

In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: October 22, 2025

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ANA OQUENDO VAZQUEZ *and* *
ARTEMIO RAMIREZ GARCIA *
on behalf of A.R. a minor child, *

Petitioner, *

No. 17-1817V

v. *

Special Master Young

SECRETARY OF HEALTH *
AND HUMAN SERVICES, *

Respondent. *

* * * * *

Diana Lynn Stadelnikas, Mctlaw, Sarasota, FL, for Petitioners.
Benjamin Patrick Warder, U.S. Department of Justice, Washington, DC, for Respondent.

RULING ON ENTITLEMENT¹

On November 20, 2017, Ana Oquendo Vazquez and Artemio Ramirez Garcia (“Petitioners”) filed a petition for compensation under the National Vaccine Injury Compensation Program (“Vaccine Act” or “the Program”), 42 U.S.C. § 300aa-10 et seq. (2018), on behalf of their minor child, A.R. Pet., ECF No. 1. Petitioners alleged A.R. suffered from Very Early Onset-Infantile Bowel Disease (“VEO-IBD”) as the result of a rotavirus vaccination administered on February 8, 2017. *Id.* at 2. Respondent argued against compensation, asserting that Petitioner could not establish a causation-in-fact claim by a preponderance of the evidence. Resp’t’s Rept. at 13, ECF No. 26.

After carefully analyzing and weighing all the evidence and testimony presented in this case in accordance with the applicable legal standards,² I find that Petitioners have provided

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

² While I have reviewed all of the information filed in this case, only those filings and records that are most relevant to the Ruling will be discussed. *Moriarty v. Sec’y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) (“We generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision.”) (citation omitted); *see also Paterek*

preponderant evidence that the rotavirus vaccine A.R. received on February 8, 2017, caused her to suffer from VEO-IBD. Accordingly, Petitioners are entitled to compensation.

I. Procedural History

Petitioners filed their petition alleging a VEO-IBD injury on November 20, 2017. Pet. On November 21, 2017, I filed an Initial Order directing Petitioners to file complete medical records and a statement of completion. ECF No. 5. Petitioner filed these records and a statement of completion on November 28, 2017. Pet'r's Exs. 1–13, ECF Nos. 6–8. Respondent filed a status report on February 27, 2018, identifying missing medical records. ECF No. 14. Petitioners filed an affidavit from Ana Oquendo Vazquez on April 4, 2018, and filed medical records on April 27, 2018. Pet'r's Exs. 14–20, ECF Nos. 15–16. Petitioners filed additional medical records in April and June 2018, and a statement of completion on July 2, 2018. Pet'r's Exs. 21–23, ECF No. 18; Pet'r's Ex. 24, ECF No. 20; ECF No. 21.

Respondent filed his Rule 4(c) report, opposing compensation, on October 10, 2018. Resp't's Rept. Respondent argued that A.R.'s symptoms had begun prior to the receipt of the rotavirus vaccine and that A.R. had tested positive for a genetic mutation, “which several treaters believed may be the cause of her inflammatory bowel disease.” *Id.* at 12. Respondent continued that none of A.R.'s treating physicians had “offered any evidence of a causal association that would meet the *Althen* standards” and thus Petitioners had failed to meet their burden under *Althen*. *Id.* at 12–13. Petitioners filed additional medical records on March 19, 2019. Pet'r's Exs. 25–29, ECF No. 37.

Petitioners filed the expert report of gastroenterologist John Santoro and accompanying medical literature on July 29, 2019. Pet'r's Exs. 31–39, ECF No. 49; Pet'r's Exs. 40–41, ECF No. 50. Petitioners filed additional medical records on October 30, 2019. Pet'r's Exs. 42–44, ECF Nos. 53–52. Respondent filed the expert report of pediatric gastroenterologist Chris Liacouras on January 10, 2020, and accompanying medical literature on March 6, 2020. Resp't's Exs. A–B, ECF No. 55; Resp't's Ex. A, Tabs 1–16, ECF No. 58. Petitioners filed more medical records on May 14, 2020, and October 27, 2020. Pet'r's Exs. 45–50, ECF Nos. 60–61; Pet'r's Exs. 51–54, ECF No. 66.

On November 10, 2020, Petitioners filed a motion to stay proceedings due to the death of Dr. Santoro, which I granted to allow Petitioners to find another expert for their case. ECF Nos. 67–68. On June 7, 2021, Petitioners filed an expert report from pediatric gastroenterologist Thomas Sferra, as well as accompanying medical literature. Pet'r's Exs. 60–75, ECF No. 74. Petitioners filed additional medical records on September 13, 2021. Pet'r's Ex. 77, ECF No. 80.

On November 18, 2021, Respondent filed a supplemental report from Dr. Liacouras and a report from immunologist Neil Romberg, as well as additional medical literature. Resp't's Ex. C, ECF No. 81; Resp't's Exs. D–E, ECF No. 82. Petitioners filed a responsive report from Dr. Sferra on June 7, 2022, and additional medical records in June and October 2022. Pet'r's Ex. 78, ECF No. 85; Pet'r's Exs. 79–80, ECF No. 86; Pet'r's Ex. 82, ECF No. 93. Respondent filed additional

v. Sec'y of Health & Hum. Servs., 527 F. App'x 875, 884 (Fed. Cir. 2013) (“Finding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.”).

reports from Dr. Liacouras and Dr. Romberg on December 9, 2022, as well as additional medical literature. Resp't's Exs. F–G, ECF Nos. 94–95.

On March 16, 2023, I scheduled an entitlement hearing between to be held on July 23–24, 2024. ECF No. 97. Petitioners filed medical records on October 24, 2023. Pet'r's Exs. 83–85, ECF No. 105. Petitioners filed their pre-hearing brief on May 28, 2024, as well as additional medical records and medical literature later that month. Pet'r's Br., ECF No. 108; Pet'r's Exs. 86–89, ECF Nos. 109–10. Respondent filed his responsive brief on July 9, 2024, and the parties filed their final pre-hearing submissions on July 16, 2024. Resp't's Br., ECF No. 112; Pet'r's Ex. 90, ECF No. 115; ECF Nos. 116–22.

A hearing in this case was held virtually on July 23, 2024. Min. Entry, dated July 23, 2024. On July 24, 2024, Petitioners submitted additional medical literature discussed during the hearing. Pet'r's Exs. 92–93, ECF No. 124. Post-hearing briefing was not conducted.

This matter is now ripe for consideration.

II. Factual History

A. Pre-Vaccination Medical History

A.R. was born at full-term with no complications on December 4, 2016, with Apgar scores of eight and nine at one and five minutes, respectfully. Pet'r's Ex. 8 at 104, 134. She weighed seven pounds, two ounces at birth. *Id.* at 104. Three days later, on December 7, 2016, A.R. was examined by nurse practitioner (“NP”) Lindsay Huie at her primary care physician’s (“PCP’s”) office. Pet'r's Ex. 1 at 5. A.R.’s examination was normal, and it was noted that A.R. was breastfeeding well. *Id.* At this visit, A.R. weighed six pounds, fifteen ounces. *Id.* at 7.

On January 11, 2017, A.R. presented to NP Huie for her one-month visit. Pet'r's Ex. 1 at 10. NP Huie noted that A.R.’s elimination was normal, with five-to-eight wet diapers and three-to-four stools per day. *Id.* at 12. A.R.’s general gastrointestinal systems were all also noted as within normal limits. *Id.* at 11. A.R. continued to breastfeed well and her weight was recorded at nine pounds, six ounces. *Id.* at 12.

B. Vaccination

A.R. presented to NP Huie for her two-month visit on February 8, 2017. Pet'r's Ex. 1 at 15. NP Huie noted she was negative for vomiting but recorded “occasional reflux” under her other symptoms. *Id.* at 16. A.R. was recorded to weigh ten pounds, two ounces, and NP Huie recommended either longer breastfeeding times or shorter intervals between feeds to increase A.R.’s weight gain. *Id.* at 19. At this visit A.R. received diphtheria, tetanus, pertussis (“DTaP”), hepatitis B, and inactivated polio vaccines, as well as a RotaTeq³ vaccine. *Id.*

³ Rotateq is a “trademark for a preparation of rotavirus vaccine, live, oral, pentavalent.” *RotaTeq*, Dorland’s Online Med. Dictionary. (hereinafter, “*Dorland’s*”). For consistency, I will refer to A.R.’s RotaTeq vaccine as a “rotavirus vaccine” for the remainder of this opinion.

C. Post-Vaccination Medical History

On February 11, 2017, A.R. was seen by Dr. David Shellington at the emergency department (“ED”) of Children’s Healthcare of Atlanta (“CHOA”) for dehydration, vomiting, and diarrhea. Pet’r’s Ex. 9 at 203. Petitioners reported that A.R. had been “vomiting after each feed for the past [six] days” and that “she started having diarrhea after each [] feeding since [four] days ago.” *Id.* Dr. Shellington’s notes also recorded that Petitioners had brought A.R. to her “PCP [five] days ago for [a] routine annual visit and was told that [A.R.] may have reflux.” *Id.* Dr. Shellington’s note specified that A.R. had received DTaP, hepatitis B, polio, and rotavirus vaccines at her PCP visit. *Id.* On examination, A.R. appeared “very dehydrated” with sunken eyes, but with no abdominal distention, pain, or fevers. *Id.* Dr. Shellington admitted A.R. to the pediatric intensive care unit (“PICU”) the same day. *Id.* at 204. While in the PICU, A.R.’s gastrointestinal panel came back negative, and her stool culture was positive for rotavirus A. *Id.* at 23. A.R. was diagnosed with rotavirus enteritis and discharged on February 14, 2017. *Id.* at 202.

The next day, on February 15, 2017, A.R. returned to the CHOA ED for continued diarrhea, worsening dehydration, and reduced breastfeeding. Pet’r’s Ex. 10 at 4532. On examination A.R. appeared lethargic and dehydrated. *Id.* Her labs returned with elevated electrolyte abnormalities and an elevated white blood cell count of 27.8. *Id.* A.R. was then readmitted to the PICU to be further evaluated for adrenal insufficiencies and a gastrointestinal illness. *Id.*

While admitted at CHOA, A.R. could not tolerate nasogastric feeds and continued to have profuse diarrhea, leading to intravenous feedings beginning on February 21, 2017. Pet’r’s Ex. 10 at 4167. On February 22, 2017, A.R.’s treating physicians opined that she may be suffering from “villous atrophy secondary to severe rotavirus enteritis.” *Id.* at 4532. Endocrinology consulted on her case and opined that “the most likely cause of her presentation and electrolyte abnormalities was pseudohypoaldosteronism^[4] secondary to her severe case of rotavirus enteritis with marked dehydration.” *Id.* at 4533. Due to A.R.’s electrolyte abnormalities she was transferred to the neonatal intensive care unit (“NICU”) from February 22, 2017, to March 6, 2017. *Id.* at 4340, 4422–66.

A.R. was examined by gastroenterologist Jeffery Lewis on February 24, 2017. Pet’r’s Ex. 10 at 4344. Dr. Lewis observed that A.R. had experienced weight loss and feeding difficulties due to her vomiting and diarrhea, even with slow-drip feeds. *Id.* He noted that A.R. “look[ed] great” and questioned whether “the original positive rotavirus was a fakeout” due to her previous rotavirus vaccine. *Id.* Dr. Lewis reiterated his observation on February 27, 2017, when he noted that he was “[u]nsure if rotavirus was [the] primary cause given that she received the vaccine less than 24 hours prior to development of symptoms.” *Id.* at 4373. Dr. Lewis also stated that A.R.’s original positive test for rotavirus was due to the vaccine and opined that A.R.’s symptoms were likely the result of “a significant and severe intestinal inflammatory condition.” *Id.*

A.R. continued to test positive for rotavirus on March 1, 2017. Pet’r’s Ex. 9 at 437. The following day, on March 2, 2017, Dr. Lewis entered a progress note in which he again opined that

⁴ Pseudohypoaldosteronism pertains to “elevated levels of aldosterone and increased plasma renin activity together with signs and symptoms of mineralcorticoid deficiency, caused by resistance of target tissues to mineralcorticoids.” *Dorland’s*.

A.R. was likely suffering from a severe intestinal inflammatory condition, and that it was “[l]ess likely [that] rotavirus [was the] primary cause given [her] prolonged symptoms and unexplained electrolyte derangements.” *Id.*

On March 7, 2017, A.R. underwent an esophagogastroduodenoscopy (“EGD”)/flexible sigmoidoscopy, which revealed superficial white plaques near the rectum and sigmoid colon, as well as mucosal abnormalities in the duodenum “described as scattered congestion, erythema, nodularity, [and] ulceration.” Pet’r’s Ex. 10 at 4563. Biopsy revealed regenerative tissue and no villi in the duodenum, “suggestive of regeneration following an acute enteritis,” and A.R.’s viral cultures were negative, but her stool was still positive for rotavirus. *Id.* at 4228, 4563 A.R.’s attending physician at the time, Dr. Jeffrey Blumenthal, noted her differential diagnosis as “possible autoimmune enteropathy vs post infectious enteritis.” *Id.* at 4563.

Dr. Blumenthal consulted with pediatric gastroenterologist Martin Martin and immunologist Lisa Kobrynski⁵ on March 14, 2017. Pet’r’s Ex. 10 at 4600. Both opined that there was concern for an underlying immune disorder. *Id.* At Dr. Kobrynski’s recommendation, an oral gamma guard was started the same day. *Id.* Dr. Blumenthal opined that A.R.’s clinical picture was suggestive of immunodysregulation polyendocrinopathy enteropathy X-linked (“IPEX”) syndrome, but “because the patient is female this [was] unlikely.” *Id.* Dr. Kobrynski also recorded that she was “unable to find any literature linking rotavirus vaccine to autoimmune intestinal processes . . . [h]owever, the persistent shedding of rotavirus may be causing ongoing gut inflammation and changes.” *Id.* at 4233. Dr. Kobrynski further noted that such persistent shedding was typically associated with T cell defects, however, A.R.’s T cell counts were not low enough to support such a diagnosis, and she recommended further monitoring to rule out this condition. *Id.*

On March 20, 2017, Dr. Blumenthal sent A.R.’s genome slides to Dr. Martin at his request to conduct genetic exome sequencing. Pet’r’s Ex. 10 at 4707. The same day, Dr. Blumenthal received confirmation that A.R. had received the RotaTeq vaccine, which he noted would explain A.R.’s positive stool findings. *Id.* A.R.’s biopsies were reviewed on March 21, 2017, which found “marked mucosal damage with damaged epithelial cells and decreased goblet cells.” Pet’r’s Ex. 24 at 16. The note associated with A.R.’s biopsies indicated that this suggested “an inflammatory process, possibly an immune related injury such as autoimmune enteropathy or a systemic immunodeficiency.” *Id.* The note also indicated that an infectious process or post-infectious injury may be considered, but there was no evidence of infectious organisms or viral inclusions. *Id.*

On March 25, 2017, A.R. was seen by Dr. Steven Liu, who noted that A.R. had received the rotavirus vaccine and that she had tested negative for the rotavirus antigen on the same day. Pet’r’s Ex. 10 at 4776. Dr. Liu also noted that Dr. Martin and reviewed A.R.’s pathology notes and reported “abnormal villus and crypts . . . apoptosis in epithelial cells . . . [o]verall findings consistent with epithelial disorder and likely related to immunodeficiency/autoimmune.” *Id.*

A.R.’s genetic exome sequencing returned on March 27, 2017, and revealed “[n]o established clinically significant variants . . . which can explain the primary clinical concerns seen

⁵ Various reports throughout the medical record spell Dr. Kobrynski’s name as “Kobrynski” and “Kabrinski.” For consistency, I will refer to her as Dr. Kobrynski throughout my opinion.

in this patient.” Pet’r’s Ex. 24 at 43. However, a “suspected mutation to WDFY4” was found, though Dr. Lewis noted it was unclear if this was significant. Pet’r’s Ex. 5 at 24. A progress note from immunologist Gerald Lee on the same day noted his impression of A.R.’s symptoms as an “[e]nteropathy of unclear etiology, rotavirus associated vs [a]utoimmune/immune dysregulation.” Pet’r’s Ex. 10 at 4822. Dr. Lee opined that “[m]itogen stimulation essentially rule[d] out T cell immunodeficiency as the cause of [her] persistent rotavirus infection,” and thus doubted that an immunodeficiency disorder was the cause of A.R.’s condition. *Id.* He further opined that immune dysregulation syndrome would be the likely cause of A.R.’s enteropathy if she failed to improve after advancing feeds and withdrawing her immune suppression. *Id.* at 4823.

A.R. underwent another EGD and sigmoidoscopy on April 18, 2017, which revealed “[d]iffusely abnormal duodenal mucosal with numerous punctate white spots, loss of vascular markings and gonestion, [m]ild gastric erythema . . . [and] Rectum-Descending colon with decreased vascular markings and mild erythema.” Pet’r’s Ex. 10 at 5148. That same day, the results of A.R.’s biopsies revealed “the possibility of autoimmune enteropathy [vs] mitochondrial storage disorder.” Pet’r’s Ex. 9 at 358. On April 21, 2017, A.R. completed an anti-enterocyte test to examine potential autoimmune causes of her enteropathy, which came back negative. Pet’r’s Ex. 10 at 5220.

A progress note from physician’s assistant (“PA”) Catherine Crenson on April 24, 2017, noted A.R. had a “compound heterozygote in the WDFY4 gene[,] though this is not known as a pathologic variation or associated with known human disease. Assumption is that she has an immune disorder leading to infantile onset IBD like picture perhaps expedited by rotavirus.” Pet’r’s Ex. 10 at 5265. A.R. was discharged on April 25, 2017, on TPN, trophic feeds, and low dose solumedrol. *Id.*; Pet’r’s Ex. 11 at 1427.

On April 30, 2017, Petitioners returned A.R. to the ED with “fever, tachycardia, . . . and mild subcostal retractions.” Pet’r’s Ex. 11 at 1427. A.R. had been wheezing the previous day and developed a fever of 101 °F with a distended abdomen. *Id.* A.R.’s diarrhea had also remained constant since her discharge, though her vomiting had resolved. *Id.* A.R. was admitted to the PICU, and her full diagnoses included:

- Feeding problem in infant
- Diarrhea
- Hypoalbuminemia
- Protein losing enteropathy
- Hyperchloremia
- Hypocalcemia
- Normocytic anemia
- Secondary hypertension
- Intestinal failure
- Severe sepsis without septic shock
- Respiratory distress
- Immunosuppressed status

- Streptococcal sepsis
- Klebsiella sepsis

Id. at 1426. “According to [the gastrointestinal department], assumption is that she has an immune disorder leading to infantile onset IBD perhaps expediated by rotavirus infection.” *Id.* at 1427. A.R. was started on broad-spectrum antibiotics and her PICC line was positive for strep genus and klebsiella. *Id.* at 1428. A.R. was evaluated by PA Kathleen McNamara on May 9, 2017. Pet’r’s Ex. 5 at 43. PA McNamara observed that A.R.’s current assumed diagnosis was an “immune disorder leading to infantile onset IBD-like picture perhaps expedited by attenuated rotavirus vaccine.” *Id.*

On May 20, 2017, A.R. was seen by immunologist Shanmuganathan Chandrakasan for evaluation for a bone marrow transplant, who opined A.R. suffered from “severe enterocolitis” due to “suspected VEO IBD with compound heterozygote for WDFY4 [variant of unknown significance (“VOUS”)]. Pet’r’s Ex. 11 at 1527. Dr. Chandrakasan also noted that A.R. had originally presented with “diarrhea which started [twenty-four hours] after [r]otavirus vaccination.” *Id.* at 1528. Dr. Chandrakasan also observed that A.R.’s EGD and colonoscopy studies were consistent with marked villous atrophy, colonic inflammation, and moderate gastritis. *Id.* Upon review of A.R.’s genome sequencing, Dr. Chandrakasan opined that she had a “suspect biallelic defect in WDFY4” and “VEOIBD with IPEX-like [gastrointestinal] biopsy phenotype.” *Id.* at 1534. However, he also noted that A.R. did “not have [a] phenotype of broader immune dysregulation.” *Id.* He further opined that “[s]ince WDFY4 is one of the BEACH domain containing proteins [], it is possible that it affects CTLA-4 mobilization, similar to [] that seen in other Tregopathies like CLTA4 haloinsufficiency and LRBA deficiency. Interestingly these two can have broader immune dysregulation and IPEX-like phenotype.” *Id.* Dr. Chandrakasan observed that “WDFY is highly expressed in immune and BM compartment,” and thus opined that it was “very likely” that a bone marrow transplant would be curative. *Id.* at 1535. However, Dr. Chandrakasan’s notes also noted that if A.R.’s genetic defect was critical for gastrointestinal barrier function, a bone marrow transplant “may not be entirely curative.” *Id.*

Following A.R.’s discharge from CHOA on May 23, 2017, she presented to gastroenterologist Dr. Lewis on May 30, 2017, and June 1, 2017, for continued diarrhea and occasional vomiting. Pet’r’s Ex. 2 at 26, 32. Petitioner reported that A.R. had been coughing before spitting up or vomiting and that A.R.’s abdomen had been distended. *Id.* In his visit notes, Dr. Lewis wrote that A.R. suffered from “intestinal failure [and] severe enterocolitis of unknown etiology/very early onset inflammatory bowel disease,” which may be explained by her WDFY4 VOUS mutation, “though this gene has not been described as causing disease in humans.” *Id.* at 35. Dr. Lewis documented vomiting and retching from A.R., but noted that she had been passing stool well. *Id.* A.R. returned to Dr. Lewis on June 12, 2017, where Petitioner reported that A.R. had been “retching [eight-to-ten times per day] and vomits [one-to-two times per day,]” with visible red streaks in her stool. *Id.* at 20. Dr. Lewis advised A.R. to continue with immunosuppressive medications and continue receiving TPN. *Id.* at 24. A.R. returned to Dr. Lewis again on June 30, 2017, where Petitioner reported a “significant amount of blood” in her stool multiple times per day. *Id.* at 14. A.R. continued to see Dr. Lewis on a weekly or bi-weekly basis for regular follow-ups throughout the remainder of 2017. *Id.* at 2–6; Pet’r’s Ex. 29 at 3.

On July 3, 2017, A.R. was admitted to CHOA for issues with anemia and dehydration. Pet'r's Ex. 5 at 188. Her history of present illness noted that A.R. had been taking Prograf and Bactrim PCP prophylaxis, but that these were stopped on June 30, 2017, as there had been no improvement in her symptoms. *Id.* A.R.'s chart further noted that she was exclusively on TPN for nutritional support and that her weight had been trending down throughout the month of June. *Id.* at 189. A.R. received intravenous fluids and a blood transfusion and was discharged the following day on July 4, 2017. *Id.*

A.R. presented to Dr. Chandrakasan at the Blood and Marrow Transplant Clinic ("BMTC") at the Aflac Cancer and Blood Disorders Center ("ACBDC") of CHOA on July 25, 2017, where she received an IVIG infusion due to low IgG. Pet'r's Ex. 12 at 496. The next day, on July 26, 2017, additional genetic testing for A.R. returned, which again noted the presence of a "heterozygous variant in the WDFY4 gene." *Id.* at 481. The report indicated that while the laboratory considered the variant to be of unknown significance, the "gene may be associated with systemic lupus erythematosus (SLE) and the risk of rheumatoid arthritis disease." *Id.*

On August 24, 2017, Dr. Benjamin Wilkins reviewed A.R.'s previous biopsies from March and April 2017, which showed villous atrophy, reactive epithelia changes, mild chronic inflammation, and rare crypt apoptosis. Pet'r's Ex. 9 at 354. Dr. Wilkins noted that no "granulomas or viral inclusions [were] identified in any specimen." *Id.* Based on these findings, Dr. Wilkins opined that A.R.'s condition "may be consistent with immune dysregulation or other form of very early-onset inflammatory bowel disease." *Id.* at 355.

A.R. was seen by her PCP, Dr. Marc Tannenbaum, on October 18, 2017, with complaints of persistent coughing. Pet'r's Ex. 25 at 14. Dr. Tannenbaum noted that A.R. was under-immunized and that A.R. "[i]nitially got ill after first [r]otavirus oral vaccine." *Id.* Petitioner reported to Dr. Tannenbaum that "a California consultant to local doctors [had] advised against immunizations because [they] may make [A.R.'s] IBD worse." *Id.* at 14–15.

On February 2, 2018, A.R. presented to Dr. Chandrakasan at ACBDC, where he noted A.R. had recently started on sirolimus and was "tolerating it well." Pet'r's Ex. 43.1 at 372. He also noted that repeat testing of A.R.'s immune functionality on January 31, 2017, showed her immune system was improving. *Id.* at 379. Dr. Chandrakasan added that he had spoken with Petitioner regarding A.R.'s vaccinations, and that he believed A.R.'s IgG and T cell profiles indicated she was safe to be vaccinated, though there was a small chance that vaccines could cause a flare in symptoms. *Id.* at 380. Dr. Chandrakasan also expressed concern regarding A.R.'s frequent hospitalizations with unexplained fever, as he believed these could be the result of immune dysregulation flares due to her inflammation still not being adequately controlled. *Id.*

At the order of Dr. Lewis, A.R. underwent another endoscopy and sigmoidoscopy on May 16, 2018. Pet'r's Ex. 42 at 279. The findings noted that A.R.'s esophagus and stomach appeared normal, however, her duodenum "appeared edematous and friable with pallor and [an] abnormal mucosal pattern." *Id.* Her colon similarly showed additional signs of inflammation. *Id.* Biopsies conducted the same day revealed "duodenal mucosa with partial villous atrophy" and "increased lymphoplasmacytic inflammation within the lamina propria." *Id.* at 284.

From June 24, 2018, to July 5, 2018, A.R. was hospitalized at CHOA “due to risk for central-line associated blood stream infection.” Pet’r’s Ex. 43.3 at 1313–18. During this visit her care team inserted a laparoscopic gastrostomy tube (“G-tube”) to assist with feedings. Pet’r’s Ex. 42 at 340.

A.R. returned to Dr. Lewis on December 12, 2018, who noted she had been experiencing chronic anemia despite intravenous iron treatments. Pet’r’s Ex. 53 at 107. Dr. Lewis also noted that A.R.’s most recent EGD and sigmoidoscopy showed “improvement in the villi and the level of inflammation.” *Id.*

On May 5, 2019, A.R. was admitted to CHOA for a haplo-identical stem cell transplant for her VEO-IBD. Pet’r’s Ex. 42 at 690. She underwent the procedure on May 10, 2019, and was discharged home on June 19, 2019. Pet’r’s Ex. 42 at 719. She received an additional infusion of hematopoietic progenitor cells (“HPC”) on May 14, 2019. *Id.* at 721. A.R. regularly followed up with the CHOA BMTC between July 3, 2019, and August 26, 2019. Pet’r’s Ex. 47.1 at 24, 150, 320, 575, 730, 888, 1046, 1051. On August 26, 2019, A.R. resumed monthly IVIG infusions, which she received through December 14, 2022. Pet’r’s Ex. 47.1 at 1051; Pet’r’s Ex. 47.3 at 2736; Pet’r’s Ex. 77.1 at 383; Pet’r’s Ex. 77.2 at 849, 942; Pet’r’s Ex. 77.4 at 1813; Pet’r’s Ex. 77.6 at 3234; Pet’r’s Ex. 77.7 at 3567; Pet’r’s Ex. 77.8 at 4288, 4625; Pet’r’s Ex. 77.9 at 4865; Pet’r’s Ex. 77.10 at 5579; Pet’r’s Ex. 77.11 at 5910; Pet’r’s Ex. 82 at 509, 746, 1082, 1688, 2446, 2994, 3235, 4129, 5141, 5506, 6055, 6065, 6398, 6639, 6937; Pet’r’s Ex. 84 at 212, 223, 468, 717, 976.

A.R. presented to BMTC on September 6, 2019, for a routine follow-up appointment for post-transplant complications. Pet’r’s Ex. 47.2 at 541. Petitioners reported that A.R. had not been experiencing any fevers since discharge, but A.R.’s feeds had not been able to increase due to her vomiting. *Id.* A.R. returned on September 16, 2019, where Petitioner reported continued vomiting, with “large volume after last feed of [the] day.” *Id.* at 990. After reviewing A.R.’s history of increased vomiting, nutritionist Katherine Keirse, L.D., attributed this to a change in the formula ratio. *Id.* A.R. presented to BMTC again on September 18, 2019, and September 23, 2019, with further complaints of persistent vomiting following feeds and tube flushes. *Id.* 1145; Pet’r’s Ex. 47.3 at 268.

On September 27, 2019, A.R. presented to the ED of CHOA for severe vomiting and bloody stools. Pet’r’s Ex. 47.3 at 558. Petitioners reported that A.R. had vomited blood clots twice the night before and was seeing blood in her stools. *Id.* A.R.’s labs indicated that her hemoglobin levels were stable and her abdominal screenings were unremarkable. *Id.* at 562. She was discharged the same day with instructions to return if symptoms continued. *Id.*

A.R. presented to the Intestinal Rehabilitation Clinic (“IRC”) for her initial appointment with gastroenterologist John-Paul Berauer on November 15, 2019. Pet’r’s Ex. 50.1 at 30. Dr. Berauer noted A.R.’s diagnosis to be “VEO-IBD secondary to WDFY4 mutation.” *Id.* Dr. Berauer noted there was an increasing concern for graft vs host disease [(“GVHD”)] with “increased hepatic transaminases, persistent diarrhea, and erythematous rash in the setting of increasing T-cell chimerism.” *Id.* at 31. Petitioners noted A.R.’s stools were improving to three-to-five times per day with greater consistency after ceasing A.R.’s anti-viral medications. *Id.*

A.R. returned to the BMTC on December 30, 2019, and was seen by Dr. Kirsten Williams. Pet'r's Ex. 50.2 at 972. Dr. Williams opined that A.R.'s persistent diarrhea was likely associated with her underlying VEO-IBD and not her GVHD and continued her on sirolimus for treatment. *Id.* at 977. Dr. Williams also noted that they would consider giving A.R. the influenza vaccine after consulting with her bone marrow transplant team. *Id.*

From January 14, 2020, to January 23, 2020, A.R. was admitted to CHOA for fever, vomiting, diarrhea, and dehydration. Pet'r's Ex. 50.4 at 408. Her blood cultures were positive for *Enterobacter*, *klebsiella*, and *staphylococcus aureus*. *Id.* at 415–16. A.R. completed a seven-day course of antibiotics and was discharged home on January 23, 2020. *Id.* at 462.

On January 30, 2020, A.R. returned to CHOA for a follow-up appointment with gastroenterologist Cary Sauer. Pet'r's Ex. 50.5 at 467. Dr. Sauer noted A.R. had suffered from Crohn's disease that was "inflammatory, non-penetrating, [and] non-stricturing." *Id.* He further noted that A.R. was "asymptomatic and doing very well." *Id.* at 468. A.R.'s plan notes from that visit also indicated that "[i]t is important that immunizations for children with IBD are current," though it also noted that immunosuppressed children should not receive the live influenza vaccine. *Id.* at 471.

A.R. continued with regular follow-ups at the BMTC between February 24, 2020, and October 7, 2020, which detailed gradual improvement of her symptoms and eventually weaned her off of TPN in August 2020. *See generally* Pet'r's Ex. 50. A.R.'s G-tube was removed on June 21, 2021, due to her increasing oral food intake. Pet'r's Ex. 79 at 11. In a July 27, 2021 letter from Dr. Lewis, he indicated that A.R.'s VEO-IBD had since resolved following her bone marrow transplant. Pet'r's Ex. 82 at 7265. A.R. continued regular follow-ups with the BMTC and CHOA through December 2022 and continued her speech and feeding therapy through January 2024. *See generally* Pet'r's Ex. 86; *see also* Pet'r's Ex. 82; Pet'r's Ex. 84.

No other relevant medical records were filed in this case.

III. Petitioners' Affidavit

On April 4, 2018, Ana Oquendo Vazquez filed a brief affidavit. Pet'r's Ex. 14. She stated that A.R. received "the [r]otavirus, pentavalent (ROTATEQ) private . . . vaccine," and did so in the United States. *Id.* at ¶¶ 1–2. She further stated that A.R. "sustained early onset infantile bowel syndrome and malabsorption triggered by the [rotavirus] vaccination," and that A.R. suffered the residual effects of the condition for more than six months. *Id.* at ¶¶ 3–4.

IV. Experts

A. Expert Qualifications

1. Petitioner's Expert, Dr. John Santoro, D.O.⁶

Dr. Santoro submitted one expert report and did not testify at the entitlement hearing. Pet'r's Ex. 31. Dr. Santoro was a gastrointestinal physician in practice with the Atlantic Gastroenterology Associates ("AGA"). *Id.* at 1. He received his D.O. from the Philadelphia College of Osteopathic Medicine. Pet'r's Ex. 32 at 1. He completed his internship and residency at John F. Kennedy Memorial Hospital in Stratford, New Jersey, and a fellowship in gastroenterology at Kennedy Memorial Hospitals University Medical Center. *Id.* at 1–2. Dr. Santoro was board certified in internal medicine and gastroenterology. *Id.* at 2.

At the time of his report, Dr. Santoro served as Medical Director of Clinical Research at AGA. Pet'r's Ex. 31 at 1. He was the Co-Director of AGA's Inflammatory Bowel Disease Center and Director of AGA's Hepatitis Treatment Center. *Id.* Dr. Santoro "cared for more than 300,000 patients during [his] 36-year tenure at AGA and at affiliated medical centers." *Id.* He was one of AGA's "two nationally known physicians specializing in treating IBD." *Id.* Dr. Santoro participated in "numerous clinic research trials . . . including IBD" and has published the results of these trials multiple times. *Id.* at 2.

2. Petitioner's Expert, Dr. Thomas Sferra, M.D.

Dr. Sferra submitted two expert reports and testified at the entitlement hearing. Pet'r's Exs. 58, 78; Tr. 11–80, 215–25. Dr. Sferra is a board-certified pediatric gastroenterologist and the Division Chief of Pediatric Gastroenterology, Hepatology & Nutrition, and the Director of the Pediatric Gastroenterology Fellowship program at University Hospitals Rainbow Babies & Children's Hospital. Pet'r's Ex. 58 at 1–2. He is also a Professor of Pediatrics at Case Western Reserve University. *Id.* at 2. Dr. Sferra completed his M.D. at Northeastern Ohio Universities College of Medicine. Pet'r's Ex. 59 at 3. He completed his residency in pediatrics and fellowship in pediatric gastroenterology at The Ohio State University Children's Hospital, where he then became Chief of Pediatrics. *Id.* at 2–3.

Dr. Sferra is "actively involved in the clinical care of children, education of medical trainees, and medical research." Pet'r's Ex. 58 at 2. He sees "over 2,000 children and adolescents per year . . . with a variety of gastrointestinal symptoms and diseases." *Id.* Dr. Sferra teaches "pediatric gastroenterology fellows, pediatric residents, and medical students in the area of gastrointestinal diseases, including the diagnosis and care of those with gastrointestinal infections and inflammatory bowel disease including the very early onset type." *Id.* Throughout his career, Dr. Sferra has "diagnosed an estimated 250 patients with inflammatory bowel disease" and been involved with the care of over 100 during the past two years. *Id.* at 1.

⁶ Petitioner's expert, Dr. Santoro, unfortunately passed away during the proceedings of this case.

3. Respondent's Expert, Dr. Chris Liacouras, M.D.

Dr. Liacouras submitted three expert reports and testified at the entitlement hearing. Resp't's Ex. A; Resp't's Ex. C; Resp't's Ex. G; Tr. 81–145. Dr. Liacouras is a board-certified pediatric gastroenterologist with more than 25 years of clinical practice. Resp't's Ex. A at 5. He is currently a Professor of Pediatrics at the Perelman School of Medicine at the University of Pennsylvania and the Children's Hospital of Philadelphia ("CHOP") in the Division of Gastroenterology, Hepatology, and Nutrition. *Id.* He is also the Medical Director of the Children's Hospital of Philadelphia's Center for Gastrointestinal Endoscopy and the Chairman of Pediatric Endoscopy for the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition. *Id.* Dr. Liacouras received his M.D. from Harvard University. Resp't's Ex. B. at 1. He completed his internship in Pediatrics, as well as his residency and fellowship in Pediatric Gastroenterology at CHOP. *Id.*

Dr. Liacouras has "extensively published in the field of pediatric gastroenterology" and has evaluated between 2,000 to 3,000 pediatric patients "every year since 1991." Resp't's Ex. A at 5. He has "personally evaluated or consulted on more than 2,000 pediatric patients who have had inflammatory bowel disease" and has been "directly or indirectly involved in the care of more than 1,500 patients with IBD and at least 50 patients with VEO-IBD." *Id.*

4. Respondent's Expert, Dr. Neil Romberg, M.D.

Dr. Romberg submitted two expert reports and testified at the entitlement hearing. Resp't's Ex. D; Resp't's Ex. F; Tr. 145–214. Dr. Romberg is an Assistant Professor of Pediatrics at the University of Pennsylvania and an attending physician at CHOP where he holds the Jeffrey Modell Endowed Chair of Pediatric Immunology Research. Resp't's Ex. D at 1. He received his M.D. from Pennsylvania State University College of Medicine. Resp't's Ex. E at 1. He completed his residency at New York University School of Medicine and his fellowship in Allergy and Clinical Immunology at Yale University School of Medicine. *Id.* He also completed a six-year research position at Yale University in the Department of Immunobiology studying immune tolerance in humans. Resp't's Ex. D at 1.

The focus of Dr. Romberg's career has been "to care for patients with inherited immunological disorders and to investigate the molecular mechanisms that underlie their diseases." Resp't's Ex. E at 1. He heads a laboratory funded by the National Institutes of Health which "investigates immunologic tolerance in humans." *Id.* Over the last five years, Dr. Romberg has "cared for approximately 80 children with inflammatory bowel disease," primarily as a consultant. *Id.* at 2. He is also "often called to consult on the sickest VEOIBD inpatients at CHOP as part of a multi-disciplinary Immune Dysregulation team." *Id.* Dr. Romberg's research laboratory also "discovered one of the monogenic forms of VEO-IBD, Autoinflammation with Infantile Enterocolitis," in 2014. *Id.*

B. Expert Reports and Testimony

1. Report of Dr. Santoro

Dr. Santoro's ultimate impression was that "the rotavirus vaccine triggered an autoantibody against [A.R.'s] intestinal epithelial cells through molecular mimicry similar to antibodies against the myelin sheath in [Guilain-Barré syndrome ("GBS")] after influenza vaccination." Pet'r's Ex. 31 at 11. "Molecular mimicry occurs when a pathogen expresses a protein that is remarkably similar in sequence or shape to a protein in the host." *Id.* Dr. Santoro explained that there is "an increased risk of IBD among persons who had critical events at birth or within the first year of life, which would be expected to lead to alterations in the gut microbiome." *Id.* He likened this to A.R.'s receipt of the rotavirus vaccine and subsequent rotavirus shedding in her stool "long after the [rotavirus] vaccination." *Id.* Dr. Santoro argued that such events "have been shown to promote alterations in the composition of the gut microbiome in the first year of life and may have important effects on its more permanent composition" and "may have impacted on the ultimate development of IBD." *Id.* at 11–12.

Dr. Santoro began by providing a brief background on IBD, noting that "[t]he exact cause of IBD is not known, but researchers believe ulcerative colitis and Crohn's disease are caused by a combination of factors that involve genetics, the environment, and an overactive or dysregulated immune system." Pet'r's Ex. 31 at 6. "It is currently believed that loss of tolerance against indigenous enteric flora is the central event in IBD pathogenesis . . . [through] defects in regulatory T-cell function, excessive stimulation of mucosal dendritic cells, [and] infections or variants of proteins critically involved in bacterial antigen recognition." *Id.* at 7 (citing Pet'r's Ex. 41).⁷ "Homeostasis in the gut involves a balance between anti-inflammatory and pro-inflammatory signals . . . [and] a failure to maintain this balance is exemplified by patients with immune dysregulation." *Id.* (citing Pet'r's Ex. 39).⁸ Dr. Santoro opined that "[i]t would not be hard to imagine that any perturbation of the immune system such as vaccination could result in dysregulation of this delicate balance and homeostasis." *Id.*

Dr. Santoro relied on Bernstein et al.⁹ to support his argument that individuals who sustain "critical events" within their first year of life are more susceptible to developing IBD due to the sensitivity of the gut microbiome at this point in life. Pet'r's Ex. 31 at 7–8 (citing Pet'r's Ex. 35). Bernstein et al. found that individuals who experience infections in the first year of life are at "increased risk for developing IBD at any age." Pet'r's Ex. 35 at 1. Because "[t]he gut microbiome undergoes the most change from birth until [one-to-two] years of age . . . events that promote alterations in the composition of the gut microbiome may have important effects on its more permanent composition." *Id.* at 2. The study ultimately concluded that "infections in the first year of life were predictive of development of IBD at any age and with the strongest association for infections in the first year of life and development of IBD before age 10 years." *Id.* at 5. The study

⁷ Zhonghui Wen & Claudio Fiocchi, *Inflammatory Bowel Disease: Autoimmune or Immune-Mediated Pathogenesis?*, 11 CLINICAL & DEVELOPMENTAL IMMUNOLOGY 195 (2004).

⁸ Bernard Khor et al., *Genetics and Pathogenesis of Inflammatory Bowel Disease*, 474 NATURE 307 (2011).

⁹ Charles N. Bernstein et al., *Events Within the First Year of Life, but Not the Neonatal Period, Affect Risk for Later Development of Inflammatory Bowel Diseases*, 156 GASTROENTEROLOGY 2190 (2019).

further noted that they did “not believe the risk posed by infections in the first year of life was secondary to persons with IBD being more likely to have an immunodeficiency disorder; disorders that can often present with an IBD-like picture.” *Id.* at 6. However, Bernstein et al. specifically noted that “[g]astrointestinal illnesses in the first year of life, including abdominal pain, were not found to be associated with later development of IBD.” *Id.* at 7.

Dr. Santoro next turned to his explanation of molecular mimicry and the development of autoimmune diseases after vaccination. He explained that “[a]lthough the triggering event in most autoimmune diseases is unknown, an infectious cause has long been postulated to explain the development of autoimmunity,” and noted that the process of molecular mimicry is one such explanation. Pet’r’s Ex. 31 at 8. Relying on Albert & Iman,¹⁰ Dr. Santoro explained his theory as follows:

Molecular mimicry occurs when a pathogen expresses a protein that is remarkably similar in sequence or shape to a protein in the host . . . this can lead to the body creating an immune response, not just to the introduce vaccine antigen, but to normal components of one’s self, thereby leading to an autoimmune reactions (sic) and disease.

Id. Dr. Santoro also pointed to examples of influenza virus proteins and H1N1 vaccinations creating similar autoimmune reactions in individuals to support the plausibility of his theory. *Id.* at 8–9. (citing Pet’r’s Ex. 40).¹¹ He also cited to Benn et al.¹² to support an overall theory that vaccines generally “have nonspecific effects on the ability of the immune system to handle other pathogens.” *Id.* at 9 (citing Pet’r’s Ex. 34). Specific to instances of IBD, Dr. Santoro cited to instances of gastrointestinal diseases following human papillomavirus (“HPV”) vaccination, noting “several flares of pre-existing IBD occurred in patients who had received [the] HPV [vaccine].” Pet’r’s Ex. 31 at 9 (citing Pet’r’s Ex. 36; Pet’r’s Ex. 37).¹³

Turning to A.R.’s case, Dr. Santoro opined that “one could expostulate that the rotavirus vaccine triggered an autoantibody against [A.R.’s] intestinal epithelial cells through molecular mimicry similar to antibodies against the myeline sheath in GBS after influenza vaccination.” Pet’r’s Ex. 31 at 11. He argued that A.R.’s receipt of the rotavirus vaccine and subsequent rotavirus shedding constitutes an event “shown to promote alterations in the composition of the gut microbiome in the first year of life,” and thus “may have impacted on the ultimate development of IBD in [A.R.]” *Id.* at 11–12. Accordingly, he argued that the rotavirus vaccine “was more likely than not responsible for [A.R.’s] development of colitis, diarrhea, and rectal bleeding.” *Id.* at 12.

¹⁰ Lori J. Albert & Robert D. Inman, *Molecular Mimicry and Autoimmunity*, 341 NEW ENGLAND J. MED. 2068 (1999).

¹¹ C. Pauwels et al., *Cytophagic Histiocytic Panniculitis After H1N1 Vaccination: A Case Report and Review of the Cutaneous Side Effects of Influenza Vaccines*, 222 DERMATOLOGY 217 (2011).

¹² Christine S. Benn et al., *A Small Jab – A Big Effect: Nonspecific Immunomodulation by Vaccines*, 34 TRENDS IN IMMUNOLOGY 431 (2013).

¹³ Denise L. Jacobson et al., *Immunogenicity and Tolerability to Human Papillomavirus-like Particle Vaccine in Girls and Young Women with Inflammatory Bowel Disease*, 19 INFLAMMATORY BOWEL DISEASE 1441 (2013).

With regard to the temporal relationship between vaccination and the onset of A.R.'s symptoms, Dr. Santoro opined that while “[t]here is no definite answer to the question in the scientific literature,” he believed the course of A.R.'s symptoms following vaccination to be “medically appropriate.” Pet’r’s Ex. 31 at 12. He noted that the timeline of three days following immunization and the onset of A.R.’s symptoms was medically appropriate, and that there is “no evidence . . . that [A.R.] suffered from inflammatory bowel disease prior to her developing it post the [r]otavirus [] vaccination and an acute rotavirus enterocolitis.” *Id.*

A. Reports and Testimony of Dr. Sferra

In his first expert report, Dr. Sferra opined that A.R.’s injury was caused by a dysregulated immune response and proposed three possible mechanisms: “disruption of the intestinal mucosal barrier during the normal immune response of the intestine to a viral infection[,] . . . molecular mimicry[, and] . . . bystander activation.” Pet’r’s Ex. 58 at 3. He noted that there was a logical sequence of cause and effect that the vaccine was the cause of A.R.’s injury because “[t]he vaccine was administered [three] days prior to the development of the most severe symptoms. This is sufficient time for the virus to replicate and induce an immune response.” *Id.* at 4. He also opined that A.R. did not have monogenic VEO-IBD,¹⁴ “thus it is more likely than an environmental trigger played an etiologic role.” *Id.* He further opined that there was an appropriate temporal relationship between the vaccine and A.R.’s injury, as “the incubation period for symptoms and thus the triggering of the immune response [to a wildtype rotavirus infection] is [one-to-three] days.” *Id.* Accordingly, “it is reasonable to conclude that the intestinal immune response toward the vaccine would occur within a similar time.” *Id.* Dr. Sferra concluded that “the [rotavirus] vaccination was a substantial factor and proximate cause of the VEO-IBD and resultant long-term gastrointestinal symptoms.” *Id.*

In his second expert report, Dr. Sferra acknowledged that A.R. had “less than optimal weight gain between the first and second months of life,” however, he noted this was not uncommon and not a concern for intervention by A.R.’s pediatrician. Pet’r’s Ex. 78 at 1. He pointed to A.R.’s medical record from her date of vaccination to show that A.R. had not been experiencing any significant symptoms of IBD prior to vaccination and had only been reported to have “occasional reflux.” *Id.* at 2 (citing Pet’r’s Ex. 1 at 15). Dr. Sferra also averred to A.R.’s whole exome sequencing, which showed “[n]o significant abnormalities . . . that would stop a protein from being produced or lead to an abnormal protein,” and thus “there is no evidence of a monogenic disease.” *Id.* at 3.

Dr. Sferra relied on Tarris et al.¹⁵ to support his theory that “viruses can be triggers of inflammation in patients with IBD.” Pet’r’s Ex. 78 at 5 (citing Pet’r’s Ex. 74). The article examined the impact of human noroviruses and rotaviruses on IBD flare-ups, noting that IBD is “influenced by microbial factors . . . [and] confounding variables such as diet, age, smoking, or psychological stress.” Pet’r’s Ex. 74 at 8. The study found that increased levels of interferons could “induce an antiviral gene expression cascade following norovirus or rotavirus infections.” *Id.* at 7. However,

¹⁴ As discussed by Dr. Sferra in his later testimony, there are generally two forms of VEO-IBD: monogenic, which is directly caused by a single genetic defect, and multigenic, where multiple genetic factors are at play. *See* Tr. 20: 24–25, 21:1–6.

¹⁵ George Tarris et al., *Enteric Viruses and Inflammatory Bowel Disease*, 13 *VIRUSES* 104 (2021).

the study also noted that “enteric viruses could alleviate intestinal inflammation via the production of IFN β , mediated by toll-like receptors.” *Id.*

Dr. Sferra also pointed to the study by Hubbard & Cadwell¹⁶ to show that viruses could indirectly cause IBD through a combination of genetic background and environmental exposures. Pet’r’s Ex. 78 at 5 (citing Pet’r’s Ex. 70) The study, which focused on analyzing the relationship between viruses, genetics, and Crohn’s disease, observed that Crohn’s disease “is associated with numerous variants rather than a single mutation.” Pet’r’s Ex. 70 at 2. However, “[d]espite the identification of many genetic susceptibility loci, they collectively account for only a third of the disease risk,” and that “pathogens represent one group of environmental factors that are likely to be a key component to inflammatory bowel diseases.” *Id.* at 4. Hubbard & Cadwell also found that “acute gastroenteritis . . . precedes diagnosis of inflammatory bowel disease in some individuals [], and there is evidence that noroviruses exacerbate inflammatory bowel disease.” *Id.* at 5. Due to the role of T cells in mediating intestinal inflammation in mouse models, the study contemplated that it would not be “difficult to imagine a scenario in which a viral infection would alter the total number and function of a subset of T cells that mediate chronic inflammatory disease.” *Id.* at 5–6. The study also observed that “a breakdown in intestinal barrier function is a hallmark of inflammatory bowel disease [] and a realistic mechanism by which a virus could trigger intestinal disease.” *Id.* at 16. However, the study cautioned that such viral triggers “would only be true for individuals of a certain genetic background.” *Id.*

During his testimony, Dr. Sferra explained the primary difference in pathology between VEO-IBD and IBD was that VEO-IBD is “more commonly caused by a single gene disorder,” meaning that it is “a single gene that has been identified that is the direct cause of the disorder.” Tr. 20:15–16, 21:1–2. Conversely, multigenic or polygenic disorders “don’t have a single genetic defect identified but also there could be . . . environmental triggers, other causes of genetic susceptibility, and also just a disruption of the immunologic process, usually due to . . . dysbiosis or alteration of the intestinal bacteria.” Tr. 21:11–16.

Addressing A.R.’s weight trends prior to vaccination, Dr. Sferra testified that A.R. was 19.5 inches long and weighed six pounds, five ounces at an age of three days, and had normal eliminations and gastrointestinal functions. Tr. 22:7, 10–11, 23:14. Dr. Sferra testified that at A.R.’s one-month visit, there were no concerns, a normal physical examination, with normal breastfeeding and elimination, and that A.R.’s length was 21.2 inches with a weight of nine pounds, six ounces. Tr. 24:11–25. He continued that at her two-month wellness visit, which was the date of vaccination, A.R. only presented with occasional reflux, and “specifically noted, no vomiting, no loss of appetite, and no diarrhea.” Tr. 26:2–5. Dr. Sferra also testified that A.R. previously was “feeding longer per side, as noted in the report, and also had more feedings overnight.” Tr. 26: 24–25. He further testified that there was nothing abnormal with A.R.’s development skills and that she weighed ten pounds, two ounces at a length of 22 inches. Tr. 27:4–8.

Dr. Sferra next testified about failure to thrive (“FTT”), which he described as “the failure or [] the lack of normal growth or prolonged inadequate maintaining normal growth in a child,” which is caused by “inadequate caloric intake, or inadequate absorption of calories or excessive

¹⁶ Vanessa M. Hubbard & Ken Cadwell, *Viruses, Autophagy Genes, and Crohn’s Disease*, 3 VIRUSES 1281 (2011).

expenditure of those calories.” Tr. 28:18–20, 29:2–3. He explained FTT was “fairly common” in the first year of life for babies, and that “at least one manuscript that reviewed this said up to 27 percent of infants meet one definition for [FTT] in year one.” Tr. 29:22–25. Dr. Sferra testified that the Cole & Lanham¹⁷ article found that when diagnosing FTT, “any single indicator has a low positive predictive value” for diagnosis, which is why weight-for-age tables are not reliable indicators of FTT. Tr. 29:17–18 (citing Resp’t’s Ex. D, Tab 7). Instead, the authors recommended “weight for length measurements” as the better method for determining failure to thrive. Tr. 30:8. Based on these metrics, Dr. Sferra testified that A.R. was not below the fifth percentile of growth based on her weight for length measurements, and thus was not suffering from FTT prior to vaccination. Tr. 30:12–15. He instead attributed A.R.’s decreased weight gain to inadequate caloric intake and not any form of IBD preceding vaccination, as “she was [had] normal elimination and . . . she had a reduc[ed] breastfeeding time per breast and also [did not receive] feedings overnight.” Tr. 30: 20–23. Dr. Sferra also testified that A.R.’s treating physician did not feel FTT was a concern at this visit because she recommended increased breastfeeding at decreased intervals, but “did not feel it necessary to give additional supplementation” through the form of additional formula. Tr. 31:12–13.

Regarding A.R.’s initial ED visit following vaccination, Dr. Sferra testified that A.R. had been seen for vomiting and diarrhea, and that “it’s reported that the vomiting was occurring after each feeding for the past six days.” Tr. 32:6–7. However, he also explained that the dates of A.R.’s reported symptoms in the record did not appear to be accurate. Tr. 32:2–8. “[T]his visit was on [February 11], but she was seen [by her pediatrician] on [February 8]. So a couple days earlier, [she] did not have [vomiting and diarrhea] recorded as a problem. And then they said they saw the pediatric five days ago, and that was an inaccurate statement.” Tr. 32:9–13. Dr. Sferra stated that A.R. was hospitalized for three days with rotavirus enteritis and that, based on his expertise, there was nothing that would have raised concerns for VEO-IBD at this point in time. Tr. 33:1–15.

When asked about A.R.’s February 15, 2016 hospitalization, Dr. Sferra testified that he believed this was “the beginning of the acute process of the very early onset IBD.” Tr. 34:17–18. He explained that a sigmoidoscopy and upper endoscopy completed on March 7, 2016, revealed “acute enteritis involving the small bowel and colon,” and immunologic staining and electron microscopy confirmed “an inflammatory enteropathy with colonic involvement.” Tr. 35:20–21, 36:6–8. At this time, A.R.’s differential diagnoses included immune-mediated injury, post-infectious allergic reaction, and allergic enteropathy. Tr. 36:12–14. Due to the accumulation of lipids in A.R.’s enterocytes, Dr. Sferra opined that A.R. had “a[n] inflammatory process that [was] affecting the gastrointestinal tract.” Tr. 37:1–3.

Dr. Sferra also explained that A.R.’s immunology team conducted “extensive studies looking at [T cells] for immunodeficiencies [which] did not find any abnormalities,” in addition to genetic testing. Tr. 38:23–25. Dr. Sferra testified that “this was a whole exome sequencing, so it looked at all the protein expression region of [A.R.’s] DNA, and there was no established clinically significant areas [] identified which could explain the primary clinical concerns in this patient.” Tr. 39:16–20. Dr. Sferra continued that when A.R.’s genetic data was reevaluated for minor abnormalities, “they did identify . . . that there was a possible abnormality in the gene called WDFY4.” Tr. 40:12–13. He explained that sequencing of the gene itself showed “there was a

¹⁷ Reminder to cite this.

mutation in only one of the two chromosomes . . . which makes it unlikely to be a disease-causing variant for this type of condition.” Tr. 40:17–20. Accordingly, because the gene would “be making a normal protein and then a mildly abnormal protein,” Dr. Sferra did not believe that it would adversely affect the function of the protein that would be made. Tr. 40:21–24. When asked about Dr. Chandrakasan’s note expressing concern about mutations in both alleles of the gene, Dr. Sferra stated the concern was invalid because “this report was done prior to the more sophisticated or the more specific testing of this gene,” and that Dr. Chandrakasan noted the gene itself was nonpathologic in humans and “not a phenotype of a broader immune dysregulation.” Tr. 41:13–21, 42:3–4. Dr. Sferra continued that Dr. Chandrakasan was the first to mention the possibility of a bone marrow transplant, and that it “can be curative if a genetic defect existed that affected the [gastrointestinal] integrity or barrier function. If not, . . . it would not be curative.” Tr. 43:6–9.

By April 2017, Dr. Sferra explained that A.R.’s imaging showed “abnormalities of the small bowel . . . with villous atrophy and active inflammation,” and “regenerative changes within her colon.” Tr. 44:1–6. At this time, he testified that A.R.’s records reflected that she was taking Entyvio, Prograf, and Rapamune to manage her illness in order to inhibit T lymphocyte activation and reduce her immune response. Tr. 44:14–25. Dr. Sferra also observed that a later review of A.R.’s April imaging and tests by Dr. Kelsen found “no granulomas or viral inclusions . . . [and] no evidence of epithelial abnormality,” which “would be consistent with an immune dysfunction or other form of very early onset IBD.” Tr. 45:15–20.

Jumping ahead to May 2018, Dr. Sferra was asked about A.R.’s endoscopy-sigmoidoscopy, which he testified revealed friability in the stomach, “but otherwise not inflamed. The duodenum was edematous and friable and had an abnormal mucosal pattern. The colon also had an abnormal mucosal pattern and was friable, suggestive of a diffuse injury or inflammation.” Tr. 46:1–7. He interpreted these results as showing “some repair and resolution of the inflammation” from the initial onset. Tr. 46: 11–12. He further observed that A.R. continued to have inflammation present at consults in January and February 2019, but that she had discontinued her steroids. Tr. 48:19–24. Following A.R.’s bone marrow transplant in May 2019, Dr. Sferra noted that A.R. continued to suffer from chronic rotavirus shedding and intermittent infections, which he attributed to her immunosuppression and injured bowel. Tr. 49:22–23. A.R. continued to receive IVIG and sirolimus, which Dr. Sferra opined was due to concerns with the bone marrow transplant and any additional intestinal inflammation. Tr. 50:14–20. He noted that another endoscopy-sigmoidoscopy conducted in August 2020 revealed “mild inflammation in the small bowel and . . . the terminal ileum had some mild inflammation . . . demonstrat[ing] that there was improvement in her disease.” Tr. 51:5–8. On cross-examination, Dr. Sferra agreed that A.R.’s VEO-IBD resolved following her bone marrow transplant. Tr. 72:14–17.

Turning to A.R.’s receipt of the rotavirus vaccine, Dr. Sferra acknowledged that he was not aware of any literature or studies that associated rotavirus with VEO-IBD. Tr. 53:12–13. Instead, he relied on an association between enteric viruses and IBD, explaining that “it’s generally recognized that a previous gastroenteritis or a viral gastrointestinal infection can be a precursor or a risk factor for inflammatory bowel disease.” Tr. 53:19–22. Dr. Sferra further pointed to the notes of A.R.’s treating physicians, primarily Dr. Lewis, who stated that A.R.’s “inflammatory bowel disease and possible immune disorder enteropathy start[ed] after the rotavirus vaccine,”

specifically noting multiple references to “onset follow[ing] the [rotavirus] vaccination.” Tr. 54:3–8.

Dr. Sferra also acknowledged that in some cases VEO-IBD is “due to a single-gene defect, but in other cases it is not.” Tr. 54:24–25. He also acknowledged that not every GI illness will put a person at risk for IBD or VEO-IBD, but “there is a known association or a risk factor of intestinal inflammation from a[n] infectious etiology that can be the precursor to inflammatory bowel disease.” Tr. 55:4–6.

Dr. Sferra next turned to his medical theories in the case, starting with dysregulation and disruption of the mucosal barrier. He explained that “dysregulation can occur via several different or perhaps interacting mechanisms, and this would be the disruption of the intestinal mucosal barrier,” which would occur “during the normal immune response to the viral infection and expose the immune system to gut resident bacteria, and that would lead to this abnormal immune response.” Tr. 57:10–16. He explained that this occurs when there “is a disruption of the flora within the gastrointestinal tract that includes . . . some viruses, and that . . . if this becomes disrupted or abnormal . . . that could lead to a breakdown in [the] intestinal barrier and subsequently to this whole process of autoimmunity or inflammatory bowel disease.” Tr. 58:1–6. He continued that in the case of A.R., it would “be the cascade of events of having the diarrhea. . . so that would . . . perhaps change the microbiome, so it’s possible that an acute gastrointestinal infection could lead to dysbiosis.” Tr. 58:11–15. He noted that naturally the microbiome is anti-inflammatory, however, “a change in the bacteria that you have [] turns [it] to a proinflammatory state. This disrupts the barrier and then allows the bacteria to come through, and these are then attacked and may then trigger this inflammatory process.” Tr. 59:1–19.

When discussing the possible environmental factors that could ignite this process, Dr. Sferra pointed to Glassner et al.,¹⁸ which listed enteric infections as a factor that could start the pro-inflammatory response, and Dr. Sferra noted that rotavirus is a kind of enteric infection. Tr. 59:20–23 (citing Pet’r’s Ex. 61 at 5). He also discussed Axelrad et al.,¹⁹ which looked “at the role of gastrointestinal pathogens and [] their effect on the microbiota of the intestines. [I]t describe[d] how a dysbiotic state or changes in the . . . bowel can lead to an immune response, and this then could lead to IBD,” specifically noting that the article listed enteric infections as an environmental trigger. Tr. 60:12–17.

He also opined that “[a]nother mechanism is molecular mimicry[,] in which the pathogen carries structural[ly] similar antigens to self-antigen and the body responds abnormally to that.” Tr. 57:17–19. He later clarified on cross-examination that he believed the vaccine A.R. received caused the rotavirus infection, which then could have led to molecular mimicry as the body attempted to fight off the infection. Tr. 224:11–19.

Dr. Sferra also posited that bystander activation could have caused A.R.’s VEO-IBD, “where you have inflammation that’s ongoing directed against the virus, but . . . the response

¹⁸ Kerri L. Glassner et al., *The Microbiome and Inflammatory Bowel Disease*, 145 J. ALLERGY CLINICAL IMMUNOLOGY 16 (2019).

¹⁹ Jordan E. Axelrad et al., *The Role of Gastrointestinal Pathogens in Inflammatory Bowel Disease: A Systemic Review*, 14 THERAPEUTIC ADVANCES IN GASTROENTEROLOGY 1 (2021).

exceeds that and triggers autoimmunity.” Tr. 57:20–22. He relied on Smatti et al.²⁰ to explain how “the inflammatory response occurs due to a pathogen and . . . [if] the brakes are not put on it . . . it could spiral out of effect and then . . . attack your own cells and cause a[n] autoimmune process.” Tr. 61:9–13. He continued that “some studies have identified particular viruses in the [gastrointestinal] tract, and . . . the attack of those viruses would lead to this bystander effect or the autoimmunity.” Tr. 61:20–24. Because rotavirus is a form of enteric virus, Dr. Sferra opined that such an infection could have caused bystander activation in A.R.’s case. Tr. 62:1–5. On cross-examination Dr. Sferra testified that he believed bystander activation to be the most likely of his proposed biological mechanisms. Tr. 77:14–17. He later summarized his proposed mechanisms as follows:

[T]he vaccine led to a rotavirus infection, a vaccine-induced infection. It was the vaccine that’s replicating within the [gastrointestinal] tract . . . and caused her symptoms of diarrhea. That in an of itself is what then either – there’s a bystander effect directly to the virus, or . . . molecular mimicry, because it’s ongoing then. Those also induced then the breakdown of the epithelial barrier. Virus infections that effect the intestinal cells breakdown the barrier because it kills those cells. Those cells die and slough off, so it is the effect. But then the immune response goes in to try to clear those cells or to repair it, and you can lead to . . . a cascade of events. Then you . . . have this process that’s ongoing, causing additional inflammatory elements to come into play. And at some point, it’s triggered to where . . . you start attacking yourself.

Tr. 224: 12–25, 225:1–7.

When asked about whether other viral pathogens had been associated with the development of IBD or VEO-IBD, Dr. Sferra explained that “there has not been strong literature saying, these are absolutely viruses that cause it. It’s more that in a particular individual that has a particular . . . genetic make up, and then the environmental factor is any virus that triggers this autoimmune response.” Tr. 62:17–21. He continued by noting that such viruses are not a direct cause of IBD themselves, but rather the specific timing of the infection and the susceptibility of the individual triggers the inflammatory response. Tr. 63:3–6.

He next turned to rotavirus as a specific trigger of bystander activation and inflammation, explaining that Blacklow & Greenberg²¹ showed that the clinical progression of rotavirus could cause severe inflammation, with an incubation period of one to three days. Tr. 64:22–25, 65:1–4 (citing Pet’r’s Ex. 75). He then opined that this was consistent with the presentation of A.R.’s symptoms, as “within three days [of vaccination] she did develop significant symptoms of vomiting and diarrhea.” Tr. 65:12–13. Dr. Sferra further acknowledged the report of A.R. experiencing diarrhea one day after receipt of the rotavirus vaccine, which he stated would not be inconsistent with the rotavirus incubation observed by Blacklow & Greenberg. 66:9–16. He continued by opining that reports of reflux in the days prior to vaccination were not sufficient to show that A.R.’s IBD pre-dated her vaccination, as “[r]eflux in neonates or infants is extremely common, and when it’s mild, as described in her medical record, that is not considered a sign of

²⁰ Maria K. Smatti et al., *Viruses and Autoimmunity: A Review on the Potential Interaction and Molecular Mechanisms*, 11 *VIRUSES* 762 (2019).

²¹ Neil R. Blacklow & Harry B. Greenberg, *Viral Gastroenteritis*, 325 *NEW ENGLAND J. MED.* 252 (1991).

IBD.” Tr. 66:8–10. He added that reflux is a gastroesophageal problem involving the stomach and the esophagus, not the intestines. Tr. 66:11–14. On cross-examination, Dr. Sferra admitted that if A.R.’s symptoms began less than 24 hours after vaccination, it would be too soon to attribute to the rotavirus vaccine. Tr. 71:11. However, when I asked Dr. Sferra about his understanding of A.R.’s symptom onset, he stated that her symptoms began “the next day” after her vaccination, with a minimum of 24 hours between vaccination and symptom onset. Tr. 73:12–20.

When asked about the difference in clinical progression for the biological mechanisms he proposed, Dr. Sferra testified that the given timeframe of 24 hours would be consistent with all three, and that he would not expect to see any difference in progression of symptoms between the three theories. Tr. 74:16. He continued that there was no evidence towards the possibility that the rotavirus vaccine significantly aggravated a pre-existing IBD condition in A.R. Tr. 74:21–25. Dr. Sferra later clarified on re-direct examination that he did believe A.R. likely had a genetic predisposition to IBD that was likely triggered by the vaccine due to A.R.’s family history of autoimmune diseases, which he relied on in addition to the timing of symptoms following vaccination. Tr. 216:7–14.

In response to a question regarding why the gastrointestinal tract was specifically involved in A.R.’s case given that bystander activation and molecular mimicry can apply to wide range of biological systems, Dr. Sferra opined that this was due to the inherent genetic predisposition that precedes IBD, and that any vaccine “that affects the [gastrointestinal] tract in a similar manner” would have caused these triggers in A.R. Tr. 76:1–6. He further testified that he had not seen any patients who developed IBD from rotavirus and that in the case of other gastrointestinal infections, he could not determine whether the infection occurred prior or subsequent to the development of IBD. Tr. 78:1–5. However, he testified that it was clear in the case of A.R. due to the timing of vaccination, as “she was healthy before and then this triggered it.” Tr. 78:11–12.

On re-direct examination, Dr. Sferra testified that a note from Dr. Lee indicated he did not believe A.R. to have an immunodeficiency disorder because he had specifically ruled out T cell immunodeficiency. Tr. 218:14–25 (citing Pet’r’s Ex. 10 at 42).

B. Reports and Testimony of Dr. Liacouras

In his first expert report, Dr. Liacouras opined that A.R.’s VEO-IBD “was more likely than not related to a combination of genetic and autoimmune abnormalities and not a single trigger, such as the rotavirus vaccine.” Resp’t’s Ex. A at 6. He stated that A.R. was experiencing “significant vomiting and decreased weight gain” prior to the receipt of the rotavirus vaccine. *Id.* Dr. Liacouras dismissed A.R.’s stool samples that tested positive for rotavirus as indicative of a rotavirus infection because “shedding of rotavirus occur[s] . . . in patients who receive[] the rotavirus vaccine” regardless of whether they suffer symptoms. *Id.* He also noted that A.R.’s treating physicians opined that rotavirus was not the cause of A.R.’s disease as her treatment progressed. *Id.*

Dr. Liacouras further argued that there was no association between enteric viruses and the development of IBD. Resp't's Ex. A at 6. He cited to Gebhard et al.,²² which concluded "that the common types of acute viral gastroenteritis do not represent a numerically significant risk factor for the activity and relapses of inflammatory bowel disease" and "vaccines directed against enteric viruses would not have a significant impact on the incidence of inflammatory bowel disease exacerbations." *Id.* at 7 (citing Resp't's Ex. A, Tab 7). He further noted that "multiple studies have been performed to evaluate possible side effect to the rotavirus vaccine," and the only significant adverse effect to be found is intussusception.²³ *Id.* (citing Resp't's Ex. A, Tab 8;²⁴ Resp't's Ex. A, Tab 9).²⁵ Dr. Liacouras also contested Dr. Santoro's reliance on A.R.'s rotavirus shedding, noting that Yen et al.²⁶ found that 21% of infants shed rotavirus following vaccination. *Id.* at 8 (citing Resp't's Ex. A, Tab 16). He continued that A.R.'s symptoms were inconsistent with typical progression of a rotavirus infection, citing to Lee et al.²⁷ which showed "25% of patients develop[ed] symptoms in 1.6 days and 75% of patients develop[ed] symptoms in 2.5 days." *Id.* (citing Resp't's Ex. A, Tab 15). Dr. Liacouras also argued that no reports existed that identified any relationship between any vaccine and IBD, and cited to studies by Angelo et al.²⁸ and Davis et al.²⁹ which showed that there was no statistically significant relationship between the HPV and measles, mumps, and rubella vaccines and the development of IBD. *Id.* (citing Resp't's Ex. A, Tab 11; Resp't's Ex. A, Tab 12).

Dr. Liacouras next took issue with Dr. Santoro's theory of molecular mimicry, arguing that it was "based solely on theory and not documented scientific evidence based on accepted large cohort studies." Resp't's Ex. A at 9. He also argued that Dr. Santoro failed to address A.R.'s vomiting and weight loss prior to vaccination. *Id.*

In his second report, Dr. Liacouras argued that the literature presented by Dr. Sferra "lack[ed] proof that the rotavirus vaccine directly causes VEO-IBD, but also contain[ed] statements that refute his hypothesis that the rotavirus vaccine caused A.R.'s disease state." Resp't's Ex. C at 3. He pointed to Dr. Sferra's reliance on Tarris et al. and noted that the study found "vaccination against major enteric viruses (i.e. rotavirus and norovirus) could be a means of improving the management of patients suffering from IBD." *Id.* (citing Pet'r's Ex. 74 at 8–9). He

²² R.L. Gebhard et al., *Actute Viral Enteritis and Exacerbations of Inflammatory Bowel Disease*, 83 GASTROENTEROLOGY 1207 (1982).

²³ Intussusception is a "prolapse of one part of the intestine into the lumen of an immediately adjoining part." *Intussusception*, DORLAND'S ONLINE MED. DICTIONARY.

²⁴ Guillermo M. Ruiz-Palacios et al., *Safety and Efficacy of an Attenuated Vaccine Against Severe Rotavirus Gastroenteritis*, 354 NEW ENGLAND J. MED. 11 (2006).

²⁵ Timo Vesikari et al., *RotaTeq, A Pentavalent Rotavirus Vaccine: Efficacy and Safety Among Infants in Europe*, 28 VACCINE 345 (2010).

²⁶ Catherine Yen et al., *Detection of Fecal Shedding of Rotavirus Vaccine in Infants Following Their First Dose of Pentavalent Rotavirus Vaccine*, 29 VACCINE 4151 (2011).

²⁷ Rachel M. Lee et al., *Incubation Periods of Viral Gastroenteritis: A Systematic Review*, 13 BIOMEDICAL CENTRAL INFECTIOUS DISEASES 446 (2013).

²⁸ Maria-Genalin Angelo et al., *Post-Licensure Safety Surveillance for Human Papillomavirus-16/18-AS04-Adjuvanted Vaccine: More Than 4 Years of Experience*, 23 PHARMACOEPIDEMIOLOGY AND DRUG SAFETY 456 (2014).

²⁹ Robert L. Davis et al., *Measles-Mumps-Rubella and Other Measles-Containing Vaccines Do Not Increase the Risk for Inflammatory Bowel Disease*, 155 ARCH PEDIATRIC ADOLESCENT MED. 354 (2001).

also noted that Hubbard et al. concluded that “although unproven, if viruses could possibly trigger the development of IBD, they would not do so directly, but instead [an] affected individual must have a specific genetic abnormality,” which he argued undercut Dr. Sferra’s opinions on causation. *Id.* (citing Pet’r’s Ex. 70). However, on cross-examination, Dr. Liacouras admitted that his larger critique of Dr. Sferra’s use of Tarris et al. was that it was “more of a review and a theory than it was a clinical study.” Tr. 121:8–9.

In Dr. Liacouras’ third report, he took issue with Dr. Sferra’s characterization of A.R.’s weight gain, arguing that “poor weight gain in an infant is not common, and is always a concern and a significant symptom.” Resp’t’s Ex. G at 3. He conceded that poor weight gain may at times be related to insufficient caloric intake, but “many times poor weight gain is the first sign of a significant medical disease, such as intestinal inflammation or IBD.” *Id.* He continued that A.R.’s vomiting and poor weight gain were the beginning of her VEO-IBD. *Id.* Dr. Liacouras also highlighted that A.R. had a family history of autoimmune disease, which “is a significant known risk factor for the development of inflammatory bowel disease.” *Id.*

At the hearing Dr. Liacouras testified that individuals with VEO-IBD can present with a variety of both gastrointestinal and non-gastrointestinal symptoms, which could include “poor weight gain, nutritional problems, [and] poor feeding.” Tr. 87:16. He continued that these symptoms are significant in the evaluation of IBD because “the [gastrointestinal] tract is essential in absorbing nutrients and things to promote growth,” and thus review of these symptoms is important to identify poor growth trends. Tr. 89:2–17. When evaluating A.R.’s recorded weights from birth to vaccination, Dr. Liacouras testified that for the first month of life, A.R. had “about the right average weight gain for an infant,” at about one ounce per day, but that her half-ounce per day growth in the second month of life was “troublesome and warranting more evaluation.” Tr. 90:10–24. He continued that although Dr. Sferra “stated that failure to thrive is a question and could be common, [] common doesn’t mean you ignore things.” Tr. 91:4–6. He noted that A.R.’s weight gain on February 8, 2017 was “concerning,” and that this was significant for patients with VEO-IBD because “retrospectively, you go back, and you see what happened, when it happened, and possibly the disease was happening earlier than you thought it did” Tr. 92:4–7. Using this logic, Dr. Liacouras testified that looking backward, he would attribute A.R.’s poor weight gain to her VEO-IBD. Tr. 92:11–12. Dr. Liacouras also noted that with regard to NP Huie’s recommendation of increased breastfeeding that “if the baby was gaining weight like [she] was in the first month, I’m sure the practice wouldn’t have changed anything.” Tr. 93:9–11.

Dr. Liacouras next discussed the study filed by Petitioner by Ouahed et al.,³⁰ which listed bloody diarrhea, frequent vomiting, failure to thrive, and fistulas among the symptoms for VEO-IBD. Tr. 93:12–20 (citing Pet’r’s Ex. 87). Dr. Liacouras also agreed with the article’s statement that assessing the full history of a patient with VEO-IBD was important to identify onset of symptoms and to “inquire about energy, appetite, tolerance of feeds, vomiting, and irritability.” Tr. 94:15–16. On cross-examination he disagreed with the article’s finding that “over 70 up to 80 percent of VEO-IBD patients will not have a specific identified causal genetic etiology,” because the article was written in 2019, and “while there certainly are cases of VEO-IBD that are not linked

³⁰ Jodie Ouahed et al., *Very Early Onset Inflammatory Bowel Disease: A Clinical Approach With a Focus on the Role of Genetics and Underlying Immune Deficiencies*, 26 INFLAMMATORY BOWEL DISEASE 820 (2019).

yet to genetic possibilities, more and more of those cases are being seen and found to have a genetic component, so that sentence by itself is not quite correct.” Tr. 121:20–23, 122:1–5. However, he later admitted that “a majority of cases [still] aren’t linked to genetics.” Tr. 138:21–22.

He then explained that A.R.’s February 11, 2017 ED visit documented vomiting after each feed since before receipt of the rotavirus vaccine, and that A.R.’s PCP characterized her symptoms as “reflux,” not vomiting. Tr. 96:11. Dr. Liacouras explained that this was because “[r]eflux is a diagnosis more than a symptom. And so this admission note talks more about and tries to characterize what was happening more, and it talks about vomiting and tried to distinguish kind of when it really started and when the diarrhea may have started.” Tr. 96:13–18. When asked whether vomiting was a symptom of a gastrointestinal issue, Dr. Liacouras testified that “[i]t can be caused by other things . . . but in general, most people think about [gastrointestinal] problems initially when you see somebody that has vomiting,” and noted that vomiting could be a symptom of VEO-IBD. Tr. 98:8–15.

On cross-examination, Dr. Liacouras admitted that he had treated cases of VEO-IBD in which no causal genetic variant could be identified and declined to testify as to whether there was any evidence that A.R.’s WDFY4 gene defect would be pathogenic for VEO-IBD. Tr. 103:10–12, 105:10–12. He further admitted that the 2021 study by Uhlig et al.³¹ did not identify WDFY4 as a genetic variant implicated in the development of IBD. Tr. 106:11–15 (citing Resp’t’s Ex. D, Tab 3). He also admitted that A.R. was never diagnosed with a primary immunodeficiency disorder. Tr. 107:1–2. However, he noted that despite the extended care A.R. received while at CHOA, “there’s often a diagnostic delay in IBD, and in retrospect, you go backwards, and you can see, when you eventually figure out what’s going on, that things started much earlier,” and given the evolving understanding of the nature of IBD, was not surprised that A.R.’s treating physicians did not identify a primary immunodeficiency disorder. Tr. 107:23–25; Tr. 108:7–8.

Dr. Liacouras also acknowledged Dr. Lewis’ opinion that the rotavirus vaccine “perhaps expedited” A.R.’s VEO-IBD. Tr. 111:23–25. However, when asked about the significance of Dr. Lewis’ repeated mentions of this possibility in his subsequent patient reports, Dr. Liacouras opined that this was “possibly within his differential diagnosis. It doesn’t mean that he knew or believed for sure that that was the cause.” Tr. 112:12–14. When asked for clarification, Dr. Liacouras stated that Dr. Lewis never came to an unequivocal decision as to whether the rotavirus vaccine caused A.R.’s VEO-IBD, and thus Dr. Liacouras used this as his own basis for stating that there was no unequivocal evidence that the vaccine caused A.R.’s injury. Tr. 136:1–4. He also opined that Dr. Lewis’ note to withhold the rotavirus vaccine from A.R. was because he was “worried that the child had an immune disorder and didn’t want to give a live virus.” Tr. 114:22–25. However, he later acknowledged that it could not be discounted that A.R.’s treaters declined to give her the rotavirus vaccine out of concern that it caused her VEO-IBD. Tr. 137:1–9.

³¹ Holm H. Uhlig et al., *Clinical Genomics for the Diagnosis of Monogenic Forms of Inflammatory Bowel Disease: A Position Paper From the Paediatric IBD Porto Group of European Society of Paediatric Gastroenterology, Hepatology and Nutrition*, 72 J. PEDIATRIC GASTROENTEROLOGY & NUTRITION 456 (2021).

When asked about monogenic causes of IBD, Dr. Liacouras testified that environmental factors could also contribute to the onset of IBD, as “there’s something or a combination that could be going on that makes the disease either occur or worsen.” Tr. 116:21–23.

Turning to A.R.’s February 8, 2017 well-baby visit, Dr. Liacouras acknowledged that A.R.’s mother reported no concerns and that A.R.’s elimination and gastrointestinal function was listed as “normal” on her physical examination. Tr. 124:16, 124:24–25, 125:8–11. However, when asked about A.R.’s diagnosis of gastroesophageal reflux at this visit, Dr. Liacouras opined that this diagnosis was incorrect, stating,

Most of the patients with gastroesophageal reflux, which is basically a condition that’s part of a lot of infants have, it’s an immaturity of the [gastrointestinal] system where the sphincter between the esophagus and stomach doesn’t work well and the stomach doesn’t empty well, and lots of kids have this effortless, kind of happy spitting that occurs shortly after birth and continues to go on. This patient had none of that, not even in this visit, but even in later histories taken at the Atlanta hospital. . . . [W]hen you have . . . VEO-IBD . . . it’s not uncommon for symptoms to occur at some point when you consider the diagnosis, but in retrospect when you look back, that other things have been going on like weight problems or even small amounts of vomiting, that then you can put together that was part of this whole process of having the disease. So that’s why . . . the weight is much more important to me and the information that there was not vomiting or effortless spitting for months and months.

Tr. 126:2–23. Dr. Liacouras also acknowledged that sub-optimal weight gain in an infant could be “part of a bunch of different possible diagnoses.” Tr. 127:18. He also admitted that he was incorrect in his initial report when he stated that A.R. suffered from diarrhea prior to vaccination, and that his provided growth curve from his initial report was incorrect. Tr. 129:1, 132:9–10.

When asked whether it was possible for the rotavirus vaccine to cause rotavirus enteritis, Dr. Liacouras declined to answer. Tr. 133:9–15. When asked about his timeline for A.R.’s onset of VEO-IBD, he opined that A.R.’s symptoms began “between one and two months,” and that the potential for multiple causes within this timeframe did not contradict his theory. Tr. 139:6, 139:11–25. He explained that

A.R.’s gradual progression of symptoms was consistent with a chronic disease like VEO-IBD, as patients “slowly start to have problems . . . [a]nd the initial symptom may be poor weight gain, because . . . it’s not involving the whole intestine. Now, a few days later or weeks later . . . you’re getting some vomiting, because it’s starting to get inflamed of certain early part of the intestine. Then it starts giving you diarrhea . . . that progression is not unheard of.

Tr. 142:8–19.

C. Reports and Testimony of Dr. Romberg

In Dr. Romberg's first expert report, he argued that Dr. Santoro's claim that A.R. was healthy prior to vaccination was incorrect, as he stated that A.R. suffered from "poor weight gain, general inflammatory signs (fever, fatigue) and [gastrointestinal] symptoms (diarrhea, vomiting, loss of appetite) . . . prior to vaccine administration." Resp't's Ex. D at 4 (citing Pet'r's Ex. 1 at 12–15). He also explained that A.R. was suffering from FTT prior to vaccination, as A.R.'s weight gain crossed the 50th and 25th percentile lines on a weight to age growth chart. *Id.* at 8–9. Accordingly, he claimed that Dr. Sferra and Dr. Santoro were incorrect to state that the rotavirus vaccine caused A.R.'s VEO-IBD because her symptoms preceded vaccination. *Id.* at 8.

Dr. Romberg also countered Dr. Sferra's assertion that A.R.'s VEO-IBD was not monogenic, citing to the increasing number of monogenic causes of VEO-IBD that have been identified since 2014 and noting that while "monogenic causes can be identified in only ~3% of IBD patients [younger than] 18 years, [they are found in as many] as 41% of infantile-onset IBD patients (onset [less than] 2 years)." Resp't's Ex. D at 6 (citing Resp't's Ex. D, Tab 3). He opined that the question was not whether A.R. had monogenic IBD, but rather "why a causative mutation was not identified." *Id.* He opined this could be due to A.R. possessing a gene mutation not known to cause VEO-IBD at the time of her exome sequencing in 2017 or that A.R. could have a somatic mutation. *Id.* at 6–7. He explained that "[i]f somatic mutations occur in a different cell type (i.e. gut) [than] those used for clinical genetic sequencing (i.e. peripheral blood or buccal samples are standard), then [whole exome sequencing] will miss them." *Id.* at 7. He also noted that whole exome sequencing only identifies variations in DNA encoding mRNA, which only accounts for approximately 1% of the human genome. *Id.* Dr. Romberg declined to comment on further biological mechanisms proposed by Petitioner's experts because "[t]hese arguments have no bearing on a case where the signs and symptoms of IBD preceded vaccine administration." *Id.* at 10.

In his second report, Dr. Romberg opined that A.R.'s treating physicians believed her WDFY4 gene mutation to be the primary cause of her VEO-IBD because her physicians described her condition as "VEOIBD immune deficiency with genetic mutation in WDFY4, IPEX-like" in 2019 when she was admitted for her bone marrow transplant. Resp't's Ex. F at 2 (citing Pet'r's Ex. 43.8 at 13). He continued that

the gut is not the primary defect in IPEX or IPEX-like diseases, the hematopoietic immune system is. Hence, it appears that Dr. Chandrakasan and A.R.'s family felt strongly enough that A.R. had a genetic disease of the immune system that they were willing to endure the considerable risks and discomfort of [a bone marrow transplant].

Id. at 3. Dr. Romberg also acknowledged that he incorrectly misinterpreted A.R.'s records from February 8, 2017, and that she was not experiencing diarrhea, constipation, and loss of appetite prior to her receipt of the rotavirus vaccination. *Id.* at 4.

At the hearing, Dr. Romberg further classified VEO-IBD into groups of children who developed IBD between the ages of two and six and those who develop IBD under the age of two,

testifying that “[k]ids that develop very early onset IBD in the first month or two of life are highly enriched in monogenic causes.” Tr. 150:19–21. When explaining the importance of reviewing an individual’s growth parameters for assessment of VEO-IBD, Dr. Romberg testified that “because the intestines are really paramount to both absorption and loss of calories . . . I think [growth parameters are] probably even a more important indicator for inflammatory bowel disease.” Tr. 152:2–5. After reviewing A.R.’s growth trajectory from January 11, 2017, to February 8, 2017, Dr. Romberg testified that “the early growth trajectory from birth to one month, which was reassuring, [] leveled off substantially, with a slow that allowed her to cross two growth curve lines. . . . That is one of the diagnostic criteria for failure to thrive.” Tr. 153:7–11. He further opined that in retrospect, he would consider this weight trend to be a symptom of A.R.’s VEO-IBD. Tr. 153:18–22.

When asked about Dr. Sferra’s proposed biological mechanisms for how the rotavirus vaccine may have caused A.R.’s injury, Dr. Romberg testified that for any of his theories to be acceptable, A.R.’s vaccination must have preceded the beginning of her symptoms. Tr. 155:12–13. However, Dr. Romberg stated that Dr. Sferra’s theories were invalid by arguing that A.R.’s weight loss was a symptom of her VEO-IBD, which preceded vaccination. Tr. 155:16–17.

Dr. Romberg further testified that while there was no known association between A.R.’s WDFY4 gene mutation and disease in humans, that does not mean that it did not cause her VEO-IBD. Tr. 156:18–22. He explained that A.R.’s mutation was described as a variant of unknown significance, which he described as “genetic variants that look suspicious but that certainly could alter protein function but have not yet had the sort of laboratory molecular biology required to prove that they are either benign or pathogenic.” Tr. 157:10–14. He continued by turning to VEO-IBD generally and stated that children who develop VEO-IBD in the infantile period tend to have a strong genetic connection to their disease. Tr. 158:12–16.

Dr. Romberg next explained whole exome sequencing, which he described as follows:

So the human genome can be divided into two fractions. One is noncoding DNA. Noncoding DNA does not encode proteins. It’s mostly structural or regulatory. And noncoding DNA comprises 99 percent of the human genome. The exome comprises the remaining 1 percent. These are nucleotides which actually encode proteins or long, noncoding RNAs. Whole exome sequencing became popular as a clinical tool over the last then years, because it enriches for just that 1 percent that is likely to be most . . . likely to cause a disease.

Tr. 159:15–25. He continued that A.R.’s whole exome sequencing did not identify a monogenic cause for her VEO-IBD and that he could not state with certainty that A.R. had monogenic VEO-IBD. Tr. 160:4–10. However, he also opined that it would be wrong to exclude a monogenic cause for A.R.’s VEO-IBD just because the whole exome sequencing did not identify a monogenic cause. Tr. 160:11–15. On cross-examination, he admitted that CHOP, his employing medical institution, acknowledged monogenic causes of VEO-IBD to be “very rare” and that “very often” they instead identify several potential causes. Tr. 199:13–23 (citing Pet’r’s Ex. 93).

Dr. Romberg next turned to Dr. Chandrakasan's opinion that A.R. suffered from "very early onset IBD with an IPEX-like [gastrointestinal] biopsy phenotype." Tr. 161:13–15. Dr. Romberg explained that IPEX stood for "immune deficiency polyendocrinopathy X-linked," and was "caused by mutations in a gene called FOXP3," which lies on an X chromosome and therefore primarily affects boys. Tr. 161:18–24. He noted that patients suffering from IPEX or IPEX-like diseases lack T regulatory cells, which "coordin[ate] immune responses[,] probably most importantly after the inflammation . . . T regs are really important for quieting things down." Tr. 162:8–11. He continued that "most IPEX patients [] start having symptoms in utero," and noted that this "provides overwhelming evidence that it is a monogenic disease of the immune system." Tr. 162:14–17. Dr. Romberg explained that "[a]round . . . the first month of life, [patients] develop really severe enterocolitis, and then by that they typically get serially polyendocrinopathy, so the different organs of the immune system other than the pancreas begin shutting down one by one." Tr. 162:22–25, 163:1–2.

Dr. Romberg then explained Dr. Chandrakasan's actual diagnosis of IPEX-like gastrointestinal biopsy phenotype, which he described as "a [gastrointestinal] biopsy in which there is bilious vomiting." Tr. 163:8–9. He further explained that the villi, which "are these little finger-like structures . . . [turn into] a fist," which also includes the "destruction of crypts[,]" which are the sort of areas between the fingers where the gut stem cells reside which allow for healing and regeneration of gut structures." Tr. 163:9–16. He also testified that one would expect to see an "infiltrate of leukocytes . . . packed full of both lymphocytes, B cells, T cells, and myeloid cells." Tr. 163:18–22. Dr. Romberg continued that an IPEX-like disorder, such as VEO-IBD or type 1 diabetes, "but you don't have a FOXP3 mutation . . . [w]e call you IPEX-like." Tr. 164:2–5.

When asked about the primary defect in IPEX-like disorders, Dr. Romberg explained the following:

Typically it does involve T regulatory cells. So FOXP3 is the master transcription factor for these cells. These cells also require IL-2 to function, so different components of the IL-2 receptor machinery, including IL-2 itself, the gamma chain, staph IB which is a saline molecule that goes through them, defects in IL-10. IL-10 is an immune suppressive cytokine that T regs secrete. All of them can cause an IPEX-like disorder.

Tr. 164:8–15. Dr. Romberg then turned to Dr. Chandrakasan's note that stated he believed a bone marrow transplant would be curative for A.R.'s VEO-IBD, as it was in other IPEX and IPEX-like disorders, stating that such treatment was the standard of care for IPEX. Tr. 165:1–6. He explained that a bone marrow transplant would be curative for a patient with VEO-IBD if the patient's "problem was in the hematopoietic compartment, because . . . the first step in transplanatation would be to remove the existing immune system with chemotherapy, and then . . . you would infuse . . . donor stem cells which . . . repopulate the hematopoietic system." Tr. 166:16–25.

Dr. Romberg next addressed a note from the end of A.R.'s hospitalization for her bone marrow transplant, which mentioned WDFY4's possible attribution to "broader immune dysregulation and IPEX-like phenotype" due to its association with BEACH domain-containing proteins. Tr. 168:1–6 (citing Pet'r's Ex. 42 at 680). Dr. Romberg explained that "[t]he BEACH

domain is another acronym that stands for beige Chediak-Higashi domain,” and that these proteins “recycle other proteins, and by recycling, then they increase the concentration of those proteins above what would otherwise be possible.” Tr. 168:10–23. He continued that:

And there is a BEACH domain containing protein called LRBA which recycles a key immunoregulatory molecule called CTLA-4. CTLA 4 is expressed highly by . . . T regulatory cells, and it’s really important in sort of quieting down the immune system. So with LRBA mutations, you will have a situation where you lack CTLA-4, and without CTLA-4, you have an IPEX-like Tregopathy. . . . A Tregopathy is any disease which is caused by the numerical deficiency or the qualitative diminishment of T regulatory cells.

Tr. 168:23–25, 169:1–12. He continued that he believed A.R.’s treaters would not have had her undergo a bone marrow transplant if they did not believe her WDFY4 gene mutation to be the cause of her VEO-IBD due the high-risk nature of the procedure, while also noting that not all forms of monogenic IBD are treatable with a bone marrow transplant. Tr. 170:3–20. Dr. Romberg also acknowledged Dr. Lewis’ letter from July 27, 2021, which noted that A.R.’s bone marrow transplant had resolved her VEO-IBD. Tr. 172:3 (citing Pet’r’s Ex. 82 at 7265). However, on cross-examination he agreed that A.R. continued to be treated for intestinal failure at CHOA following her bone marrow transplant. Tr. 176:7–11. He later clarified that he did believe the bone marrow transplant resolved A.R.’s VEO-IBD, but that her continued hospitalizations were the result of the time it took her gut to fully heal following the operation. Tr. 194:10–19.

Dr. Romberg then turned to the recommendation against vaccines for A.R. in March 2022 due to her hypogammaglobulinemia, which he described as low antibody concentrations in the blood. Tr. 172:5–13. He explained that advising against immunizations in these instances was reasonable given the immune-compromised state of patients, which would present generally efficacy concerns, as well as safety concerns in the case of live vaccines. Tr. 173:1–14.

On cross-examination, he stated that it was “a demonstrable fact” that A.R. suffered from failure to thrive prior to vaccination. Tr. 176:24–25. He noted that despite the fact A.R.’s feeding schedule was changed between her January and February 2017 well-baby visits, he did not believe this was the reason for her poor weight gain. Tr. 178:21–22. He also agreed that NP Huie’s notes from A.R.’s February 8, 2017 visit lacked any urgency and that “[t]he follow-up schedule [was] consistent with someone who’s not concerned about the patient.” Tr. 181:7–8. When asked why there was no mention of failure to thrive in A.R.’s medical records by her treating physicians following her hospital admission, he stated that failure to thrive is “a diagnosis that you would use until you understood what the underlying cause of failure to thrive is, and then the underlying cause would be used in place of failure to thrive.” Tr. 182:3–7.

When questioned about his use of weight charts to diagnose A.R. with failure to thrive, Dr. Romberg admitted that he used only weight charts and not weight-to-length charts as recommended by Cole & Lanham. Tr. 184:12–13 (citing Resp’t’s Ex. D, Tab 7). When reviewing the CDC’s weight-to-length chart for girls, Dr. Romberg admitted that A.R.’s weight-to-length trends stayed relatively consistent with the 50th percentile for growth and never crossed below the 5th percentile or below two percentile lines prior to vaccination. Tr. 189:3–8 (citing Pet’r’s Ex.

92). He later testified that he believed weight charts to be a better metric than weight-to-length charts because “[i]t’s very difficult to get a length in an infant that is reliable . . . we call it length, not height, because usually the baby is supine, and you try to stretch the baby out as best as you can, but it is not a very reliable measurement.” Tr. 202:21–25. When asked whether the fact that A.R.’s weight-height measurements tracking along the same percentile was itself evidence of consistency, he explained that “accuracy and reproducibility are different things,” and stated that “a wrong answer given multiple times is reproducible, but not accurate.” Tr. 203:13–25. He declined to answer when asked if pediatricians should not use weight-to-length measurements, but stated the metric he would rely upon the most would be weight. Tr. 204:1–17. However, he later testified that if A.R.’s weight-to-length measurements had been maintained following her February 8, 2017 well-baby visit, they would have crossed below the 5th percentile growth curve as well. Tr. 205:23–25.

When asked about his opinion that A.R. may have developed her VEO-IBD through an acquired mutation rather than an inherited mutation, Dr. Romberg acknowledged that there was no such evidence in the record. Tr. 190:1–2. He further testified that there was no evidence of a family history of IBD or monogenic disease, consanguinity, atypical infections consistent with primary immunodeficiency disease, malignancies, or multiple intestinal atresias, which Uhlig et al. identified as clinical features that should prompt a physician to consider a monogenic cause of IBD. Tr. 192:1–25 (citing Resp’t’s Ex. D, Tab 3). The only factor Dr. Romberg identified consistent with the article’s findings was A.R.’s early onset of symptoms. Tr. 193:10–11.

Dr. Romberg next addressed whether A.R.’s disease could have resulted from a multi-factorial process instead of a single cause even if she suffered from a primary immunodeficiency. He explained that there are two types of diseases, “[one] is a disease in which you have IBD every time . . . [a]nd then there are other diseases in which it’s not the primary feature.” Tr. 193:20–25. He continued that he would consider IL-10 receptor deficiencies a sole-cause disease, while a CTLA-4 mutation could be a multi-factorial disease. Tr. 194:1–4.

Dr. Romberg also admitted that the only symptom A.R. exhibited prior to vaccination that his employer, CHOP, identifies as a signal of VEO-IBD was poor weight gain, and not other symptoms such as bloody stool, abdominal pain, fevers, fatigue, cramping, or diarrhea. Tr. 200:5–16. He also acknowledged that CHOP does not identify vomiting as a potential symptom of IBD. Tr. 200:17–25.

When asked about whether the Rotateq vaccine can cause rotavirus, Dr. Romberg admitted that it was possible. Tr. 207:12–19. However, he also testified that “[e]verybody sheds rotavirus after rotavirus vaccination,” and that the difference between shedding and an active infection was “that there is no other explanation for the symptoms of enterocolitis.” Tr. 208:3–4. Thus, he believed the rotavirus enterocolitis diagnosis was a mistake due to the nature of rotavirus shedding following vaccination in some cases. Tr. 207:5–11. In A.R.’s case, Dr. Romberg opined that the other explanation for A.R.’s symptoms was not a rotavirus infection, but rather a pre-existing case of VEO-IBD. Tr. 208:17. He continued that his primary indicators to support his position was A.R.’s poor growth pre vaccination and A.R.’s diarrhea post vaccination, as he did not believe that 24 hours was a reasonable timeframe for A.R. to develop such symptoms following vaccination. Tr. 210:6–9. He supported his opinion by testifying that a case series examined children with

severe combined immune deficiency and received the Rotateq vaccine, but did not exhibit symptoms until several weeks after vaccination. Tr. 210:20–25, 211:1–6.³²

V. Applicable Legal Standards

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

A. Factual Issues

A petitioner must prove, by a preponderance of the evidence, the factual circumstances surrounding her claim. § 13(a)(1)(A). To resolve factual issues, the special master must weigh the evidence presented, which may include contemporaneous medical records and testimony. *See Burns v. Sec’y of Health & Hum. Servs.*, 3 F.3d 415, 417 (Fed. Cir. 1993) (explaining that a special master must decide what weight to give evidence including oral testimony and contemporaneous medical records). Contemporaneous medical records, “in general, warrant consideration as trustworthy evidence.” *Cucuras v. Sec’y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993); *but see Kirby v. Sec’y of Health & Hum. Servs.*, 997 F.3d 1378, 1382 (Fed. Cir. 2021) (rejection the presumption that “medical records are accurate and complete as to all the patient’s physical conditions”); *Shapiro v. Sec’y of Health & Hum. Servs.*, 101 Fed. Cl. 532, 538 (2001) (“[T]he absence of a reference to a condition or circumstance is much less significant than a reference which negates the existence of the condition or circumstance.”).

There are situations in which compelling testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec’y of Health & Hum. Servs.*, 69 Fed. Cl. 775, 779 (2006) (“[L]ike any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking.”); *Lowrie v. Sec’y of Health & Hum. Servs.*, No. 03-1585V, 2005 WL 6117475, at *19 (Fed. Cl. Spec. Mstr. Dec. 12, 2005) (“[W]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent.” (quoting *Murphy v. Sec’y of the Dep’t of Health & Hum. Servs.*, 23 Cl. Ct. 726, 733 (Fed. Cl. 1991))). Ultimately, a determination regarding a witness’ credibility is needed when determining the weight that such testimony should be afforded. *Andreu v. Sec’y of Health & Hum. Servs.*, 569 F.3d 1367, 1379 (Fed. Cir. 2009); *Bradley*, 991 F.2d at 1575.

Despite the weight afforded medical records, special masters are not bound rigidly by those records in determining onset of a petitioner’s symptoms. *Valenzuela v. Sec’y of Health & Hum.*

³² Respondent did not submit this article as an exhibit and it was not made available to the Court or Petitioner after the hearing. Tr. 211:7–8.

Servs., No. 90-1002V, 1991 WL 182241, at *3 (Fed. Cl. Spec. Mstr. Aug. 30, 1991); *see also Eng. v. Sec’y of Health & Hum. Servs.*, No. 90-1754V, 1994 WL 67704, at *3 (Fed. Cl. Spec. Mstr. Feb. 18, 1994) (Section 13(b)(2) “must be construed so as to give effect also to § 13(b)(1) which directs the special master or court to consider the medical records (reports, diagnosis, conclusions, medical judgment, test reports, etc.), but does not require the special master or court to be bound by them.”).

B. Causation-In-Fact

To establish causation-in-fact, a petitioner must demonstrate by a preponderance of the evidence that the vaccine was the cause of the injury. § 300aa-13(a)(1)(A). A petitioner is required to prove that the vaccine was “not only a but-for cause of the injury but also a substantial factor in bringing about the injury.” *Moberly*, 592 F.3d at 1321–22 (quoting *Shyface v. Sec’y of Health & Hum. Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)).

In the seminal case of *Althen v. Sec’y of Health & Hum. Servs.*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278–79 (Fed. Cir. 2005). The *Althen* test requires petitioners to set forth: “(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury.” *Id.* at 1278. To establish entitlement to compensation under the Program, a petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *Id.* “[C]lose calls regarding causation are resolved in favor of injured claimants.” *Id.* at 1280. Further, evidence used to satisfy one prong of the test may overlap to satisfy another prong. *Capizzano*, 440 F.3d at 1326.

Under the first prong of *Althen*, a petitioner must offer a scientific or medical theory that answers in the affirmative the question: “can the vaccine[] at issue cause the type of injury alleged?” *See Pafford v. Sec’y of Health & Hum. Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *mot. for rev. den’d*, 64 Fed. Cl. 19 (2005), *aff’d*, 451 F.3d 1352 (Fed. Cir. 2006). To satisfy this prong, a petitioner’s theory must be based on a “sound and reliable medical or scientific explanation.” *Knudsen v. Sec’y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such theory must only be “legally probable, not medically or scientifically certain.” *Id.* at 548–49. Petitioners are not required to identify “specific biological mechanisms” to establish causation, nor are they required to present “epidemiologic studies, rechallenge[] the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities.” *Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). Scientific and “objective confirmation” of the medical theory with additional medical documentation is unnecessary. *Althen*, 418 F.3d at 1278 – 81; *see also Moberly*, 592 F.3d at 1322. However, as the Federal Circuit has made clear, “simply identifying a ‘plausible’ theory of causation is insufficient for a petitioner to meet her burden of proof.” *LaLonde v. Sec’y of Health & Hum. