test result was not informative (Tr. 190-91). Additionally, while he cited literature showing that there may be pre-clinical inflammatory markers of ulcerative colitis, Dr. Longman acknowledged that these inflammatory markers represent only a predisposition to ulcerative colitis, rather than an actual subclinical disease process. (*Id.* at 188-89.) Dr. Longman acknowledged during cross-examination that he has "no evidence to suggest that [petitioner] had ulcerative colitis prior to 2017" and agreed that symptom onset was not prior to July of 2017. (*Id.*

> of coincidence or another cause prevents the claimant from proving the vaccine caused the injury by preponderant evidence.

440 F.3d at 1327.

at 189-90.) Moreover, while he considers the development of ulcerative colitis to represent a longer process, Dr. Longman agrees that the process can be subject to "watershed" events that can cause the initial onset of symptoms. (*Id.* at 164-65, 176.) This effectively agrees with Dr. Cromwell's opinion that ulcerative colitis can be subject to triggers in addition to genetic susceptibility and other environmental factors. (*Id.* at 48.) Thus, even if some preclinical disease process was occurring, this would not be dispositive.

Second, despite symptoms having first occurred post-vaccination, Dr. Longman contests that the colitis demonstrated in this case would have occurred in the post-vaccination time period. Specifically, Dr. Longman explained that ulcerative colitis starts characteristically in the rectum and progresses proximally, *i.e*. higher in the colon. (Tr. 175.) Looking at petitioner's histology (Ex. 7, p. 50), he opines that it evidences chronic condition. (Tr. 176.) He further noted that petitioner's CT scan showed descending colitis, which then progressed proximally to ascending colitis by the time of his colonoscopy. (Ex. D, p. 3 (citing Ex. 3, p. 10; Ex. 13, p. 2; Ex. 14).) However, petitioner's CT scan was not performed until September 21, 2017 (Ex. 13, p. 1), nearly two months after the initial onset of his condition, his colonoscopy occurred about a month after that on October 18, 2017 (Ex. 14, p. 1), which is also when the pathology sample was collected (Ex. 7, p. 50). Although Dr. Longman repeatedly stressed that ulcerative colitis represents an unfolding process, rather than an acute presentation, he did not adequately explain why these findings would suggest that the time-course of petitioner's condition would be earlier than petitioner asserts. Rather, he testified that there is significant variance in symptom presentation among ulcerative colitis patients and that some patients do develop symptoms "much more quickly," which he explained to mean "on the order of weeks to months." (Tr. 177-78.) There were "weeks to months" between the time of petitioner's vaccination and the time of the CT scan and colonoscopy from which Dr. Longman seeks to discern the chronicity of his condition. Moreover, Dr. Longman's report observes that petitioner's condition progressed from the time of his CT scan to the time of his colonoscopy. (Ex. D, p. 3.) Thus, it is not the case, as Dr. Longman seems to imply, that the full extent of petitioner's colitis was present at the time of symptom onset.

Third, both of respondent's experts question whether the pattern of tissue destruction in petitioner's case is consistent with molecular mimicry. Specifically, they contend that if petitioner's theory were correct, then petitioner should have experienced a pan-colitis because one should expect that if antibodies are in equilibrium throughout the colon, then the affected areas should also be uniform. (Tr. 194-95, 218.) Petitioner, by contrast, had inflammation from the rectum to the ascending colon that spared parts of the right colon and secum. (*Id.* at 194-95.) Dr. Ahmed disagreed that his theory would necessarily result in a uniform tissue destruction, indicating that it is common in autoimmunity for auto-antigens to be expressed in various tissue while having a "very localized response" to specific tissue and that tropomyosin may be expressed on a gradient within the colon, such that mimicry may first occur in the tissue with the most expression of auto-antigens. (*Id.* at 226-28.) Dr. Cromwell also reasonably explained that respondent's experts' view does not account for the fact that bacterial flora are not

