In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 17-1158V

(to be published)

NIKKO CERRONE,	*	
	*	Chief Special Master Corcoran
Petitioner,	*	Filed: May 8, 2022
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Gary Alan Krochmal, Law Offices of Gary A. Krochmal, PLLC, Farmington Hills, MI, for Petitioner.

Mallori Browne Openchowski, U.S. Department of Justice, Washington, DC, for Respondent.

ENTITLEMENT DECISION[1]

On August 28, 2017, Nikko Cerrone filed this action seeking compensation under the National Vaccine Injury Compensation Program (the "Program").[2] ECF No. 1. Petitioner alleges that the human papillomavirus ("HPV"), influenza, and Hepatitis A ("Hep. A") vaccines he received on October 7, 2015, caused him to incur ulcerative colitis ("UC"). A two-day entitlement hearing in the matter was held in Washington, D.C., on May 24-25, 2022.

Having reviewed the record, all expert reports and associated literature, and listened to those witnesses and experts who testified at the hearing, I hereby deny an entitlement award. As discussed in greater detail below, Petitioner has not preponderantly established that any of the

[1] The parties may object to the published Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire Decision will be available to the public in its current form. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758, codified as amended at 42 U.S.C. §§ 300aa-10 through 34 (2012) [hereinafter "Vaccine Act" or "the Act"]. Individual section references hereafter will be to § 300aa of the Act (but will omit that statutory prefix).

vaccines can cause UC, that they did so herein, or that the timeframe in which his UC manifested (when measured against the date of vaccination) was medically acceptable.

I. Fact History

Prior Medical History and Receipt of Vaccinations

Mr. Cerrone was sixteen years old when he was evaluated by his primary care physician ("PCP") for right jaw and ear pain on October 7, 2015. Ex. 1 at 3, 14. He weighed 165.5 pounds at the time. *Id.* at 14. At this visit Petitioner received the three vaccines at issue: HPV (under the "Gardasil" tradename), influenza (the "Flumist" formulation),[3] and Hep A.[4] *Id*. Before vaccination, Petitioner's medical history was significant for attention deficit hyperactivity disorder, and Petitioner had been taking medication for the condition. *Id*. There is no contemporaneous medical record evidence of any immediate vaccine reactions.

The following month, Petitioner had two visits to the ER for physical injuries. Ex. 2 at 31 (November 10, 2015 ER visit for lacerated lip), 34 (November 3, 2015 left wrist injury while playing football and reports of "left wrist pain due to injury"). He also had a primary care visit on November 12, 2015, that reported his previous injuries and two ER visits. Ex. 1 at 13. During this visit he weighed 164 pounds. *Id.*

The aforementioned records say nothing about a vaccine reaction, and there is no other medical record evidence for the remainder of 2015 establishing any alleged post-vaccination symptoms relevant to this claim. Petitioner has, however, personally averred in his affidavit that he experienced three events relevant to his claim. Affidavit, dated October 12, 2017 (ECF No. 19-1) ("Cerrone Aff. I"); Affidavit, dated March 20, 2018, (ECF No. 28) ("Cerrone Aff. II"). First, he maintains that during November 2015, his stamina decreased, and he could not lift weights with the same repetition or run distances as far or fast. Cerrone Aff. II at 2. Second, he states his stability became an issue, and he fell for no reason during a football game during that same month. *Id.* Third, Petitioner reports that in late December he first observed bloody stools, but was too embarrassed to tell his mother.[5] *Id.* at 1.

[3] Flumist is a "live attenuated influenza vaccine" ("LAIV") that is administered as a nasal spray. *D'Tiole v. Sec'y of Health & Hum. Servs.*, No. 15-085V, 2016 WL 7664475, at *1 n.4 (Fed. Cl. Spec. Mstr. Nov. 28, 2016), *mot. for review den'd,* 132 Fed. Cl. 421 (2017), *aff'd,* 726 F. App'x 809 (Fed. Cir. 2018) (noting that Flumist "contains live, but attenuated (meaning reduced in virulence), strains of the wild flu virus.").

[4] The records indicate that Petitioner had been receiving yearly flu vaccinations since 2007. Ex. 1. at 1–3.

[5] Petitioner also noted (though with no clear date or time at which this occurred) that he was having a hard time playing sports because of his low energy level and strength. Cerrone Aff. I at 5. Such symptoms (plus continued rectal bleeding and diarrhea) made it difficult for him to attend college classes. *Id.*

Diagnosis of UC After Appearance of Gastrointestinal Symptoms

On February 10, 2016, Petitioner returned to his PCP's office with complaints of a sore throat and congestion. Ex. 1 at 4, 12. He was diagnosed with pharyngitis, had a normal physical exam (with no evidence of unexpected weight loss), and at this time administered a second dose of Gardasil vaccine. *Id*. (normal abdominal examination noted). This record (like those before it) references no gastrointestinal issues either. And no medical records for the prior five to six weeks have been offered, and thus there is no contemporary evidence prior to this date from the beginning of 2016 that Petitioner was experiencing any symptoms consistent with his UC.

A few days later, however, on February 13, 2016 (now more than four months after vaccination), Petitioner presented to the Monroe Regional Hospital ("Monroe") emergency room in Monroe, Michigan complaining of three weeks of bright red blood in his stools, with particularly exacerbated symptoms over the past several days.[6] Ex. 2 at 25–26. He was diagnosed with hematochezia[7] and discharged. *Id*. at 27, 29–30 (normal hemoglobin and hematocrit values recorded). On February 17, 2016, Petitioner underwent a stool panel. Ex. 1 at 57–58. The next day (February 18th), he followed up with his PCP, recounting a history of blood in his stool for three to four weeks. *Id.* at 11. He was referred for a gastrointestinal ("GI") evaluation. *Id*.

Petitioner underwent a flexible sigmoidoscopy[8] performed by gastroenterologist Lesa Chopra, D.O., on March 14, 2016, which showed proctosigmoiditis with a few ulcerations and contiguous inflammation to 25 cm. Ex. 3 at 11. His weight had now dropped significantly from what he had been the month before (down to 158 pounds), and at a follow-up with Dr. Chopra on March 24, 2016, Petitioner was formally diagnosed with UC. *Id*. at 6–7, 11. Dr. Chopra also concluded that the biopsies taken during the sigmoidoscopy were consistent with irritable bowel disease ("IBD"). *Id*. at 6. By this time, Petitioner was experiencing persistent daily rectal bleeding despite use of a suppository. *Id*.; *see also* Ex. 1 at 10 (March 30, 2016 PCP visit reiterating the UC diagnosis and persistent bloody stools).

[6] This history (which is consistent with the PCP record from February 18, 2016) would place onset of Petitioner's symptoms approximately fifteen weeks after his October 7, 2015, receipt of the HPV vaccine, or by the last week of January 2016. Ex 1 at 11. During this February 18, 2016 visit, Petitioner's weight was 170.8 pounds. *Id.*

[7] Hematochezia is the medical term for the passage of bloody stools. *Hematochezia,* Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=21736&searchterm=hematochezia (last visited May 8, 2023).

[8] A sigmoidoscopy is an inspection of the sigmoid colon through a sigmoidoscope. *Sigmoidoscopy,* Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=45800&searchterm=sigmoidoscopy (last visited May 8, 2023).

UC Treatment

On May 19, 2016, Petitioner returned to the Monroe ER for a lower GI bleed and acute abdominal pain. Ex. 2 at 19–24. He gave a history of bloody stools for five months with associated diarrhea, constipation, abdominal pain, and hemorrhoids (putting onset anywhere between mid-December 2015 to mid-January 2016. *Id*. Petitioner's mother reported that he had been "doubled over" with pain, but it had since resolved. *Id*. Petitioner also had a facial rash for one day after recent completion of a course of oral steroids that reportedly did not help with his symptoms. *Id*.; Ex. 3 at 1. He was started on another suppository and fiber, and discharged to follow up with Dr. Chopra the following week. Ex. 2 at 23–24.

Petitioner thereafter continued treatment through the early fall of 2016, but his rectal bleeding did not diminish. Ex. 3 at 1-4 (May and August 2016 treatment visit). In the interim, on June 24, 2016, Petitioner saw his PCP for testing after he swam in a lake with high levels of *E. coli*. Ex. 1 at 8. He reported abdominal pain and diarrhea the day before. *Id*. At that visit, Petitioner received a third Gardasil vaccination. *Id*. at 4, 8. There is no medical record evidence suggesting any reaction to this dose of vaccine, and Petitioner has not alleged it exacerbated his symptoms.

That September, Petitioner was seen in the Monroe ER for chest pain and shortness of breath, which was diagnosed as costochondritis with no need for further cardiology workup. Ex. 2 at 13, 18–19; 100. He also reported a recent upper respiratory infection two weeks earlier. *Id*. at 13. A history of IBD with iron deficiency anemia, abdominal pain, melena,[9] and hematochezia was noted. *Id*. at 13–14. Petitioner was on steroids for UC and being followed by a GI specialist, but they could not control or stop his bleeding and diarrhea. *Id*. at 88. He was reportedly still eating okay and functioning well. *Id*.

On October 3, 2016, Petitioner was evaluated by Nirmal Kaur, M.D., at the Henry Ford IBD Center. Ex. 4 at 9. At that visit, Petitioner indicated specifically (for the first time in the medical record)[10] "that he began having some intermittent rectal bleeding during *December* of 2015," but did not seek further evaluation or workup at that time. *Id* (emphasis added). He subsequently began having "nausea with epigastric pain as well as worsening frequency of blood in his stools." *Id*. By March 2016, Petitioner had daily pain with associated nausea. *Id*.

[9] Melena is the passage of dark-colored, tarry stools, due to the presence of blood altered by the intestinal juices. *Melena,* Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=30249&searchterm=melena (last visited May 8, 2023).

[10] Petitioner reported a history of bloody stools beginning in December 2015 on multiple subsequent occasions. Ex. 4 at 17; Ex. 5 at 15, 24, 1247; *but see* Ex. 1 at 11; Ex. 2 at 25. The history also indicates that Petitioner was first seen by Dr. Chopra on February 26, 2016, although Dr. Chopra's records (filed collectively as Petitioner's Exhibit 3) do not appear to contain a record of this visit.

In October 2016, Petitioner was continuing on his medication, but still had five to six stools per day with visible blood in every bowel movement. Ex. 4 at 9. He now weighed 140 pounds—a 20-pound unintended weight loss since March 2016. *Id.* at 14. Dr. Kaur discussed with Petitioner and his mother the concerns for "active disease that is not controlled on his current therapy." *Id.* at 11. Another endoscopic evaluation with flexible sigmoidoscopy was planned. *Id.* A repeat endoscopy performed on October 6, 2016 showed "Mayo 2 colitis from rectum, 35 cm." and Mr. Cerrone was switched again to another new medication. Ex. 5 at 15.

From October 2016 to the present, Petitioner has continued to obtain treatment for his UC, which on some occasions presented acutely and required in-patient treatment. *See, e.g.*, Ex. 2 at 9–12; Ex. 5 at 12–13, 15 (October 2016 hospitalization). By November 2016, pancolitis[11] was observed, and Petitioner underwent a colectomy with a diverting ileostomy[12] on December 12, 2016. Ex. 5 at 1247, 1265–70, 2788, 2918–19. He required additional emergency or in-patient care in early 2017. Ex. 2 at 1; Ex. 5 at 3064–66, 3377–89. He has otherwise continued to follow up with his specialists and PCP for his UC. *See generally* Exhibit 69.

II. Witness Testimony and Expert Reports

A. Petitioner's Experts

1. *David Rosenstreich, M.D.* – Dr. Rosenstreich, a licensed clinician and immunologist (though not a gastroenterologist), prepared two written reports and an affidavit, and testified for Petitioner in support of the contention that the three vaccines he received (HPV, Flumist, and Hep. A) can cause UC, and did so to him. *See generally* Tr. at 6–143, 324–34. Report, dated September 12, 2018, filed as Ex. 8 (ECF No. 39-2) ("Rosenstreich First Rep."); Report, dated October 22, 2019, filed as Ex. 48 (ECF No. 63-2) ("Rosenstreich Second Rep."); Affidavit, dated July 15, 2020, filed as Ex. K (ECF No. 97-2) ("Rosenstreich Aff.").

Dr. Rosenstreich obtained his undergraduate degree from the City College of New York and his medical degree from New York University School of Medicine. *Curriculum Vitae,* filed as Exhibit 35 on September 13, 2018 (ECF No. 42-2) ("Rosenstreich CV") at 1. He is currently a Professor in the Departments of Medicine, Otolaryngology, and Microbiology/Immunology at the Albert Einstein College of Medicine. Tr. at 6; Rosenstreich CV at 1; Rosenstreich First Rep. at 1. He is also the Director of the Division of Allergy & Immunology in the Department of Medicine

[11] Pancolitis is defined as inflammation of the entire colon. *Pancolitis,* Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=36502&searchterm=pancolitis (last visited May 8, 2023).

[12] A colectomy is excision of a segment of the colon and ileostomy is establishment of a fistula through which the ileum discharges directly to the outside of the body. Stedman's, supra note 2 at 407, 946.

at the Albert Einstein College of Medicine and Montefiore Medical Center. Tr. at 6; Rosenstreich CV at 1; Rosenstreich First Rep. at 1.

Dr. Rosenstreich actively sees patients with vaccine-induced problems and performs differential diagnostic techniques. Tr. at 7. His clinical work does not focus on the care and treatment of GI patients, however, and he does not diagnose patients with UC or IBD. *Id.* at 103–04. He has also never provided a diagnosis where a vaccine or combination of vaccines was suspected to have caused UC. *Id.* at 133. Dr. Rosenstreich is board certified as an Internal Medicine specialist by the American Board of Internal Medicine and as an Allergy/Immunology specialist by the American Board of Allergy and Immunology. *Id.* at 6–7; Rosenstreich CV at 2; Rosenstreich Aff. at 1; Rosenstreich First Rep. at 1. He also has an additional qualification in Diagnostic Laboratory Immunology. Rosenstreich CV at 2; Rosenstreich Aff. at 1; Rosenstreich First Rep. at 1. Dr. Rosenstreich has published over 200 scientific papers in the field of allergy and immunology and has edited 4 books in the fields of clinical allergy and basic immunology. Tr. at 7; Rosenstreich First Rep. at 2. The focus of his publication and research work is not on reporting vaccine-related autoimmune problems, though he mentioned one recent paper specific to the COVID-19 mRNA vaccines. Tr. at 104–05.

Dr. Rosenstreich accepted Petitioner's UC diagnosis,[13] given Petitioner's colonoscopy findings and disease pathology. Tr. at 11–12. He defined UC to be an immunologically-mediated inflammatory disease[14] of the large intestine. *Id.* at 12–13, 16, 333; Rosenstreich First Rep. at 5; S. Friedman & R. Blumberg, *Harrison's Principles of Internal Medicine* 8 (McGraw-Hill Global Education Holdings 19th ed. 2015) ("Friedman"); R. Ungaro et al., *Ulcerative Colitis*, 389 Lancet 1756, 1756 (2017), filed as Ex. 10 (ECF No. 39-4) ("Ungaro"). In UC, immune tolerance[15] is broken and regulatory processes in the gut fail. Tr. at 62; Rosenstreich First Rep. at 5. In particular, gastrointestinal T cell lymphocytes[16] become immunologically activated, increase in number, and

[13] Although the experts agree on the diagnosis, they use UC and IBD interchangeably throughout their discussions.

[14] Dr. Rosenstreich differentiated autoimmune diseases from *immune-mediated* diseases. An autoimmune disease is where the antigen sparking an aberrant immune reaction is part of the patient's makeup (even if something else might trigger the antigen beforehand—like a vaccine), whereas an immune-mediated disease occurs due to the impact of an external agent. Tr. at 13–14; Ex. 38. UC, Dr. Rosenstreich explained, is *both* an autoimmune disease and immune-mediated disease; there are autoantibodies against epithelial cells, which are self antigens, and there is an immune reaction against external or commensal gut bacteria (external antigens). Tr. at 15–17; *see, e.g.*, Friedman at 4; Ungaro at 1757–59; I. Ordas et al., *Ulcerative Colitis*, 380 Nature 1606, 1607 (2012), filed as Ex. 12 (ECF No. 39-6). Respondent's experts agreed with Dr. Rosenstreich that UC is an inflammatory immune-mediated disease, even though they did not concede a vaccine can be causal of it *ab initio*. Tr. at 17–19.

[15] Immune tolerance is where the body does not recognize the antigen and thus does not have an immune response. Tr. at 61. Breaking immune tolerance means the gut bacteria is now exposed to the systemic immune system improperly. *Id.* at 66.

[16] The T cell lymphocytes are located in the lamina propria of the intestine underneath the epithelial cells. Tr. at 64. These cells monitor antigens that are in the gut and protect against infection. *Id.*

initiate an intense reaction against gut microbial constituents, with production of large amounts of inflammatory cytokines such as tumor necrosis factor. Tr. at 62; Rosenstreich First Rep. at 5. This produces UC's characteristic symptoms—blood in the stool and diarrhea, and in severe cases symptoms can also include incontinence, fatigue, increased frequency of bowel movements, and abdominal discomfort. Ungaro at 1759.

There is not one single understood trigger of UC. Rather, UC has various infectious and/or genetic etiologies, although for the majority of patients its etiology cannot be determined. Tr. at 20–24, 26, 58–59; Rosenstreich First Rep. at 5, 7–8; K. Gradel et al., *Increased Short and Long-Term Risk of Inflammatory Bowel Disease After Salmonella or Campylobacter Gastroenteritis*, 137 Gastroenterology 495, 495, 499–500 (2009), filed as Ex. 11 (ECF No. 39-5) ("Gradel") (finding particular genetic mutations increase the risk of developing IBD);[17] B. Khor et al., *Genetics and Pathogenesis of Inflammatory Bowel Disease*, 474 Nature 307 (2011), filed as Ex. 18 (ECF No. 40-3) ("Khor") (reviewing the genetics of IBD in this genome-wide association study and finding 200 different genes that could be associated in IBD patients, compared to patients without the disease). In addition, Dr. Rosenstreich maintained, specific environmental factors (e.g., smoking, antibiotics, vaccines, or infections) can in a susceptible host (meaning someone with likely, if unidentified, genetic propensities) come together to cumulatively/interactively disrupt immunologic homeostasis,[18] producing a chronic state of dysregulated inflammation common to IBD/UC. Tr. at 57–58, 118; Rosenstreich First Rep. at 5; Khor at 314–15.

Next, Dr. Rosenstreich sought to explain how the three vaccines Mr. Cerrone received could theoretically cause UC. Tr. at 28. By his own admission, he reached his opinion by reasoning "backwards" from UC's symptomatic presentation, characterized by colonic inflammation, to the vaccines. *Id.* at 76, 117–18. And he ultimately invoked the effects, or proposed impact, of the differing vaccines involved (one of which—Flumist—is administered nasally) at different stages of his theory, attempting to associate these sub-conceptions with what Petitioner's experience revealed.

First, Dr. Rosenstreich broadly referenced the mechanistic theory of molecular mimicry often invoked to explain the pathophysiologic process of an autoimmune disease, identifying it as the most likely explanation for chronic disease inflammation in this case. Rosenstreich First Rep. at 7; Rosenstreich Second Rep. at 5. In particular, he proposed that (in the context of the immune

[17] Also cited as Respondent's Exhibit AA.

[18] Dr. Rosenstreich defined immunological homeostasis to be the balance between immune stimulation and immune suppression. Tr. at 61. This is disrupted with an infection or vaccine when excessive stimulation sets up a negative feedback with immune regulation and suppresses the reaction that would otherwise shut down an autoimmune/aberrant process. *Id.*

stimulation[19] generally attributable to vaccination) some cross-reactivity of antibodies or T cells, due to vaccine antigens and "intestinal epithelial cell antigens" being similar—sequentially or structurally—to each other,[20] allowed gut bacteria to penetrate the intestinal mucosa, setting up a chronic immune-mediated reaction to the bacteria characteristic of UC. Tr. at 67, 75–76, 139–42, 325; Rosenstreich First Rep. at 5–7; Ungaro at 1758; I. Ordas et al., *Ulcerative Colitis*, 380 Nature 1606, 1608 (2012), filed as Ex. 12 (ECF No. 39-6).

The antigen-specific signal sufficient to spark cross-reactivity due to mimicry could have come from any of the three vaccines Petitioner received, Dr. Rosenstreich maintained. Tr. at 76, 139. However, he particularly focused on the possibility that the Gardasil vaccine contained proteins that could mimic intestinal brush-border proteins, noting that there are often "unexpected similarities" between viral proteins and relevant UC proteins. *Id.* at 77–78; Rosenstreich First Rep. at 7; Rosenstreich Second Rep. at 6; C. Natale et al., *Computer-Assisted Analysis of Molecular Mimicry Between Human Papillomavirus 16 E7 Oncoprotein and Human Protein Sequences*, 78 Immunology & Cell Biology 580, 580 (2000), filed as Ex. 21 (ECF No. 40-6) ("Natale"). Respondent's experts later disputed this possibility, observing the plain fact that intestinal proteins are not found in the HPV vaccine—including the specific HPV viral strain discussed in Natale—but Dr. Rosenstreich emphasized that he only raised the *possibility* of this occurring, and could not provide specifics to corroborate his speculation. Tr. at 77–79 ("[i]n this case, I have no idea what they are, but they can exist").

Alternatively, Dr. Rosenstreich offered an analogy to what is scientifically known about how a *Campylobacter jejuni* bacterial infection can result (via molecular mimicry) in the production of autoantibodies driving Guillain-Barré syndrome ("GBS"). Tr. at 72; Rosenstreich First Rep. at 7; N. Shahrizaila & N. Yuki, *Guillain-Barre Syndrome Animal Model: The First Proof of Molecular Mimicry in Human Autoimmune Disorder*, J. Biomedicine & Biotechnology 1–4 (2010), filed as Ex. 20 (ECF No. 40-5) ("Shahrizaila"). Though the host structure for target antigens would be different for GBS (the GM1 antigen, as opposed to the epithelial cells for UC), there is scientific support for the proposition that a *C. jejuni* infection results in the production of

[19] At each of the sites of vaccination (three in total here), the vaccine antigens would be taken up by antigen-presenting cells locally, where they probably migrated into the regional lymph nodes and stimulated activation of B cells, which produced antibodies and T cells. Tr. at 67–68. The antibodies and T cells then enter circulation in the body and return to the site of injection to cause a local reaction. *Id.* This ongoing stimulation creates memory T cells and memory B cells—which can also be cross-reactive if the antigen that underlies the B or T cells is a mimic of a self structure or amino acid sequence. *Id.*

[20] Molecular mimicry would occur during the immune system's adaptive response—a phase Dr. Rosenstreich differentiated from the initial, innate response. Tr. at 83–84. The innate immune reaction is the first line of immunologic defense—a nonspecific reaction to invading pathogens, in which immune cells rapidly, but generally, react to danger signals to start releasing cytokines and initiate an immune reaction. *Id.* The adaptive arm occurs thereafter, and features more specificity to the precise antigenic attackers. *Id.*

cross-reactive antibodies capable of causing myelin damage in GBS—and the same mechanism was plausible herein. Tr. at 73; Rosenstreich First Rep. at 7; Shahrizaila at 2–4.

In addition to molecular mimicry, Dr. Rosenstreich opined that the three vaccines Petitioner had received also probably induced the activation of other immune cells through less immunologically-specific mechanisms. Some, he proposed, might be attributable to the alum adjuvant included in some of the vaccines at issue.[21] Tr. at 82–83; Rosenstreich First Rep. at 7. Such adjuvants increase vaccine immunogenicity because they stimulate cells like macrophages, which then releases cytokines like interleukin 1 that augment immune reactions. Tr. at 83. Without them, the vaccine antigens alone often will not stimulate a very powerful response sufficient to encourage the intended response. *Id*.[22] In addition, an aberrant immune reaction could occur as a result of polyclonal activation and or bystander activation.[23] *Id.* at 81; Rosenstreich First Rep. at 7. Less specific immune cells, located in the lamina propria of the gut, could be stimulated by an ongoing intense immunologic inflammatory context, becoming activated and producing cytokines that would only further the inflammatory reaction. Tr. at 81–82.

To support the theory, Dr. Rosenstreich discussed or referenced several different items of medical literature. Tr. at 29. First, he considered the vaccine package inserts, starting with Gardasil. This package insert revealed that the vaccine's manufacturers had looked at the incidence of IBD in patients in a vaccinated group versus control group. *Id.* at 30–31, 126–28; Gardasil Package Insert, filed as Ex. 13 on Sept. 12, 2018 (ECF No. 39-7) ("Gardasil Package Insert"), at 8–9.[24] Although Dr. Rosenstreich admitted that the HPV vaccine trials found no difference overall in the IBD incidence for vaccine recipients compared to patients who had received an alum control, the fact that Petitioner had at the same time *also* received Flumist—a live attenuated influenza vaccine, or "LAIV"—was a significant confounding factor, since suggested it would cause "different degrees of immune stimulation and immune dysregulation." Tr. at 30–31.

On cross examination, Dr. Rosenstreich was confronted with the fact that some clinical trial findings disclosed in the Gardasil Package Insert were *inconsistent* with vaccine causation.

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[21] The Flumist vaccine does not contain an adjuvant. *D'Tiole*, 2016 WL 7664475, at *9.

[22] *Johnson v. Sec'y of Health & Hum. Servs.*, No. 14-254V, 2018 WL 2051760, at *10 (Fed. Cl. Spec. Mstr. Mar. 23, 2018). (explaining the immunologic function of the alum adjuvant).

[23] "Bystander activation occurs when immune system cells that were previously suppressed, or anergic, are broken down by an existing/ongoing immune response to infection (or an autoimmune response to vaccination), causing immune tolerance created by those cells to similarly be destroyed and thereby allowing the dysregulation of the immune response to continue or expand." *Lozano v. Sec'y of Health & Hum. Servs.*, No. 15-369V, 2017 WL 3811124, at *4 (Fed. Cl. Spec. Mstr. Aug. 4, 2017), *mot. for review den'd,* 958 F.3d 1363 (Fed. Cir. 2020), *aff'd,* 958 F.3d 1363 (Fed. Cir. 2020).

[24] The Gardasil Package Insert was filed by Petitioner twice (as Exhibit 13 and 45), and also filed by Respondent as Exhibit JJ, Tab 2.

Tr. at 126-29. In particular, for a subgroup of the trial sample (specifically, 9 to 26 year old boys, which would have included Petitioner, comparing more than three thousand vaccinated individuals versus approximately 2,300 who received an alum or saline placebo), not only was there no increased incidence for IBD seen in the vaccinated population, but the incidence for the vaccinated group was lower. *Id.* at 128; Gardasil Package Insert at 9 (Table 10). Dr. Rosenstreich questioned the reliability of these results, however, because some of the control group received an alum adjuvant alone, which was concerning to him as alum could (in theory) cause an aberrant immune response. Tr. at 128; Rosenstreich First Rep. at 2, 9; G.P. de Chambrun et al., *Aluminum Enhances Inflammation and Decreases Mucosal Healing in Experimental Colitis in Mice*, 7 Mucosal Immunology 589, 589 (2014), filed as Ex. 49 (ECF No. 63-3) ("Chambrun I").

Dr. Rosenstreich went on to address the package inserts for the two other vaccines. The Flumist Package Insert noted that because that vaccine is a LAIV formulation, it functions through introduction of weakened live viral particles, causing different degrees of immune stimulation and dysregulation. Tr. at 32; Rosenstreich First Rep. at 6; Flumist Quadrivalent Package Insert, filed as Ex. 14 on Sept. 12, 2018 (ECF No. 39-8) ("Flumist Package Insert"), at 12–13. Thus, the response to it would be more akin to the impact of a wild virus infection, with the attendant dangers. Flumist Package Insert at 12. And the Hep. A Package Insert revealed that it included (like the HPV vaccine) an alum adjuvant—meaning that Petitioner had received a "double dose" of alum at the time he was vaccinated (and thus a greater risk of an adverse response due to excessive inflammation). Tr. at 33; Rosenstreich First Rep. at 6, 9; Rosenstreich Second Rep. at 2. HAVRIX Package Insert, filed as Ex. 15 on Sept. 12, 2018 (ECF No. 39-9) ("Hep. A Package Insert"), at 9. While the Flumist and Hep. A package inserts did not reveal any concern that IBD was a quantifiable side effect of those vaccines, they also did not disclosure pre-release testing relevant to that question. Tr. at 129. And there was no evidence that any studies about the effects of receiving all three vaccines at one time had ever been conducted. *Id.* at 330; Rosenstreich First Rep. at 6, 9; Rosenstreich Second Rep. at 8.

Second, Dr. Rosenstreich discussed a number of case reports that he deemed supportive of a causal relationship between the vaccines Petitioner received and his UC. Tr. at 33–34. He acknowledged that case reports lack the same scientific evidentiary value as full-scale epidemiologic studies, but deemed them nevertheless to be reliable "signals" to the scientific community of a potential vaccine-UC relationship worthy of further consideration. *Id.* at 46–47, 55, 326. Dr. Rosenstreich later admitted, however, that if case reports deserved weight even though they amount to an "n-of-one" study (a one-person sample), then larger studies involving bigger sample populations could not simply be rejected as incapable of detecting the rare event of a vaccine injury. *Id.* at 138.

In one case report, pancolitis (an infection of the entire colon) was observed after administration of a flu vaccine to a 70-year-old woman with a history of diabetes. Tr. at 36–37,

130; L. Luca et al., *Pancolitis After Influenza Vaccination*, 59 Allergy 362, 367 (2004), filed as Ex. 27 (ECF No. 41-3) ("Luca"); Rosenstreich First Rep. at 7. The Luca patient had received at least six prior flu vaccines, developing onset of GI symptoms within hours of receipt of an additional dose. Tr. at 130; Rosenstreich Second Rep. at 3; Luca at 367. Dr. Rosenstreich admitted, however, that Mr. Cerrone's flu vaccine had been administered in a different manner—and that his onset was not nearly as sudden. Tr. at 131. In another case report, a patient developed panniculitis[25] after a flu vaccine that he had previously tolerated, indicating a delayed hypersensitivity reaction.[26] *Id.* at 37–38; C. Pauwels et al., *Cytophagic Histiocytic Panniculitis After HlNl Vaccination: A Case Report and Review of the Cutaneous Side Effects of Influenza Vaccines*, Dermatology 217, 217–19 (2011), filed as Ex. 28 (ECF No. 41-4) ("Pauwels").[27] Pauwels also referenced 17 cases of systemic vasculitis, an immune-mediated inflammatory reaction, in association with the flu vaccine. Tr. at 38–39; Pauwels at 218. Dr. Rosenstreich deemed such evidence to establish an association between the flu vaccine and different, but comparable, forms of immune-mediated inflammatory reactions. Tr. at 39.

Third, Dr. Rosenstreich referenced VAERS reports[28] establishing an association between vaccines and UC. He was able to identify 75 specific reports of colitis[29] associated with the administration of either the Gardasil, flu, or Hep. A vaccines. Tr. at 40, 42, 135; Rosenstreich First Rep. at 8; Rosenstreich Second Rep. at 5. He also found five VAERS reports associating colitis with the Gardasil vaccine alone. Tr. at 42–43.[30] In testimony he represented that there were other VAERS reports of patients who had received multiple vaccines at the same time and then experienced UC, but none were filed.[31] *Id.* at 43–45. As with case reports, Dr. Rosenstreich admitted that VAERS reports were not capable of establishing causality (especially in the absence

[25] Panniculitis is an inflammatory reaction of subcutaneous fat. *Panniculitis,* Dorland's Medical Dictionary Online, https://www.dorlandsonline.com/dorland/definition?id=36598&searchterm=panniculitis (last visited May 8, 2023).

[26] Dr. Rosenstreich explained that immediate reactions are those mediated by antibodies and immunoglobulins, similar to an allergic reaction whereas delayed reactions are skin or pathological reactions that take several days to develop, which are usually mediated by activated T cells. Tr. at 38.

[27] Pauwels was filed by Petitioner twice, as Exhibit 28 and Exhibit 42.

[28] The Vaccine Adverse Event Reporting System ("VAERS") is a database maintained by the Center for Disease Control ("CDC") to compile information from the public about reactions to immunizations listed on the Vaccine Injury Table, Section 14(a).

[29] Colitis is different from UC, Dr. Rosenstreich acknowledged, since it was more likely to be time-limited in overall course. Tr. at 125.

[30] These are set forth in Ex. 29, which appears to be a self-made document referencing the five VAERS reports with a short write-up. The exhibit has no other citations, however, so the accuracy of its contents cannot be verified simply from its face.

[31] During the hearing, Respondent noted that proof of these instances had not been filed. Tr. at 44. I informed Petitioner's counsel they could file such evidence after the hearing. Tr. at 45. This did not occur.

of information about background rates of disease instances or total vaccines administered in a specific population group), but he deemed them nevertheless of value in suggesting causation. *Id.* at 41, 56, 124–26, 326–27; Rosenstreich Second Rep. at 8–9. At the same time, he acknowledged reliability problems with such data; in particular, an adverse event report is not verified before its creation, meaning the underlying truth of a VAERS report cannot be ascertained merely from its *existence*. Tr. at 45–46, 124–25, 136–38.

Besides these categories of evidence, Dr. Rosenstreich highlighted a meta-analysis study[32] filed by Respondent, focusing on the occurrence of IBD after receipt of a specific live vaccine (poliomyelitis). Tr. at 53; G.P. de Chambrun et al., *Vaccination and Risk for Developing Inflammatory Bowel Disease: A Meta-Analysis of Case–Control and Cohort Studies*, 13 Clinical Gastroenterology & Hepatology 1405, 1405 (2015), filed as Ex. Y (ECF No. 53-11) ("Chambrun II"); Rosenstreich Second Rep. at 9. Chambrun II sought to combine the findings from eight case control studies plus three cohort studies (although none involved the HPV or Hep. A vaccines). Tr. at 53; Chambrun II at 1405, 1410. It proposed that there was potential higher risk of IBD after receiving multiple vaccines at the same time. Chambrun II at 1413. Dr. Rosenstreich also maintained that live vaccines might add to this risk, although only the Flumist vaccine contained live viral components. Tr. at 54–55. Importantly, however, Chambrun II's *overall* conclusion was that the childhood vaccines it considered were *not likely* to increase the risk of IBD—and to the extent receiving multiple vaccines at one time was itself a risk factor, Chambrun II's authors deemed that partially attributable to the fact that many of the studies incorporated into the meta-analysis had not focused on single vaccine causality. Chambrun II at 1412–13, 1414.

Dr. Rosenstreich disputed the value of other literature offered by Respondent's experts—in particular articles that purportedly found no increased risk of UC after receipt of the HPV vaccine. Tr. at 47–48; J. Skufca et al., *The Association of Adverse Events With Bivalent Human Papilloma Virus Vaccination: A Nationwide Register-Based Cohort Study in Finland*, 36 Vaccine 5926, 5926 (2018), filed as Ex. CC (ECF No. 53-15) (showing no significant increased risk of UC in 11 to 13-year-old girls with the Gardasil vaccine) ("Skufca"). In his view, studies like Skufca were ultimately not sensitive enough to detect a rare occasion like a vaccine injury, especially since genetics and previous medical history can make an individual unusually susceptible to an adverse event. Tr. at 48. He also criticized studies that in essence confirmed the safety of certain of the vaccines at issue. *See, e.g.*, M-G. Angelo et al., *Post-Licensure Safety Surveillance for Human Papillomavirus-16/18-AS04-Adjuvanted Vaccine: More Than 4 Years of Experience*, 23 Pharmacoepidemiology & Drug Safety 456, 463 (2014), filed as Ex. R (ECF No. 53-4); ("[c]linical studies conducted during vaccine clinical development are essential, but usually too limited in size

[32] A meta-analysis is defined as "a method for systematically combining pertinent qualitative and quantitative study data from several selected studies to develop a single conclusion that has greater statistical power." Himmelfarb Health Sciences Library, *Meta-Analysis*, https://himmelfarb.gwu.edu/tutorials/studydesign101/metaanalyses.cfm (last visited May 8, 2023).

to detect rare [adverse events]. . . .") ("Angelo"). Had such studies established a risk, the vaccine would not have been approved in the first place—but that did not mean that a vaccine could never be causal of injury in rare circumstances. Tr. at 48.

Dr. Rosenstreich next focused on Mr. Cerrone's medical history, arguing that his experiences were consistent with the causation theory. Tr. at 9, 57; Rosenstreich First Rep. at 8–9. As a general matter, Dr. Rosenstreich felt it likely that Petitioner was a genetically-susceptible host. Khor, he noted, had identified 200 potential genes that may drive IBD—with only three or four needed for disease to occur. Tr. at 58, 60; Rosenstreich First Rep. at 5, 7, 9; Rosenstreich Second Rep. at 2–3; Khor at 315; Ungaro at 1756. He acknowledged, however, that there was no testing evidence from this case that would establish whether Petitioner actually possessed any risk factors for IBD. Tr. at 118–19, 121; Rosenstreich First Rep. at 2; Ex. 72 at 13. There was also no notation in the records that he had a family history of IBD (although Petitioner's mother's status as an adopted child greatly diminished the possibility of obtaining such evidence on a family basis). Tr. at 118–19. In effect (and as admitted elsewhere), Dr. Rosenstreich was reasoning backward from the *fact* of injury to his conclusion of genetic susceptibility (an especially problematic approach given that unvaccinated patients develop IBD, while the majority of patients that receive vaccines do not). *Id.* at 120.

It was also possible, Dr. Rosenstreich opined, that other environmental factors had contributed to Petitioner's development of UC. For example, Mr. Cerrone may have developed a clinically-inapparent viral infection such as cytomegalovirus or enterovirus, which could have altered his intestinal microbial constituents and magnified the aberrant response to vaccination. Tr. at 121; Rosenstreich First Rep. at 9. However, Dr. Rosenstreich could not identify any record evidence in support of this contention. Tr. at 122. Indeed, part of Petitioner's workup for his UC involved an analysis of his stool; infectious agents were checked, but none of the usual stool pathogens were found.[33] *Id*.

Dr. Rosenstreich derived additional evidence in support of his opinion from witness statements. In particular, Petitioner had alleged in his affidavit an increased loss of stamina a few weeks after his vaccination but before the onset of his clinical GI symptoms (bloody stools on December 27th). Cerrone Aff. II at 2. Stability was also an issue, according to Petitioner's affidavit, and Petitioner reported falling during a pickup football game on November 3, 2015, fracturing his wrist. Tr. at 107; Cerrone Aff. II at 2. Dr. Rosenstreich deemed these incidents significant, considering them manifestations of ongoing systemic inflammation even before Petitioner's more obvious GI-associated symptoms. Tr. at 94–96, 105, 107, 114–15; Rosenstreich Second Rep. at 1, 9.

[33] Dr. Rosenstreich also could not opine on other, more direct potential factors that might have impacted the development of UC, such as Mr. Cerrone's diet or the quality of his drinking water. Tr. at 121.

At the same time, however (and as Dr. Rosenstreich admitted), these symptoms[34] of loss of stamina and lack of stability were not mentioned in any of the contemporaneous medical records. Tr. at 106–07. Indeed, from October 7, 2015 (date of Petitioner's vaccinations) until January 2016, there are in the record *no* primary care appointment or medical encounters reporting malaise, stability, or stamina issues. *Id.* at 107–08. Petitioner had previously reported instances of fatigue prior to vaccination (for example, on December 17, 2014), suggesting he would have done so later if such concerns existed. *Id.* at 112–13; Ex. 1 at 15. Nevertheless, Dr. Rosenstreich still opined the references to post-vaccination symptoms (again reiterating fatigue) were significant. Tr. at 113; Rosenstreich Second Rep. at 1, 8. K. Ozawa et al., *Suspected Adverse Effects After Human Papillomavirus Vaccination: A Temporal Relationship Between Vaccine Administration and the Appearance of Symptoms in Japan*, 40 Drug Safety 1219, 1227 (2017), filed as Ex. 31 (ECF No. 41-7) ("Ozawa") (discussing general fatigue, along with headache, limb pain, and weakness as possible Gardasil vaccine-related adverse effects).

Petitioner's purported worsening of symptoms after the receipt of his second HPV vaccine dose on February 10, 2016, was also evidence supporting causation, Dr. Rosenstreich maintained. Tr. at 96–97, 328; Rosenstreich Second Rep. at 8. He maintained that the immune response after a second exposure to vaccination is inherently faster/more robust. Tr. at 97–98, 116; Rosenstreich First Rep. at 6, 10; Rosenstreich Second Rep. at 8; C-A. Siergrist, *Vaccine Immunology*, Vaccines 17, 23 (2008), filed as Ex. 77 (ECF No. 90-3) ("Siergrist"). However, Dr. Rosenstreich struggled to comport this alleged worsening with the *lack* of evidence of a reaction after Petitioner received a third Gardasil dose in June 2016 (by which time Petitioner was receiving treatment for his UC).[35] Tr. at 116, 328. Dr. Rosenstreich also acknowledged that Petitioner's treating physicians had not expressed concern about the role of any vaccines in causing his UC, and in fact *recommended* he received vaccinations even after his UC diagnosis. *Id.* at 117.

Finally, Dr. Rosenstreich proposed that the timeframe for Petitioner's symptoms onset was medically acceptable. Tr. at 334; Rosenstreich First Rep. at 8. To do so, he began by setting forth his understanding of the progression of UC. The intestinal epithelial damage associated with UC's symptoms would begin, he maintained, after sufficient activated T cells are present in the gut. Tr. at 92–93; Rosenstreich First Rep. at 8. And it would take approximately 30 days post-insult to develop inflammation, and for the body to reach peak antibody response. Tr. at 93, 140–42;

[34] Dr. Rosenstreich continuously emphasized Petitioner's alleged fatigue as well, although fatigue was not actually mentioned in Petitioner's affidavit as a symptom in November of 2015 (in comparison to complaints of stability or stamina problems). Cerrone Aff. II at 2. Low energy level and decreased strength, by contrast, were, though the timeline of those symptoms is unclear. Cerrone Aff. I at 5.

[35] At most, Dr. Rosenstreich maintained that it was hard to discern the impact of this third HPV vaccine dose, since by this time Petitioner was both quite ill and receiving treatment—factors that might have obscured what the reaction was. Tr. at 329; Rosenstreich Second Rep. at 8.

Siergrist at 23. After that immune response is at its maximum, there would be an aberrant process of cell death and regrowth in the gut, progressing to the point where the immune system destroys enough cells to cause holes in the gut because the cells cannot regrow fast enough to counter existing bacteria. Tr. at 93; Rosenstreich First Rep. at 8.

An influx of such commensal bacteria would take a while to peak as well before their damage potentiality would be realized. Tr. at 93–94; Siergrist at 23. Dr. Rosenstreich then proposed another 20 days would likely pass before there is full-blown destruction of the gut epithelium and visible bleeding. Tr. at 94. Throughout this 80-day process, a patient might be experiencing inflammation of a sub-acute nature. *Id.* at 90, 94. (Of course, Dr. Rosenstreich had also opined that the fatigue had clinically manifested in November 2015 was part of the vaccine reaction process leading to the more obvious and specific UC manifestations, although the record reveals no other instances of obvious inflammation from the date of vaccination until late December 2015 at the earliest).

Here, Petitioner had been vaccinated in October 2015, and approximately 81 days later experienced bloody stools on or around December 27th.[36] This, Dr. Rosenstreich proposed, was an indication that Petitioner was experiencing colitis-associated inflammation. Tr. at 27, 86, 333; Rosenstreich First Rep. at 8. There was subsequently an unbroken sequence between the bleeding Petitioner reports first experiencing on December 27th and his ultimate diagnosis a few months later. Tr. at 86–88; Rosenstreich First Rep. at 8.

Such a timeframe was consistent with Petitioner's literature, Dr. Rosenstreich contended. Gradel, for example, had observed a delay between the time of recovery from patients' IBD-initiating infection (during which time they were presumably asymptomatic—although some of the studied sample had been hospitalized) and when they began to experience IBD symptoms, with the temporal gap peaking at around four to five months.[37] Tr. at 25–27, 89; Rosenstreich Second Rep. at 4; Gradel at 498; Angelo at 463–64. Further support for the timeframe question was found in a study specific to the flu-GBS association. *See* L. Schonberger et al., *Guillain-Barré Syndrome Following Vaccination in the National Influenza Immunization Program, United States, 1976–1977,* 110 Am. J. Epidemiol. 105, 112 (1979), filed as Ex. 16 (ECF No. 39-10) ("Schonberger"). Although Schonberger documented an increased risk for GBS concentrated primarily within the five-week period after vaccination, some cases occurred as much as nine or ten weeks after. Tr. at 90–91; Schonberger at 105, 112 Figure 4 (determining that from week ten the relative risks no

[36] Though this first instance of bloody stools did not lead to Petitioner visiting a physician, he reported this event in his affidavit. Tr. at 87; Cerrone Aff. II at 1.

[37] Gradel also found that a prior gastroenteritis infection can cause IBD with up to a one-year latency period. Tr. at 122; Gradel at 499. Dr. Rosenstreich did not give an outer limit on what he would consider a medically acceptable timeframe for vaccine-caused UC, however, maintaining that it would have to be evaluated on a case-by-case basis in the end. Tr. at 122–23.

longer remained significantly different, but observing some cases after). In fact, Schonberger observed cases as late as 12 weeks (84 days) after vaccination. Tr. at 332, 334; Rosenstreich Second Rep. at 4; Schonberger at 112–13. This was also consistent with findings in Respondent's literature. Tr. at 49–51; Angelo at 460 (noting that for GI disorders, the authors found four cases beginning at five weeks after vaccination, as well as two cases around 17 weeks and one case around 36 weeks).

2. *John J. Santoro, D.O.* – Dr. Santoro, a gastrointestinal physician, prepared one written report and an affidavit (but did not testify at trial)[38] for Petitioner in support of the contention that the three vaccines Petitioner received can cause UC, and did so in this case.[39] *See generally* Report, dated August 16, 2019, filed as Ex. 36 (ECF No. 59-2) ("Santoro Rep."); Affidavit, dated July 15, 2020, filed as Ex. 81 (ECF No. 90-7) ("Santoro Aff."). Dr. Santoro's report was not discussed at length in Petitioner's pre- or post-hearing briefs, and for the most part the opinion he offered was duplicative of Dr. Rosenstreich's reports and testimony. But because it remains in evidence, I will address his points briefly.

Dr. Santoro reiterated the dates and evidence provided in the medical records, and provided background comments on IBD consistent with Dr. Rosenstreich's reports and testimony. Santoro Rep. at 3–8. Dr. Santoro also suggested a theory of molecular mimicry due to the presence of serum and mucosal autoantibodies against intestinal epithelial cells (described in further detail by Petitioner's other expert. *Id.* at 9–10. Dr. Santoro opined that one of Petitioner's vaccines caused his UC because there were no other antecedent or concurrent events that could explain his symptoms, and there was no evidence in his medical records that he suffered from IBD prior to his vaccinations. *Id.* at 10–11. And though there is no definite answer in the medical literature for an appropriate temporal relationship between IBD and the vaccines, Dr. Santoro found from his experience that patients might have several months of indolent symptoms before a firm diagnosis can be made, given the waxing and waning nature of the disease—thus suggesting the timeframe for Petitioner's onset was acceptable. *Id.*; D-W. Lee, et al., *Diagnostic Delay in Inflammatory*

[38] Dr. Santoro is deceased. He obtained his undergraduate degree from the LaSalle College in Philadelphia, PA and graduated with his doctorate of osteopathic medicine from the Philadelphia College of Osteopathic Medicine. *Curriculum Vitae,* filed as Exhibit 47 on August 16, 2019 (ECF No. 60-4) ("Santoro CV") at 1. He then completed a rotating internship in internal medicine at the John F. Kennedy Memorial Hospital, and a residency in internal medicine and fellowship in gastroenterology at the University of Medicine & Dentistry in Stratford, NJ. Santoro CV at 1. He was a Medical Director of clinical research at Atlantic Gastroenterology Associates and the Co-Director of the groups Inflammatory Bowel Disease Center. Santoro CV at 3; Santoro Rep. at 2. He also held a clinical Associate Professorship at Rowan University School of Osteopathic Medicine. Santoro CV at 3; Santoro Rep. at 2. He cared for more than 300,000 patients and specialized in diagnosing, treating, and researching various gastrointestinal diseases like IBD. Santoro Rep. at 2. He was board certified in internal medicine and gastroenterology by the American Osteopathic Board of Internal Medicine. Santoro CV at 2; Santoro Aff. at 1.

[39] Dr. Romberg argued that Dr. Santoro was not qualified to opine on the molecular underpinnings of inflammatory diseases. Tr. at 262–63; Romberg Second Rep. at 2.

Bowel Disease Increases the Risk of Intestinal Surgery, 23 World J. Gastroenterology 6474, 6478–80 (2017), filed as Ex. 46 (ECF No. 60-3).

B. Respondent's Experts

1. *Chris Liacouras, M.D.* – Dr. Liacouras, a practicing pediatric gastroenterologist, prepared two written reports and an affidavit for Respondent, and also testified for Respondent in support of the contention that Petitioner's UC was not vaccine-associated. *See generally* Tr. at 146–211. Report, dated May, 31, 2019, filed as Ex. O (ECF No. 53-1) ("Liacouras First Rep."); Report, dated January 21, 2020, filed as Ex. HH (ECF No. 71-1) ("Liacouras Second Rep."); Affidavit, dated December 11, 2020, filed as Ex. LL (ECF No. 97-2) ("Liacouras Aff.").

Dr. Liacouras received his undergraduate degree from Johns Hopkins University and his medical degree from Harvard University. Tr. at 146; *Curriculum Vitae,* filed as Exhibit NN on May 19, 2022 (ECF No. 120-1) ("Liacouras CV") at 1. He is currently a Professor of Pediatrics at the Children's Hospital of Philadelphia ("CHOP"), University of Pennsylvania School of Medicine. Tr. at 146; Liacouras CV at 2. He also currently holds hospital positions as a co-director at the Center for Pediatric Eosinophilic Disorders, a director and medical director at CHOP Exton Specialty Center, and a pediatric gastroenterologist at the Children's Hospital of Philadelphia at three satellite locations. Liacouras CV at 3. He has over 30 years of clinical and endoscopic experience treating children and adolescents with gastrointestinal, liver and dietary disorders, including more than 2,500 patients with inflammatory bowel. Liacouras Aff. at 1. Dr. Liacouras sees approximately two to 3,000 patients a year in both an inpatient and outpatient setting, with approximately 85 percent of his work devoted to such patient care. Tr. at 147. He is licensed to practice medicine in Pennsylvania and is board certified in pediatric gastroenterology, hepatology, and nutrition by the American Board of Pediatrics. Liacouras Aff. at 1. He has approximately 80-90 peer-reviewed articles and has helped write or organize several textbooks in pediatric gastroenterology. Tr. at 148–49.

Dr. Liacouras accepted that Petitioner most likely suffered from UC. He defined UC as a chronic, ulcerative condition of the colon (often grouped in the same category as IBD because they are treated similarly).[40] Tr. at 149–51, 154; Liacouras First Rep. at 4. UC is considered an autoimmune or immune-mediated disease but its etiology is largely unknown, with genetic, environmental, autoimmune and bacterial factors all possible explanations. Tr. at 150, 188–90, 204, 208; Liacouras First Rep. at 3, 6, 8; Liacouras Second Rep. at 4. It causes severe irritation of the mucosa and submucosa of the colon. Tr. at 149–50. UC occurs somewhere around one to five patients for every 10,000 patients—common enough that the diagnosis occurs frequently in Dr.

[40] Colitis alone, by contrast, just means inflammation of the colon, and is most commonly an acute, short lived, self-resolving condition, whereas UC is severe and chronic. Tr. at 150–51; Liacouras First Rep. at 7.

Liacouras's practice. *Id.* at 152. In pediatric patients, it presents with some degree of rectal bleeding accompanied by diarrhea and abdominal pain. *Id.* at 151; Liacouras First Rep. at 4; Liacouras Second Rep. at 2.

The bleeding associated with UC can be severe enough that patients develop anemia or weight loss, which can lead to other systemic features like fatigue or lethargy. Tr. at 152; Liacouras First Rep. at 4–5. The average age of onset is around 10-12 years old, but patients can present with UC at any age. Tr. at 152–53; L. Higuchi & A. Bousvaros, *Clinical Presentation and Diagnosis of Inflammatory Bowel Disease in Children*, UpToDate 1, 2–3 (2020), filed as Ex. LL, Tab 1 (ECF No. 97-3). Treatment ranges from oral medicines to surgery, relying on biologic therapies in severe cases. Tr. at 153–54; Liacouras First Rep. at 3–4.

Mr. Cerrone's disease progression, Dr. Liacouras contended, helped establish why his vaccinations were likely unrelated to his UC. In the month following vaccination, Petitioner was seen by medical providers in the ER twice.[41] Tr. at 155–56; Liacouras First Rep. at 2; Ex. 2 at 30 (November 10, 2015 ER visit for laceration of his lip), at 34 (November 3, 2015 ER visit for left wrist injury). Yet at these times he did not mention or demonstrate any GI symptoms (in fact, his GI evaluations were normal). Tr. at 156–58; Liacouras First Rep. at 1, 2, 6; Ex. 1 at 13; Ex. 2 at 30, 34. Indeed, even later records (after Petitioner's purported onset, moreover) revealed few issues relevant to UC. Thus, on February 10, 2016, Petitioner had a primary care visit for a sore throat, cough, and congestion, but his examinations revealed no abnormal abdominal findings nor evidence of UC symptoms. Tr. at 158–59; Ex. 1 at 12. He also now received his second dose of HPV vaccine, with no evidence of any reaction. Tr. at 159; Liacouras First Rep. at 2; Ex. 1 at 12.

The first record that formally memorialized an instance of lower gastrointestinal bleeding was from February 13, 2016. Tr. at 159; Liacouras First Rep. at 2–3; Ex. 2 at 20, 25–26. But other than general GI complaints (discussed as blood in his stool for the last three weeks), Petitioner displayed no evidence of dizziness, weakness, or fatigue, and his abdominal exam was otherwise normal. Tr. at 159; Liacouras First Rep. at 2; Ex. 2 at 20, 25–26. Only by mid-March 2016 was there evidence from testing of significant issues fully reflective of UC (thus suggesting the severity of his problem had progressed considerably over this timeframe). Tr. at 161–62; Ex. 3 at 11. By March 2016, Petitioner was 158 pounds, and he dropped more weight in the ensuing months. Tr. at 162–63; Ex. 3 at 6; Ex. 5 at 14. But even after significant treatment for UC, Petitioner was still allowed to receive a third HPV vaccine dose. Liacouras First Rep. at 2; Ex. 1 at 4, 8.

[41] In fact, Petitioner was evaluated no less than *four times* between the date of his first Gardasil vaccine dose on October 7, 2015, and the first reported visit for abdominal complaints on February 13, 2016. Liacouras First Rep. at 5.

Given Petitioner's medical history and disease progression (as best evidenced by the record),[42] Dr. Liacouras deemed it unlikely that the vaccines Petitioner received (alone or in concert) had caused his UC, since there was no real evidence of any disease process until much longer after vaccination. Tr. at 179, 208; Liacouras First Rep. at 3, 7–8; Liacouras Second Rep. at 3. There was virtually no medical record of anything GI-associated from October 2015 to the end of January/early February 2016. At best, Petitioner *alleged* that he had experienced decreased stamina and loss of stability in November 2015, but Dr. Liacouras characterized such symptoms as associated with UC *only* when presenting with (or in the wake of) significant anemia—which the record did not reveal to exist in the fall of 2015. Tr. at 167–68; Liacouras First Rep. at 8. And in Dr. Liacouras's view, there were plenty of other causes of fatigue or loss of stamina for teenagers, and Petitioner had previously reported fatigue prior to vaccination (allowing the question of why he had not done so formally in November 2015). Tr. at 168; Ex. 1 at 15. In addition, none of Petitioner's treaters had counseled against his receipt of additional HPV vaccine doses despite his UC diagnosis. Tr. at 177–79; Ex. 3 at 7 (documenting as a preventative measure that Petitioner should receive the pneumococcal vaccine every five years and the annual flu vaccine); Ex. 5 at 1135 (talking about ordering Hep. B and varicella vaccines as per the GI recommendations). In fact, patients with active IBD are routinely vaccinated. Liacouras First Rep. at 5. And Dr. Liacouras could not find record evidence that Petitioner's second or third HPV doses had caused a worsening of UC symptoms (although the record does clearly establish general worsening between February and March 2016). Tr. at 169–70.

Dr. Liacouras only briefly discussed the alleged causal association (or lack thereof) between the vaccines and UC, leaving the immunologic issues such matters raised to Respondent's other expert, Dr. Romberg. Tr. at 171, 191–93, 196, 200–01, 209. He indicated, however, that he had been unable to locate in his own literature searches evidence associating vaccines with UC, adding that in fact the *contrary* seemed to be better supported. *Id.* at 173–76, 203–04; Liacouras First Rep. at 5, 7; Liacouras Second Rep. at 2, 4; Skufca at 5926 (evaluating several hundred thousand individuals and finding no significant evidence indicating there were any adverse effects related to the development of UC or fatigue after receipt of the HPV vaccine); S. Dezfoli & G. Melmed, *Vaccination Issues in Patients with Inflammatory Bowel Disease Receiving Immunosuppression*, 8 Gastroenterology & Hepatology 504, 507–08 (2012), filed as Ex. Z (ECF No. 53-12) ("Dezfoli") (concluding that there was no increased risk associated abnormalities for IBD after the Hep. A or HPV vaccines); R. Davis et al., *Measles-Mumps-Rubella and Other Measles-Containing Vaccines do not Increase the Risk of Inflammatory Bowel Disease*, 155 Archives Pediatrics & Adolescent Med. 354, 354 (2001), filed as Ex. T (ECF No. 53-6) ("[c]hildren vaccinated with MMR who were older than 18 months were at significantly *decreased*

[42] In Dr. Liacouras's view, Dr. Rosenstreich relied too much on Petitioner's affidavits and amended petition *rather than* the contemporaneous medical records. Liacouras First Rep. at 6.

risk for IBD")(emphasis added); Chambrun II at 1414 ("results of this meta-analysis do not support a role of childhood immunization or H1N1 vaccination in the development of IBD").

Dr. Liacouras' opinion also included consideration of Petitioner's onset and its relationship to causation. He noted that symptoms of UC typically progress between a few weeks to up to two months after what might be considered an instigating trigger (like an infection). Liacouras First Rep. at 4.[43] In his view, the records best supported the conclusion that Petitioner's UC symptoms began around mid to late January 2016—or about three to four months after his October 7, 2015 vaccinations. Tr. at 169; Liacouras First Rep. at 6. Dr. Liacouras acknowledged that Petitioner alleged his symptoms began earlier, in late December 2015 (even if they were not formally reported or treated at that time), but in his opinion even such an onset would not make vaccine causation more likely. Tr. at 169, 209; Cerrone Aff. II at 1.

Dr. Liacouras also disputed the evidence offered by Dr. Rosenstreich for the contention that UC can occur anywhere between five weeks to almost a year after instigation in patients. Angelo, for example (which Respondent filed but Dr. Rosenstreich attacked) did not look at this issue. Tr. at 175; Angelo at 460–64. At most, Angelo showed the possibility of UC in the sample group of patients, but it did *not* correlate the risk to the HPV vaccine using a case control group or patient. Tr. at 176; Angelo at 463. In fact, Dr. Liacouras would expect even more cases of UC in the normal population if an association with the vaccine was likely, given the commonality of this disease. Tr. at 176. Angelo ultimately had failed to identify any significant relationship between the development of UC and the HPV vaccine, undermining the significance of any proposed risk interval. *Id.*; Angelo at 464.

2. *Neil Romberg, M.D.,* – Dr. Romberg, an immunologist and medical doctor focused on the care for children with immunological disorders, testified on behalf of Respondent, and submitted two expert reports and an affidavit. *See generally* Tr. at 211–323; Report, dated May, 6, 2019, filed as Ex. A (ECF No. 50-1) ("Romberg First Rep."); Report, dated January 14, 2020, filed as Ex. GG (ECF No. 70-1) ("Romberg Second Rep."); Affidavit, dated December 11, 2020, filed as Ex. JJ (ECF No. 98-2) ("Romberg Aff."). Dr. Romberg did not find a casual association between the vaccines Petitioner received and UC.

Dr. Romberg received his undergraduate degree from the University of Michigan, and his medical degree from Pennsylvania State University, College of Medicine. Tr. at 211; *Curriculum Vitae*, filed as Ex. MM (ECF No. 119-1) ("Romberg CV") at 1.[44] He completed a pediatric residency and a chief residency in pediatrics at New York University, School of Medicine and

[43] Respondent cited to Ex. FF by an author named Croft, but this pages for this exhibit are cut off and it is unclear on the authors name or title of the article.

[44] This is the most updated version filed by Respondent.

completed his training at Yale University, School of Medicine, with a three-year allergy clinical immunology fellowship. Tr. at 211; Romberg CV at 1. Dr. Romberg is currently an Assistant Professor of Pediatrics at the University of Pennsylvania and an attending physician at the Children's Hospital of Philadelphia where he holds the Jeffrey Modell Endowed Chair of Pediatric Immunology Research. Romberg CV at 1; Romberg First Rep. at 1. He is licensed to practice medicine in New York, Connecticut, and Pennsylvania, and is board certified by the American Board of Pediatrics and the American Board of Allergy and Clinical Immunology. Tr. at 214; Romberg First Rep. at 1; Romberg CV at 2. Dr. Romberg has published approximately 40-50 peer-reviewed publications. Tr. at 217.

Dr. Romberg deferred to Dr. Liacouras regarding Petitioner's UC diagnosis, and instead focused on Petitioner's three mechanistic theories. He understood them to be as follows: that (a) the innate immune system would mount an overly exuberant response to vaccine components (due in part to the alum adjuvant); (b) molecular mimicry between antigenic vaccine components and epithelial cell structures would results in a cross-reaction against the gut, damaging it and also encouraging an inflammatory setting; and (c) the vaccines could also induce an immune response that upsets the equilibrium between the mucosal immune system in the gut and the mensural bacteria. Tr. at 220–21, 281; Romberg First Rep. at 4. Although Dr. Romberg admitted he could not say with certainty that there was absolutely a zero percent chance the vaccines at issue could induce such processes resulting in disease, in his estimation the chance *approached* zero, given the submitted literature and evidence. Tr. at 320–21.

First, Dr. Romberg addressed Petitioner's contentions about the role of the innate immune system in the context of this case. Tr. at 221, 309. The innate immune system, he explained, responds quickly after it detects evidence of pathogens or other damaging external factors. *Id.* at 222, 310–11. By contrast, the adaptive response moves slowly and secondarily, and is more selective about what it recognizes as a foreign invader. *Id.* at 223. Thus, where the innate immune system typically responds the same every time (and quickly as well), the adaptive immune system has features of immunological memory, and thus will only react more rapidly to antigenic stimuli it has encountered before. *Id.* at 223, 275.

Dr. Romberg opined that an aberrant innate response would not be hidden or remain subacute for a lengthy period of time. Rather, hyperactivation of the innate response (for example, due to the alum adjuvant) would result in clinical manifestations or other evidence that could be obtained from testing. Tr. at 225. The immune response to alum (which occurs within minutes of vaccination) has been well described and characterized. *Id.* When alum is detected by a protein called NLRC3, it stimulates a macromolecular structure called the inflammasome, leading to the upregulation of certain proinflammatory cytokines. *Id.*; Romberg First Rep. at 7; S. Eisenbarth et al., *Crucial Role for the Nalp3 Inflammasome in the Immunostimulatory Properties of Aluminum Adjuvants*, 453 Nature 1122, 1122 (2008), filed as Ex. K (ECF No. 50-11). If those cytokines stay

in the tissue, they cause fever or "induration" (swelling and redness at the injection site).[45] Tr. at 225; Romberg First Rep. at 7. Subsequently, the antigens sparking the innate response will be taken to lymph nodes, where they interact with the B and T cells and start the adaptive immune response. Tr. at 225–26, 285; Romberg First Rep. at 7. To get a more systemic reaction that can result in disease or worse symptoms, there must be an uncontrolled series of events. Tr. at 226.

Dr. Romberg similarly did not accept the argument that the alum adjuvant might have heightened the initial vaccine response, deeming the fact that Petitioner received two vaccines with the adjuvant simultaneously as not atypical. Tr. at 228. Dr. Rosenstreich had cited a study regarding oral ingestion of large amounts of aluminum in mice and its relation to IBD (Chambrun I), but this was not a comparable situation to vaccination in Dr. Romberg's estimation. *Id.*; Chambrun I at 589. The studied mice in Chambrun I had been force-fed large amounts of aluminum for 31 days, in comparison to the amounts Petitioner had received in a single day. Tr. at 229; Romberg Second Rep. at 5–6. And the dosage mattered, since the amount of alum contained in vaccines is far dwarfed by what the experimental mice had received. Tr. at 230, 303; Romberg Second Rep. at 5–6. Most importantly, Chambrun I's authors determined that exposure to alum *alone* did not cause colonic inflammation, so its own results did not support Dr. Rosenstreich's contentions. Tr. at 229–30, 306–07; Romberg Second Rep. at 5–6; Chambrun I at 590 (citing supplementary Figure 1, and noting "[t]hese four weeks' oral administration of aluminum did not induce any macroscopic, histological, or molecular colonic inflammation"). As Dr. Romberg later admitted, however, Chambrun I does also state that the dose and route of aluminum administration used in the study had relevance to human exposure, even if the study methodology used artificial conditions so that effects could be reasonably evaluated for experimental purposes. Tr. at 304; Chambrun I at 597.

In addition, the receipt of multiple vaccines on a single day, Dr, Romberg opined, was not itself likely to encourage an aberrant reaction. In fact, the immune system can easily handle multiple vaccines at once without the occurrence of any immune-mediated harm. Tr. at 252. The CDC has no difficulty recommending multiple vaccines be administered at a single pediatric visit, and many vaccines are intentionally formulated to be multi-antigen (like the DTaP or pneumococcal vaccine, which contains several pneumococcal serotypes). *Id*. Thus, Petitioner's receipt of three vaccines at one time was not contrary to accepted pediatric standards of care. *Id.* at 252–53.

[45] Fever is the number one sign that a specific proinflammatory cytokine, IL-1β, is circulating in the blood and has reached (or at least communicated with) the brain. Tr. at 226; *Pek v. Sec'y of Health & Hum. Servs.*, No. 16-0736V, 2020 WL 1062959, at *5, n.8 (Fed. Cl. Spec. Mstr. Jan. 31, 2020) (defining IL-1β as a "type of cytokine that mediates antigen-specific responses through direct activation of lymphocytes"). The clinical/symptomatic response is malaise and fatigue. Tr. at 226.

Second, Dr. Romberg deemed unpersuasive the component of Petitioner's causation theory positing an autoimmune cross-reaction due to molecular mimicry. As he explained, molecular mimicry is a theory of mistaken identity in which the immune system reacts to the protein of an exogenous antigen (like a vaccine or infection), creating an immune response to that protein—but where the original antigenic agent has some resemblance (whether due to amino acid sequence or structure) to a self-protein component or structure.[46] Tr. at 230; Romberg First Rep. at 4. This can lead to the immune system mistakenly attacking the self tissue, due to its component resemblance to a pathogenic microbe or other foreign invader. Tr. at 230–31.

In Dr. Romberg's view, however, while molecular mimicry has a reasonable scientific basis as a theory, it does not follow that it is the likely mechanism in any given autoimmune disease process. Tr. at 231; Romberg First Rep. at 5; C. Benoist & D. Mathis, *Autoimmunity Provoked by Infection: How Good is the Case for T Cell Epitope Mimicry?,* 2 Nature Immunology 797, 797–98 (2001), filed as Ex. F (ECF No. 50-6) ("Benoist"); L. Albert & R. Inman, *Molecular Mimicry and Autoimmunity*, 341 N Eng. J. Med. 2068, 2073 (1999), filed as Ex. G (ECF No. 50-7). Rather, evidence supporting its role must be identified. Some in the immunologic field rely on a four-pronged framework[47] to determine if molecular mimicry is the likely disease mechanism. Tr. at 231, 287; Romberg First Rep. at 5; Benoist at 797–98; C. Ang et al., *The Guillain-Barré Syndrome: A True Case of Molecular Mimicry*, 25 Trends Immunology 61, 62–65 (2004), filed as Ex. H (ECF No. 50-8) ("Ang").[48]

The first criterion of this framework, Dr. Romberg explained, looks for epidemiologic support for a vaccine-injury association generally. Tr. at 231, 287. The second asks whether autoreactive T cells or B cells that might recognize some sort of a human target have been identified. *Id*. at 240–41, 300; Romberg First Rep. at 6. The third criterion looks for a proposed antigen on the vaccine/infection side that might sufficiently resemble a self structure to spark a cross-reaction (in the wake of the immune system's reaction to the initial foreign antigen). Tr. at 241, 300. And the fourth criterion evaluates whether an animal model exists that could reproduce

[46] Dr. Romberg provided more detail for his explanation of molecular mimicry in his first report. As he noted, the concept is that an immune cell mistakes a self-antigen loaded in an HLA molecule for a foreign antigen and mounts an inflammatory response. Romberg First Rep. at 4; Tr. at 286–87. As different HLA alleles present antigens differently, autoimmune diseases occur more often in people with certain HLA alleles, and so molecular mimicry may provide an explanation why some people develop inflammatory diseases when others do not. Romberg First Rep. at 4.

[47] This framework was originally created by Dr. Diane Mathis, and has since been relied upon by immunologists interested in autoimmune diseases as a way to gauge whether molecular mimicry actually might "explain" a disease's pathogenesis. Tr. at 242; Benoist at 797–98; Ang at 62–65.

[48] Dr. Rosenstreich, by contrast, maintained that this four-prong framework demanded a degree of proof far in excess of what would be deemed sufficient in the context of a Vaccine Program injury claim. Rosenstreich Second Rep. at 5–6. This point has merit, as I discuss below (although I take some notice of the framework as generally illuminating the kinds of evidence needed to support molecular mimicry as explanatory of an autoimmune process).

experimentally the proposed autoimmune process relying on molecular mimicry. *Id*. at 241–42. The ability to meet all four provides strong support for molecular mimicry as relevant to a disease process, in Dr. Romberg's view—whereas if none are fulfilled, the argument that molecular mimicry is part of the disease process is unpersuasive. *Id.* at 243.

In this case, Dr. Romberg maintained, none of these criteria could be met. Tr. at 243; Romberg First Rep. at 5. First, he could identify no persuasive or reliable epidemiologic evidence establishing a vaccine association generally, noting that the placebo-controlled clinical trial data discussed in the Gardasil Package Insert undercut contentions of a relationship. Tr. at 233; Gardasil Package Insert at 8–9. In these seven clinical trials, development of new autoimmune diseases were assessed two and six months after either administration of a vaccine or placebo. Romberg First Rep. at 5; Gardasil Package Insert at 8–9. The study compared 10,944 females who had received the Gardasil vaccine compared to 9,412 females receiving a placebo, but found only seven cases in the Gardasil group, versus ten cases in the placebo group, of IBD. Tr. at 234; Romberg First Rep. at 5; Gardasil Package Insert at 8. The same analysis was done for males (though in fewer numbers, with 3,093 males in the vaccine group and 2,303 in the placebo group). Tr. at 234; Romberg First Rep. at 5; Gardasil Package Insert at 9.

In discussing this evidence from the Gardasil Package Insert, Dr. Romberg rejected Dr. Rosenstreich's concerns that alum in the placebo group doses might have impacted a reaction alone. Tr. at 234, 296. If, he reasoned, alum was the "bad actor" prompting IBD, there would be cases *just* in the alum group and not in the saline group (whereas if it was the protein that caused disease there would be evidence in the group receiving the vaccine, as opposed to the controls).[49] *Id.* at 235. In fact, the study saw *fewer* cases of IBD in the placebo group than in the treatment group, suggesting there is probably no effect of the alum adjuvant. *Id.* at 235, 296–97. This clinical trial study evidence thus negated any HPV vaccine association—and Petitioner had offered no other evidence *pro* or *con* relating to Flumist or Hep A.[50] *Id.* at 293; Romberg First Rep. at 5.

Second, Dr. Romberg maintained that no evidence established *what* autoreactive T cells or autoantibodies would be driving a cross-reactive process. Tr. at 241; Romberg First Rep. at 6. Indeed, there was no evidence of the presence of any such potential offending T or B cells in

[49] The Gardasil Package Insert also disclosed that in seven clinical trials (five amorphous aluminum hydroxy sulfate ("AAHS") controlled, one saline placebo controlled, and one uncontrolled), there were 15,706 patients in the Gardasil group, 13,023 patients in the AAHS control group, and only 594 patients in the saline placebo group, which Dr. Romberg admitted was generally large enough to detect rare events for the saline placebo group. Tr. at 297–98; Gardasil Package Insert at 4.

[50] By comparison, Dr. Romberg noted that there were many good examples where molecular mimicry likely *does* contributes to autoimmune human diseases, such as in the context of Streptococcal infection-associated rheumatic fever, or the infections/flu vaccine association with GBS. Romberg First Rep. at 5. In such cases, reliable and persuasive epidemiological data exists that links the exposure with onset of disease. *Id*.

Petitioner's blood. Romberg First Rep. at 6. Dr. Rosenstreich had cited to a case report, Luca, to suggest that colitis could be T cell-induced after receipt of the flu vaccine, but Luca not only involved a totally different version of the vaccine (which was injected rather than administered intranasally like Flumist) but also featured onset *within two hours* (not 11 weeks). *Id.* at 6–7; Luca at 367. Nor was Dr. Rosenstreich able, in Dr. Romberg's view, to identify what the mimic for the vaccine antigen even was. At most, Petitioner proposed that the HPV16 E7 protein was molecularly similar to an intestinal brush-border transport protein, but the former protein is not contained in the HPV vaccine—let alone the other two. Tr. at 214, 241; Romberg First Rep. at 7; Rosenstreich First Rep. at 7; Gardasil Package Insert at 12 (listing a complete list of ingredients in the vaccine).

The final criterion was also unmet, in Dr. Romberg's estimation. He noted the existence of many animal models for IBD (identifying his familiarity with 66 models as of the date of his first report), but he was aware of none that had attempted to induce IBD or UC via Gardasil, Hep. A, any form of seasonal flu vaccine, or the components thereof (including the alum adjuvant). Tr. at 242, 302–03; Romberg First Rep. at 6. Though Dr. Romberg acknowledged that more research on rare conditions was always called for, he emphasized that IBD is a major topic for biomedical research and is frequently evaluated, so in his view the absence of research evidence on this subject was telling. Tr. at 243. On the other hand, clinical guidelines routinely recommended that IBD/UC patients be vaccinated. Tr. at 235–36; K. Chaudrey et al., *Updates in Vaccination: Recommendations for Adult Inflammatory Bowel Disease Patients*, 21 World J. Gastroenterology 3184, 3184 (2015), filed as Ex. I (ECF No. 50-9). If vaccines were factors in contributing to IBD, adverse events would be far more commonly reported. Tr. at 236–37.

Dr. Romberg went on to discuss the case report evidence relied upon under Petitioner's theory, deeming them to generally be worthy of relatively little evidentiary weight. Tr. at 237. In the hierarchy of scientific/medical evidence, he contended, the most persuasive and reliable proof was to be found in meta-analyses of placebo-controlled blinded studies of a large number of patients. *Id.* at 231–32, 290. Below this level would be placebo-controlled blinded studies, followed by epidemiologic evidence like case control series. *Id.* at 232. At the bottom would be case series reports, with single-patient case reports the least persuasive category of causation evidence. Indeed, in Dr. Romberg's estimation many in the scientific community might not deem the latter to be of any evidentiary value at all, given the lack of controls and individual patient samples. *Id.* at 233.

Besides lacking general value as causation evidence, Dr. Romberg deemed the specific case reports cited by Dr. Rosenstreich to be unpersuasive or unhelpful to Petitioner's case. Luca, for example, involved a single patient who could be distinguished from Mr. Cerrone in terms of

age, gender, preexisting conditions, and timeframe for onset.[51] Tr. at 238; Luca at 367. The same was true for Pauwels. Tr. at 238–39; Romberg Second Rep. at 8; Pauwels at 217–19. That case report involved a wholly-different disease (panniculitis), not to mention a form of the flu vaccine with a different composition and method of administration. Tr. at 239; Romberg Second Rep. at 8. Flumist accesses the mucosal immune system in the nose, with the intention of creating a controlled infectious process therein, distinguishing it from a peripherally-administered intramuscular vaccine which aims to send the vaccine antigens more directly into the lymphatic system.[52] Tr. at 239–40; Romberg Second Rep. at 8. Dr. Romberg also deemed the VAERS data establishing 75 cases of post-vaccine colitis to be unsurprising, given the passive nature of this kind of evidence. Tr. at 240; Romberg First Rep. at 5. He deemed unverified reporting of adverse events to be no better than a last resort, useful only when there is no other data relevant to causal issue. Tr. at 240. Yet in this case, such data exists (although it is unhelpful to Petitioner's case) *Id.*; Romberg First Rep. at 5.

Dr. Romberg found equally unpersuasive Dr. Rosenstreich's contention that the vaccines (alone or in concert) could somehow interfere with gastrointestinal equilibrium. In making this argument, Dr. Rosenstreich had analogized the impact of the relevant vaccines to infectious agents understood to induce autoimmune disease, such as *C. jejuni*. But because the HPV vaccine is not (nor does it contain) an intraluminal microbe, the nature and source of this balance disruption could not be illuminated either way. Tr. at 245–46. Otherwise, Dr. Romberg denied that vaccines had been credibly linked to the abnormal imbalance between commensal bacteria and the immune system characteristic of IBD. *Id*.

Another argument raised by Petitioner but questioned by Dr. Romberg was the possibility that Petitioner's second HPV vaccine dose,[53] received on February 10, 2016, evidenced rechallenge,[54] or a quicker adaptive immune response upon second exposure, since the medical record showed that Petitioner's UC progressed drastically from mid-February to March 2016. Tr. at 243–44, 314–16; Romberg Second Rep. at 8–9. In Dr. Romberg's view, the very concept of rechallenge in this case (in which the first dose did not result in evident clinical manifestations for

[51] Dr. Romberg also noted that the Luca case report did not appear to have been peer-reviewed, and its assertions about the patient considered and her condition could not be verified. Romberg First Rep. at 6.

[52] In addition, Dr. Romberg explained, with a live vaccine there is a delayed innate immune response (around five to eight days) because the live viruses in the vaccine need to replicate several times before an immune reaction will occur. Tr. at 239.

[53] Dr. Romberg was unaware whether Mr. Cerrone had also previously received the Hep. A or Flumist vaccines, so he focused on the HPV vaccine in addressing this issue. Tr. at 244.

[54] *See generally Nussman v. Sec'y of Health & Hum. Servs.*, No. 99-500V, 2008 WL 449656, at *9 (Fed. Cl. Spec. Mstr. Jan. 31, 2008), *aff'd,* 83 Fed. Cl. 111 (2008) (defining challenge-rechallenge as "when a person (1) is exposed to one antigen, (2) reacts to that antigen in a particular way, (3) is given the same antigen again, and (4) reacts to that antigen similarly").

over two months) was belied by the fact that Mr. Cerrone received a *third* HPV vaccine dose on June 24, 2016, after his diagnosis and while he was being actively treated, but showed no renewed or worsened symptoms thereafter. *Id.* at 244–45, 315; Romberg Second Rep. at 9.

Dr. Romberg was questioned on cross examination about Dezfoli, a ten-year old abstract review article. Tr. at 315–16. Although Dezfoli concluded that IBD patients receiving immunosuppressive treatments were not put at risk by receipt of the HPV or Hep. A vaccines, it *did* classify LAIVs like Flumist to be contraindicated. Dezfoli at 505, 509-10. Dr. Romberg maintained, however that in Dezfoli the flu vaccine had been administered to 575 IBD patients who were receiving immunosuppressive therapy, with no control group. Tr. at 316; Dezfoli at 506. IBD patients are known to have flares, and therefore it was not surprising to Dr. Romberg that Dezfoli observed flares in five percent of the sample post-vaccination. Tr. at 316; Dezfoli at 506. Thus, whether there was a likely causal connection with that specific vaccine was not reliably established. Tr. at 316. And Dezfoli's authors stressed generally that their recommendations flowed from the broader view that generally "live vaccines should be avoided among patients who are immunosuppressed," as opposed to a determination that this category of vaccine posed causal risks for disease initiation. Dezfoli at 509, 510.

Dr. Romberg concluded with a discussion of whether Petitioner's UC onset was medically acceptable under the circumstances. He acknowledged that the medical record in this case *could* support an onset as having occurred between 81 to 100 days after vaccination. Tr. at 224, 319–20; Romberg First Rep. at 7–8. But Dr. Romberg found it difficult to identify what period might be most medically reasonable, based on the evidence submitted. Tr. at 246–47. Schonberger, for example, best supported a post-vaccination onset for the autoimmune disease it focused on (GBS) of around 21 days,[55] but it involved a distinguishable vaccine and injury. *Id.* at 247; 289–292; Romberg First Rep. at 7–8; Schonberger at 112.

Dr. Romberg also pointed out that Schonberger's results had been corroborated by animal models[56]—but there was little comparable evidence that could shed light on what the proper timeframe for vaccine-caused UC/IBD would be. Tr. at 248. At best, one could look to an IBD-specific mouse model, and to that end he referenced the Dextran Sulfate Sodium model. *Id.* at 248–49; Romberg Second Rep. at 7; B. Chassaing et al., *Dextran Sulfate Sodium(DSS)-Induced Colitis in Mice*, 104 Current Protocols Immunology 1, 1 (2015), filed as Ex. GG, Tab 3 (ECF No. 70-4) ("Chassaing"). But the response observed in Chassaing was significantly faster—occurring within three to four days. Tr. at 249–51; Romberg Second Rep. at 7; Chassaing at 8. Another study had

[55] Specifically, Schonberger indicates that most GBS cases after the flu vaccine occurred around 13-17 days, with their latest happening 41 days. Schonberger at 112.

[56] Dr. Romberg acknowledged that animal testing was not fully comparable to what would be expected to occur with humans, but noted that were reasonable models that could provide fair comparison to comparable diseases in humans (specifically pointing to one that was used in mice as a proxy for peripheral neuropathies in humans, like GBS). Tr. at 249–50; Romberg First Rep. at 7–8.

reached a similar conclusion. *See, e.g.*, E. Antoniou et al., *The TNBS-Induced Colitis Animal Model: An Overview*, 11 Annals Med. & Surgery 9, 13 (2016), filed as Ex. GG, Tab 4 (ECF No. 70-5) (describing a separate mouse colitis model for Crohn's disease, and finding that test subjects demonstrated colon-impacting symptoms within three days, dying by day seven). Thus, what evidence existed relevant to UC did not support even the shortest vaccine-symptoms interval possible in this case (81 days). Tr. at 251; Romberg Second Rep. at 7.

Dr. Romberg commented about what the medical record said (or did not) about onset and vaccine association with Petitioner's UC. He did not see any evidence of local inflammatory symptoms such as induration, redness, or fever after the October 2015 vaccination date. Tr. at 226, 280, 319; Romberg First Rep. at 3, 7. And Petitioner's contentions that he had experienced loss of stamina that November had not been contemporaneously reported to any of his providers. Tr. at 227–28. Dr. Romberg also noted (like Dr. Liacouras) that teenagers might experience fatigue or low energy for a number of reasons unrelated to vaccination (e.g., growth, hormonal activity, or sleep disturbances). *Id*. at 227. And these kind of symptoms were not commonly associated with gut inflammation in any event. *Id.* at 226–27; Romberg First Rep. at 5.

IV. Procedural History

After the case's initiation in August 2017, Petitioner filed medical records, affidavits, an amended petition, and statement of completion by October 2017. Respondent's Rule 4(c) Report was filed on February 28, 2018, contesting Petitioner's right to compensation. ECF No. 25. Expert reports were subsequently filed through early 2020, and thereafter the special master to whom the case had been assigned requested a briefing from the parties in advance of potential adjudication to determine a ruling finding for entitlement, a decision denying entitlement, or an order scheduling the case for a hearing. ECF No. 78. Petitioner submitted his brief on July 15, 2020, Respondent filed her response on December 11, 2020, and Petitioner replied on February 26, 2021. ECF Nos. 90, 97, 102.

The case had been set for an October 2021 trial, but was transferred to me due to a conflict of interest involving the prior special master. I subsequently set the matter for a two-day hearing for May 2022. ECF No. 115. The trial occurred as scheduled, and the parties submitted post hearing briefs on August 5, 2021. ECF Nos. 133–34. The matter is now ripe for resolution.

V. Applicable Legal Standards

A. *Petitioner's Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table

Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[57] In this case, Petitioner does not assert a Table claim.

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Hum. Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005): "(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."

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical

[57] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Hum. Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Hum. Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Hum. Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

theory. *Andreu v. Sec'y of Health & Hum. Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras*, 121 Fed. Cl. at 245.

In discussing the evidentiary standard applicable to the first *Althen* prong, the Federal Circuit has consistently rejected the contention that it can be satisfied merely by establishing the proposed causal theory's scientific or medical *plausibility*. *See Boatmon v. Sec'y of Health & Hum. Servs.*, 941 F.3d 1351, 1359 (Fed. Cir. 2019); *see also LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) ("[h]owever, in the past we have made clear that simply identifying a 'plausible' theory of causation is insufficient for a petitioner to meet her burden of proof" (citing *Moberly*, 592 F.3d at 1322)); *Howard v. Sec'y of Health & Hum. Servs.*, No. 16-1592V, slip op. at *6 (Fed. Cl. Feb. 27, 2023) (confirming that "[t]he standard has been preponderance for nearly four decades"). Otherwise, petitioners *always* have the ultimate burden of establishing their Vaccine Act claim with preponderant evidence. *W.C. v. Sec'y of Health & Hum. Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell v. United States*, 133 Fed. Cl. 782, 793 (2017) (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Medical records and statements of a treating physician, however, 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. Section 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 & Hum. Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates

that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Hum. Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Dept. of Health & Hum. Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review denied*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 F. Appx. 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Hum. Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for rev. denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Legal Standards Governing Factual Determinations*

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

As noted by the Federal Circuit, "[m]edical records, in general, warrant consideration as trustworthy evidence." *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Hum. Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Hum. Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). A series of linked propositions explains why such records deserve some weight: (i) sick people visit medical professionals; (ii) sick people attempt to honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Hum. Servs.*, No. 11–685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Hum. Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Hum. Servs*., No. 03–1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are often found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Hum. Servs*., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, the Federal Circuit has also noted that there is no formal "presumption" that records are accurate or superior on their face to other forms of evidence. *Kirby v. Sec'y of Health & Hum. Servs.,* 997 F.3d 1378, 1383 (Fed. Cir. 2021). There are certainly situations in which compelling oral or written testimony (provided in the form of an affidavit or declaration) may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Hum. Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Hum. Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Hum. Servs.*, No. 90–2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y of Health & Hum. Servs.*, 110 Fed. Cl. 184, 203–04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). Under *Daubert*, the factors for analyzing the reliability of testimony are:

> (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community.

Terran, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

In the Vaccine Program the *Daubert* factors play a slightly different role than they do when applied in other federal judicial settings, like the district courts. Typically, *Daubert* factors are employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable or could confuse a jury. By contrast, in Vaccine Program cases these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of

expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)); *see also Isaac v. Sec'y of Health & Hum. Servs.*, No. 08–601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Hum. Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. *Consideration of Medical Literature*

Both parties filed numerous items of medical and scientific literature, but not all such items factor into the outcome of this decision. While I have reviewed all the medical literature submitted, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical record filed. *Moriarty v. Sec'y of Health & Hum. Servs.*, No. 2015–5072, 2016 WL 1358616, at *5 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.,* 527 F. App'x 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

ANALYSIS

Petitioner was unable to meet any of his causation prongs under *Althen*.

I. *Althen Prong One*

At the outset, I reiterate that the evidentiary standard for the first *Althen* prong is *preponderance*. *Boatmon*, 941 F.3d at 1359 (Fed. Cir. 2019); *LaLonde,* 746 F.3d at 1339. Although Petitioner has not directly challenged this legal conclusion, his briefing emphasized other commentary and characterizations that the Federal Circuit has provided about the "can cause" prong—and that in turn might stand for a slightly different, and effectively lower, standard. *See generally* Petitioner's Post-Hearing Brief, dated August 5, 2022 (ECF No. 133) ("Br."), at 1–19. Thus, his post-trial brief repeatedly notes that the theory offered by an expert must merely be "reputable" (suggesting in turn that *only* evidence that the theory was *not* reputable—i.e., that it would not warrant publishing in peer-reviewed articles, or would otherwise be soundly rejected by the medical community—would be sufficient to rebut Petitioner's showing), or that a "plausible" theory suffices. Br. at 1–3, 11–12.

It is firmly established in the Vaccine Program that no particular class or type of evidence *must* be included in the mix of proof (circumstantial and direct) a petitioner offers. *See Perekotiy v. Sec'y of Health & Hum. Servs.*, No. 16-997V, 2020 WL 12904810, at *13 (Fed. Cl. Spec. Mstr. Apr. 20, 2020), *mot. for review denied*, No. 16-997V, 2020 WL 5887548 (Fed. Cl. Sept. 17, 2020) (citing *Andreu*, 569 F.3d at 1378–79) ("[p]etitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory"). Thus, for example, I cannot (and would not) dismiss a case for failing to offer any epidemiologic evidence supporting a vaccine-injury association.

But the evidence a claimant offers must, in totality, always accomplish one thing in the end: *preponderantly establish that the vaccine(s) at issue more likely than not can cause the relevant disease.* Thus, the reputable quality of individual items of literature offered in the case, or plausibility of a theory, does *not* mean this burden has been carried, unless the overall *weight* of evidence (which includes evidence Respondent in rebuttal) balances out in a claimant's favor. It is not demanding certainty to find that certain items of literature or studies, no matter where published, do not sufficiently aid Petitioner in crossing the preponderant "line," especially after all the evidence is weighed together. Application of any other standard amounts to asking that the burden of proof *be lowered*. *See L.C. v. Sec'y of Health & Hum. Servs.*, No. 17-722V, 2021 WL 3630315, at *19 (Fed. Cl. Spec. Mstr. July 2, 2021) (citing *Hodges v. Secretary of Health & Hum. Servs.*, 9 F.3d 958, 961 (Fed.Cir.1993) ("while 'the [Vaccine Act] does the heavy lifting' when a claimant seeks to establish a Table injury, in the causation-in-fact context 'the heavy lifting must be done by the petitioner, and it is heavy indeed')).

Here, it was not preponderantly demonstrated that UC can be vaccine-caused—and if so, that the immunologic processes would work as proposed to cause it (even if UC is immune-

mediated, as the experts generally agreed). The associations between the specific vaccines in question and UC, for example, were not well-established with sufficient evidence. Respondent, by contrast, offered several individual reliable items of evidence (including studies performed in association with initial vaccine safety trials) that found no causal relationship. *See, e.g.*, Skufca at 5926; Dezfoli at 507–08; Chambrun II at 1414; Gardasil Package Insert at 8–9.[58] While Petitioner was never obligated to identify his own favorable epidemiologic evidence or direct proof of a vaccine association, the existence of some evidence going the other way was reasonably included in my evidentiary weighing process. Chambrun II was especially inconsistent with Petitioner's theory, since it specifically found no association between two of the three vaccines at issue and IBD (and only deemed the LAIV a risk factor because of its inclusion of live viral components—a danger at best in the context of *existing* IBD, and/or where a patient is receiving immunosuppressive therapies).

The individual mechanistic theories offered by Dr. Rosenstreich were also inadequately supported by reliable evidence, and ultimately were unpersuasive. His contention that molecular mimicry, in particular, as an explanation for some of the processes leading to UC relied too much on borrowing its substantiation with respect to other autoimmune diseases, even though the theory is not a "one size fits all" credible explanation for all alleged vaccine-caused injuries. *See McKown v. Sec'y of Health & Hum. Servs.,* No. 15-1451V, 2019 WL 4072113, at *50 (Fed. Cl. Spec. Mstr. July 15, 2019) ("[b]ut merely chanting the magic words 'molecular mimicry' in a Vaccine Act case does not render a causation theory scientifically reliable, absent *additional evidence* specifically tying the mechanism to the injury and/or vaccine in question") (emphasis in original).

In addition, a variety of additional evidence needed to bulwark Petitioner's claim was not provided. On the issue of molecular mimicry, for example, Dr. Rosenstreich's theory 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. Dr. Rosenstreich could not identify what specific components of any of the relevant vaccines might be at the center of such a process. He at most posited the possibility of some cross-reaction between antibodies or T cells reacting to HPV vaccine components and epithelial cells in the gut, even though the study relied upon for this contention involved a protein not included in Gardasil. *Compare* Gardasil Package Insert at 12

[58] There was some discussion at trial about the Gardasil Package Insert in particular, and the clinical trials it disclosed did bear on whether IBD was a likely adverse event. But package inserts are generally afforded very little weight in Vaccine Program cases as proof of causation. *Christiansen v. Sec'y of Health & Human Servs*., No. 08-244V, 2012 WL 6766650, at *12 (Fed. Cl. Spec. Mstr. Nov. 13, 2012). All vaccines covered by the Program are considered "safe" for administration in an overall sense, but that fact never rebuts an individual claim that a vaccine might have caused a *specific* injury (or even that in rare circumstances some vaccines might cause certain injuries more often). I thus have not given this item of evidence significant weight in my overall balancing.

with Natale at 580.[59] The fact that many other autoimmune diseases can proceed this way does not make up for this omission.

In so finding, I am not requiring Petitioner's evidentiary showing to meet the "four factors" Dr. Romberg relied upon in explaining why he did not deem molecular mimicry established as the likely immune process underlying vaccine-caused UC. These factors do not constitute a court-established test that must be met in Vaccine Act cases, independent from or in addition to a claimant's general obligation to establish the "can cause" prong preponderantly. The factor that looks for epidemiologic support for molecular mimicry, in particular, is *not* something Petitioners must ever demonstrate to prevail on the first *Althen* prong, as I have noted above (even though epidemiologic evidence, to the extent it exists and is otherwise relevant to a claim, *does bear* on a Petitioner's success, and may be considered by a special master). My finding that Petitioner has not persuasively established vaccine-caused molecular mimicry can result in UC is not a function of my determination that *all* of these factors could not be satisfied.

However, Dr. Romberg persuasively explained why he took into account such factors in assessing whether molecular mimicry reasonably applied in this case. His consideration of them does not amount to his requiring certainty, or otherwise invalidates his opinion. In fact, he expressly noted that he could *not* say for certain that Petitioner's theory was wrong, even if he rejected it overall. Tr. at 320–21. Rather, the factors reflect what knowledgeable members of the relevant scientific community would deem important when determining if molecular mimicry explains a likely disease process. I differentiate that from *my own* legal analysis of the evidence (which would permit me to find causation even in the absence of reliable epidemiologic proof).

The role the innate response might play in the disease process—and specifically how it would lead into, or encourage, a molecular mimicry-driven cross reaction—was also not persuasively or reliably established by Dr. Rosenstreich. Little probative evidence was offered to show an aberrant innate response would likely spark UC. Alum per se as an adjuvant ingredient was not shown to constitute a risk factor—even when included in more than one vaccine, as here. Reliance on alum as doing so bordered on the discredited Program theory of "ASIA" (autoimmune syndrome induced by adjuvants). *See, e.g.*, *McGuinness v. Sec'y of Health & Hum. Servs.*, No. 17-0954V, 2021 WL 5292343, at *17 n.17 (Fed. Cl. Spec. Mstr. Oct. 20, 2021); *Morris v. Sec'y of Health & Human Servs.,* No. 12-415V, 2016 WL 3022141, at *12 (Fed. Cl Spec. Mstr. Apr. 1, 2016); *Rowan v. Sec'y of Health & Human Servs.,* No. 10-272V, 2014 WL 7465661, at *16 (Fed. Cl. Spec. Mstr. Dec. 8, 2014), *mot. for review den'd*, 2015 WL 3562409 (Fed. Cl. May 18, 2015); *D'Angiolini v. Sec'y of Health & Human Servs.,* No. 99-578V, 2014 WL 1678145, at *60 (Fed. Cl. Spec. Mstr. Mar. 27, 2014), *mot. for review den'd*, 122 Fed. Cl. 86 (2015), *aff'd*, 645 F. App'x 1002 (Fed. Cir. 2016). And such an immune-driven process would most likely be associated with a

[59] In fact, Natale's purpose to no small extent was to use its findings to argue for the importance of developing therapies (*including* vaccines) that would allow the immune system to generate antibodies against the studied HPV16 E7 oncoprotein—thus underscoring the fact that the existing version of the vaccine (and certainly the one at issue in this case) *does not perform this function because it does not contain such an antigen.* Natale at 580, 584.

closer-in-time reaction (i.e., some evidence of inflammation) or evidence of greater disease manifestation, both of which are absent from the record (and indeed Dr. Rosenstreich was arguing for a sub-acute process that would take more than two months to manifest with any recognizable UC symptoms).

The argument about gut bacteria/immune equilibrium balance being impacted by vaccination was similarly not bulwarked with evidence that this balance could be disrupted by vaccination(s) received several weeks before onset. And Petitioner over-relied on classes of evidence—case reports or VAERS data—to support a vaccine-injury relationship that are not generally given much weight in Program cases, for the reasons provided by Respondent's experts. *See, e.g.*, *Tompkins v. Sec'y of Health and Human Servs.*, No. 10–261V, 2013 WL 3498652, at *16 (Fed. Cl, Spec. Mstr, June 21, 2013) ("VAERS is a stocked pond," and its individual reports lack scientific reliability), *mot. for review den'd,* 117 Fed. Cl. 713 (2014); *Campbell v. Sec'y of Health & Hum. Servs.,* 97 Fed. Cl. 650, 668 (2011) ("[c]ase reports do not purport to establish causation definitively, and this deficiency does indeed reduce their evidentiary value," even if they should receive some weight). Such proof simply records instances in which UC, or a comparable condition, *temporally* followed vaccination—not that evidence was derived (in a study or test or some kind) that lent support to a causal association. The fact that any one case report was published in a peer-reviewed journal, or serves as a signal worthy of further study, does not suddenly elevate this class of evidence into something meriting greater weight.[60] And case reports for distinguishable illnesses or involving different kinds of patients (Luca or Pauwels) were even less probative.

[60] In this vein, I do not find persuasive Petitioner's citation to a 2012 publication by the Institute of Medicine (the "IOM") suggesting that case reports can stand as "strong mechanistic evidence" that can outweigh epidemiologic studies involving larger numbers of subjects or vaccinations. Br. at 9 (citing Committee to Review Adverse Effects of Vaccines, *Adverse Effects of Vaccines: Evidence and Causality*, 1, 46–47 (K. Stratton et al. eds., 2012), filed as Ex. 85 (ECF No. 116-3) ("Stratton")). The citation has been taken out of context. Putting aside the fact that Petitioner purported to file *the entire text* of a work more than 800 pages at length, the quote selected comes from a discussion of the authors' different "causality conclusions" for specific vaccines and injuries, and their explanations for certain terms they employ therein. The cited section notes that they would employ the term "convincingly supports" where vaccine causality evidence included "one case report in which *convincing evidence exists* that the vaccine indeed did cause the adverse event," adding that they would also consider "the detection of laboratory-confirmed, vaccine-strain virus compelling evidence to attribute the disease to the vaccine-strain virus and not other etiologies." *Id.* (emphasis added). Stratton's authors here also discussed the fact that they would associate a vaccine with a specific adverse event despite epidemiologic evidence going the other way, *but* only where that evidence proved of "limited confidence or insufficient." Stratton at 47.

Thus, the cited portion from Stratton does not stand for the proposition that case reports *alone*—lacking other corroborative proof, and without "laboratory-confirmed, vaccine-strain virus compelling evidence"—would carry the day, that case reports always do so, or that they inherently outweigh epidemiologic studies that are *not* of "limited confidence or insufficient." Rather, it deems them significant when presented with *other* highly-reliable scientific evidence linking the vaccine to an injury. It does not establish a basis for elevating case reports to a level of reliable or probative evidence they are not presently provided in Program cases.

Overall, Dr. Rosenstreich's opinion was not bulwarked with enough reliable independent scientific/medical evidence to be persuasive—and the opinion he offered did not gain credibility from demonstrated study of the immunologic issues it involved. Certainly (and ignoring his lack of specific GI experience) Dr. Rosenstreich had sufficient qualifications to offer an opinion on the purported immunologic processes due to vaccination that theoretically could cause UC. But he relied on no specific research or experience of his own that could be brought to bear in support of his theory (which applies to the specific context of a gastrointestinal disease). Although Dr. Rosenstreich acted in good faith in offering the theory he did, his opinion ultimately seemed more designed to serve the needs of Petitioner in this case than to reflect an independently trustworthy view. Thus, (as he admitted a trial), he had attempted to support the theory based on reasoning backward from the injury (Tr. at 76), and relied on literature searches conducted *for this case* rather than his own expertise in immunologic/autoimmune illness (Tr. at 10).

Respondent's testifying experts, by contrast, were collectively more credentialed, better able to connect their testimony to their personal expertise, and proved significantly more persuasive in explaining why the three vaccines Petitioner received could not likely cause UC, based on their experiential understanding of the medical scientific issues as well as fair readings of the filed literature. They persuasively rebutted Petitioner's contention that his causation theory was "legally probable," and did not (as Petitioner has contended) apply a standard of certainty in so determining. Br. at 9. And I found their rejection of Petitioner's theory to be derived less from a claim-oriented desire to assist their side to prevail, but more to reflect their own independent and honest assessment of the theories and facts at issue.

Petitioner's theory ultimately rested on a combination of the temporal association with injury (as association that relies on a somewhat *attenuated* temporal period), the case and VAERS reports of post-vaccination UC, and the theory's "biological plausibility." Tr. at 101. This does not amount to a preponderant showing, even if individual items of evidence offered in this case had their own specific reliability or reputability—or even if the core idea that vaccines could cause UC has some degree of plausibility.

II. *Althen Prong Two*

The record does not permit the conclusion that any of the vaccines in question likely "did cause" Mr. Cerrone to experience UC. First, no treaters ever proposed any association between the vaccinations and Petitioner's subsequent diagnosis. In fact, doctors expressed no hesitancy (and in some cases even recommended) administering the remaining two doses of HPV vaccine in commonly-prescribed regimen, as evidenced by the record. Ex. 1 at 4, 8, 12; Ex. 3 at 7; Ex. 5 at 1135. Second (and as noted above), the medical record is not consistent with Petitioner's theory. There is no evidence of any initial vaccine reaction that would reflect the start of an inflammatory process, for example; no testing evidence that Petitioner possessed any putatively-causal

autoantibodies (ignoring that Petitioner never identified what they might be);[61] and no record corroboration of the symptoms Petitioner reports experiencing in November 2015 (symptoms which, it should be emphasized, are nonspecific for UC, not uncommon for teens to experience, and which if present in UC would likely follow other manifestations—not precede them).[62] It cannot even be concluded that Petitioner's alleged fatigue and stamina issues were related to his onset of UC several weeks later.

Petitioner's rechallenge argument was similarly unsupported by the record. It is admittedly the case that Petitioner more obviously worsened symptomatically after his receipt of a second HPV vaccine dose in February 2016, and close in time to it as well. But the temporal gap between *any* likely UC-related symptoms (which occurred no earlier than the end of December) and the first HPV dose exceeded *two months*, evidencing no initial "challenge" that could reasonably be measured against his medical history after the second dose. In addition, some of the initial records (in February 2016) where Petitioner first complained of rectal bleeding suggest it had been ongoing since mid to later January—even *prior* to the second HPV vaccine dose, and thus somewhat undermining the contention that he had in fact worsened after it. Ex 2 at 25–26. It is as likely that Petitioner was already progressing symptomatically, independent of the second dose. And then, importantly, the third dose Petitioner received that summer reveals no further rechallenge at all. This case thus does not provide the sort of facts where an initial vaccination prompts an identifiable reaction, with a second, more pronounced reaction after the second vaccine exposure, thereby supporting vaccine causality.

III. *Althen Prong Three*

The timeframe (measured from vaccination) in which Petitioner's UC symptoms manifested has not been shown to be medically acceptable. Although my first prong determination impacts how the third *Althen* prong is resolved (because Petitioner cannot show the vaccines can

[61] It also has not been established that Petitioner was genetically susceptible to injury of this kind. Although Petitioner argues in his brief, with the support of his expert, that it "is probable that [he] has genes that uniquely make him susceptible…", there is nothing in the record to support this assertion. Br. at 19. He uses evidence from the Luca case report, noting that the patient there had skin test results supportive of such findings. Luca at 362. But such testing did not occur in this case.

[62] Although I can accept for purposes of argument that Petitioner's reported November 2015 symptoms did occur as alleged, their lack of record corroboration limits their evidentiary utility—and Dr. Rosenstreich's straightforward reliance on their accuracy, over the actual records from the timeframe, is harmful somewhat to his opinions. For example, it was not until November 3, 2015, when Petitioner fractured his wrist that there was a contemporaneous medical record from the emergency room. Tr. at 108–09; Ex. 2 at 34. However, on this encounter Petitioner reports *only* symptoms from pain and dull aching from the injury. Tr. at 111; Ex. 2 at 34. The next medical visit once again lacked the reporting of symptoms discussed in Petitioner's affidavit. Tr. at 111–12. Less than ten days later, Petitioner was back in the ER on November 10th for a lacerated lip while at the movie theater. Tr. at 111; Ex. 2 at 30–31. During this visit there was no record of fatigue, loss of stability, strength, or stamina. Tr. at 112.

cause UC, the onset of his UC is immaterial), this prong itself was not preponderantly established, given Dr. Rosenstreich's theory.

Although some of Petitioner's symptoms allegations lack record corroboration, I accept his contention that he first began to experience bloody stools in late December 2015 (December 27th specifically, even though he delayed in reporting them to treaters for more than a month). Dr. Liacouras (the most credentialed and qualified GI disease expert who offered an opinion in this case) seemed comfortable with a December onset, even if he noted the medical records better supported onset beginning in January 2016. Petitioner therefore needed to establish that an 81-day (or more than 11 weeks) post-vaccination onset was medically acceptable. Petitioner offered some reliable evidence to support a several-week onset (albeit for a variety of autoimmune diseases, most of which are facially distinguishable from UC, like Schonberger). Indeed, Gradel (which was specific to IBD and UC) posited a risk period of months to a year or longer (although it based its findings not on vaccinations but gastroenteritis caused by bacterial infections, attenuating its relevance to this context). Gradel at 498–99. The timeframe in this case from vaccination to obvious UC manifestations falls within the four to five-month period Dr. Rosenstreich seemed to allow as medically acceptable overall. Tr. at 89–90.

But Petitioner's actual causation theory—which relied on a somewhat-confusing and overlapping combination of innate and adaptive aberrant immune responses, occurring at different stages—is ultimately not consistent with such a lengthy timeframe, nor does sufficient reliable science support it. The theory as presented, and as connected to Petitioner's actual history, relies on his experiencing a mix of clinical and subacute reactions—with initial inflammation largely due to the HPV vaccine alone or alum found in it plus the Hep. A vaccine, followed later by cross-reactive autoantibody production, and then immune system balance dysfunction in the gut. But the actual record does not reflect Petitioner's theory for how, and when, UC would unfold or manifest due to receipt of the Hep. A, HPV, and Flumist vaccines.

For example, the aspect of Petitioner's theory that focuses on an innate response (likely stimulated by the alum adjuvant) would reasonably involve some kind of reaction close-in-time to the October vaccinations. But the medical record itself shows *no immediate reaction to vaccination at all*, nor does it support the conclusion that a lengthy sub-acute process was underway, manifesting only in late December. There is simply no medical record support that would establish an aberrant, subacute immune response was occurring in November or most of December 2015, that would (a) later manifest 81 days after vaccination, but (b) remain tolerable another four to six weeks, before becoming severe enough to encourage Petitioner to seek emergency treatment. Dr. Romberg, by contrast, persuasively established that a theory relying on an innate immune response as aberrant and/or contributing to a later-manifesting disease should have record corroboration of some initial reaction. Tr. at 225–26.

To get around this record omission, Petitioner alleges he *did* experience symptoms associated with his later-diagnosed UC: fatigue or stamina loss/strength issues in November 2015.

Dr. Rosenstreich agreed (as indicated in his testimony from Petitioner's rebuttal case) that the initial symptoms alleged by Petitioner were important to his theory's validity. Tr. at 333 (admitting that disregarding the witness testimony of November fatigue or stamina issues would "weaken" his feelings about the theory, and that Petitioner's "descriptions of his symptoms I think are an important part of my understanding of the development of his disease").

But not only are these witness contentions lacking in corroboration (there is no medical records reflecting stamina or fatigue issues), but these kinds of symptoms have not been shown to be precursors of the more typically-expected UC symptoms. On the contrary, and as Dr. Liacouras established, if stamina loss and fatigue occur in the context of UC, they would likely manifest only later, as a result of anemia associated with bleeding caused by gut inflammation. Tr. at 152, 167–68. At most, Petitioner offered some evidence specific to the HPV vaccine that unconvincingly links it to fatigue.[63] And even if Petitioner had persuasively demonstrated that a common HPV vaccine reaction is fatigue or stamina loss, he did not also show that this symptom (which otherwise has not been associated with UC generally) could be *both* the transient product of one of the three vaccines received, and also a precursor of the kinds of symptoms classically associated with UC's onset.

The other components of Petitioner's causation theory relevant to onset timeframe were also unsupported by sufficient reliable independent proof. He relied heavily on case reports, for example, that were facially inconsistent with the timeframe at issue, with one in particular involving an extremely short onset period not at all compatible to what occurred herein. Luca at 367. Other case reports involved distinguishable injuries. *See generally* Pauwels. Indeed, on the question of onset generally, Petitioner referenced several items of literature having nothing to do with UC. *See, e.g.*, Schonberger at 112. I do not accept the suggestion that "any" autoimmune and vaccine-caused illness is likely to occur in the same timeframe—such that findings in Schonberger, for example, can be readily transposed to the present case.[64]

At the same time, animal models specific to IBD and UC suggested a very rapid response time after insult—less than one week. *See, e.g.*, Chassaing at 7–8. While I do not in this case make a finding, generally, as to what period of time post-vaccination would be most "medically acceptable" for vaccine-caused UC—and as noted, the 81-day post-vaccination timeframe is

[63] In particular, Dr. Rosenstreich offered Ozawa, which discusses purported dysautonomic effects of the HPV vaccine in Japanese girls. Ozawa at 1220. I have had the occasion in several prior cases to address Ozawa (specific to claims that the HPV vaccine causes a variety of orthostatic issues), but have noted that it is not a reliable or persuasive item of literature. *See, e.g.*, *McDonald v. Sec'y of Health & Hum. Servs.*, No. 15-612V, 2023 WL 2387844, at *5, 11, and 22 (Fed. Cl. Spec. Mstr. Mar. 7, 2023).

[64] Schonberger is not fully supportive of Petitioner's timeframe contentions in any event. It showed the autoimmune process causing GBS peaking within two to three weeks, dwindling down significantly to no real risk by 10 weeks (less than the 11-week period herein). First Romberg Rep. at 7; Schonberger at 112 Figure 4.

consistent with Dr. Rosenstreich's opinion—this kind of evidence at least shows that a lengthy timeframe has reliability issues that Petitioner's evidence did not fully address or refute.

In the end, Petitioner's onset contentions ultimately amount to an attenuated version of what many claimants argue—that the *fact* of post-vaccination illness (even at some distant time after vaccination) inherently implicates the vaccine. This kind of *post hoc* reasoning, however, has never been deemed evidentiarily persuasive in the Program. *Pafford,* 451 F.3d at 1358. It is even less so when the timeframe exceeds two months,[65] but where the medical record does not corroborate the purported immune process at work.

CONCLUSION

A Program entitlement award is only appropriate for claims supported by preponderant evidence. Here, Petitioner has not made such a showing. Petitioner is therefore not entitled to compensation.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the Clerk of the Court **SHALL ENTER JUDGMENT** in accordance with the terms of this Decision.[66]

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran
Chief Special Master

[65] Notably—and somewhat contradictory to Schonberger—most special masters have been unwilling to deem the onset of GBS after the flu vaccine medically acceptable if onset exceeds six to eight weeks, or up to 56 days. *See Chinea v. Sec'y of Health & Hum. Servs.*, No. 15-095V, 2019 WL 1873322, at *29 (Fed. Cl. Spec. Mstr. Mar. 15, 2019) (citing *Barone v. Sec'y of Health & Human Servs.,* No. 11-707V, 2014 WL 6834557 (Fed. Cl. Spec. Mstr. Nov. 12, 2014) (eight weeks is the longest reasonable timeframe for a flu/GBS injury)). An onset of nearly four weeks longer, as here, would readily be rejected, underscoring why (even if I accepted Petitioner's invocation of Schonberger in a distinguishable context) the timeframe at issue is too great.

[66] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment if (jointly or separately) they file notices renouncing their right to seek review.