evenly distributed throughout the colon, having a greater density going from the right to the left side. (*Id.* at 234-35.) He suggests that, because the cytotoxic damage from the antibody response interplays with the gut biome, a gradient pattern is not necessarily unexpected.[28] (*Id*.) As noted under *Althen* prong one, the literature filed in this case posits that ulcerative colitis is explained by multiple factors, including both autoimmunity and the status of the gut microbiota. (Gajendran et al., *supra*, at Ex. E, Tab 2, p. 8.) In any event, in making this point, Dr. Longman himself stressed that petitioner's own presentation as "very typical" of ulcerative colitis. (Tr. 194.) Given that petitioner has satisfied *Althen* prong one, Dr. Longman is not persuasive in contending that antibodies implicated as having a demonstrated pathogenic role in the development of ulcerative colitis should be assumed to be incapable of resulting in the "very typical" presentation of that condition.

Fourth, and finally, respondent's experts contest the idea that the development of the antibody response theorized by Dr. Ahmed could unfold over the course of a week. (Tr. 182-83, 204-05.) Dr. Bates explained that, if petitioner's theory is correct, then the antigen injected at petitioner's arm would need to travel to the draining lymph node, get captured by antigen-presenting cells and presented to T-cells. (*Id.* at 203.) Then the T-cells would have to migrate to the B-cell follicle where a germinal center would be created leading to the production of B-cells. (*Id.*) Those antibodies would need to be produced at a high enough level to cause disease and would have to travel through the bloodstream to the colon where they could then cause cytolysis. (*Id.* at 204.) Dr. Ahmed described the steps involved in his theory in a manner similar to Dr. Bates. (*Id.* at 98-99.) However, Dr. Bates opined that "I can't wrap my head around how those antibodies could be stimulated to a high enough level to cause that sort of pathology by day six." (*Id.* at 215.) Dr. Longman likewise opined that, while he agreed the adaptive immune response could be active within seven days, he did not agree that it would result in actual colitis within that timeframe. (Ex. D, pp. 3-4.)

Dr. Ahmed disagreed with the assertion that the seven-day onset was too short for this process to occur and noted that respondent had not cited any literature supporting that assertion. (Tr. 139-40, 231.) He cited a mouse model study demonstrating weight loss just six days after immunization with an increase in disease severity at around day ten. (*Id.* at 153, 229-30 (discussing EAE Model Description, *supra*, at Ex. 88).) Dr. Bates felt this model was unrepresentative of ulcerative colitis, because it involved a T-cell mediated rather than B-cell mediated process, suggesting a B-cell process would necessarily take longer. (*Id.* at 204.) However, according to the IOM,[29] the latency between antigen exposure and primary antibody response can be as

[28] Notably, this explanation is consistent with respondent's description of the pathogenesis of ulcerative colitis within his prehearing brief. (ECF No. 81, p. 14, n. 5.) Respondent's understanding is that the immune process at issue arises in locations where changes in microbiota and a decreased mucosal layer disrupt the intestinal barrier and attract immune cells. (*Id.*)

[29] The Institute of Medicine (known as the National Academy of Medicine since 2015) is the medical arm of the National Academy of Sciences. The National Academy of Sciences ("NAS") was created by Congress in 1863 to be an advisor to the federal government on scientific and technical matters (*see* An Act to Incorporate the National Academy of Sciences, ch. 111, 12 Stat. 806 (1863)), and the Institute of

little as seven days for a naïve exposure, with the production of B-cells ramping up (identified as the "logarithmic phase") by the fourth day. (2012 IOM Report, *supra*, at Ex. 57, p. 87.) Ultimately, Dr. Longman agreed on respondent's behalf that the adaptive immune response at issue would be active within the seven days between petitioner's vaccination and his onset of symptoms. (Ex. D, pp. 3-4.) And, while Dr. Bates questioned the timing relative to petitioner's theory, he otherwise explained that, even if it often takes between two weeks to a month, immunization can stimulate autoimmunity in as little as ten days (Tr. 204-05), which is not a significant difference from the approximately seven days at issue in this case.[30] In that regard, special masters are cautioned against setting hard and fast deadlines for onset. *Paluck v. Sec'y of Health & Human Servs.*, 786 F.3d 1373, 1383-84 (Fed. Cir. 2015). Although Dr. Longman opined that, even if the immune process at issue was active, petitioner's condition would not manifest by that time, this point is clouded by the preceding point. Dr. Longman was unpersuasive to the extent he seemed to suggest that the full extent of petitioner's colitis would have been present from the time of symptom onset.

But in any event, while the parties stipulated (ECF No. 77) and the experts assumed (Tr. 20, 80, 176, 214-15) that onset of petitioner's condition occurred about one week post-vaccination, this represents only the earliest possible timing of onset. In his affidavit, authored nearly two years into the course of his ulcerative colitis, petitioner recalled that he first felt ill and observed blood in his stool six days post-vaccination, later experiencing onset of nausea by July 25, 2017, and abdominal pain about a week after that. (Ex. 27, pp. 1-2.) However, the contemporaneous treatment records indicate that when petitioner first sought urgent care for what would later be diagnosed as ulcerative colitis on August 28, 2017, he described onset of bloody stool of only one month, which would place his earliest symptom at about the end of July, approximately two weeks post-vaccination. (Ex. 5, p. 1.) Moreover, at that time, he was specifically screened for nausea and abdominal pain and denied having these symptoms. (*Id*.) When petitioner followed up with his primary care provider on September 7, 2017, he reported a six-week history of progressive symptoms, which would place the initial onset at about July 27, 2017, ten days post-vaccination. (Ex. 4, p. 5.) Accordingly, petitioner's hindsight account likely compresses the period of time over which his symptoms initially manifested. Based on the most contemporaneous medical records, it is more likely that petitioner's first symptoms of ulcerative colitis occurred about ten days to two weeks post-vaccination.

In light of all of the above, and considering the record as a whole, I find that petitioner has preponderantly demonstrated that the onset of his symptoms of ulcerative colitis occurred during a post-vaccination period of time from which it is appropriate to draw a causal inference and, further, that a logical sequence of cause and effect

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Medicine is an offshoot of the NAS established in 1970 to provide advice concerning medical issues. When Congress enacted the Vaccine Act in 1986, it directed that the IOM conduct studies concerning potential causal relationships between vaccines and illnesses. *See* § 300aa-1 note.

[30] I do not find it necessary to resolve whether the presence of an adjuvant in the vaccine would have speeded up the immune response, as Dr. Ahmed additionally suggested.

preponderantly supports his July 17, 2017 Hepatitis A vaccination as a cause or trigger of the condition.

d. Factor unrelated to vaccination

Once petitioner has met his own prima facie burden of proof, respondent may still demonstrate by a preponderance of evidence that the injury was nonetheless caused by a factor unrelated to the vaccination. § 300aa-13(a)(1)(B); *Deribeaux v. Sec'y of Health & Human Servs.*, 717 F.3d 1363, 1367 (Fed. Cir. 2013). In order to meet his burden, respondent must demonstrate by preponderant evidence "that a particular agent or condition (or multiple agents/conditions) unrelated to the vaccine was in fact the sole cause (thus excluding the vaccine as a substantial factor)." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1354 (Fed. Cir. 2008) (emphasis omitted). Here, however, respondent has not presented any such argument. (ECF No. 81, p. 17.)

VI. Conclusion

After weighing the evidence of record within the context of the Vaccine Program, I find by preponderant evidence that petitioner suffered ulcerative colitis, resulting in cavernous venous thrombosis, caused-in-fact by the Hepatitis A vaccination he received on July 17, 2017. A separate damages order will be issued.

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master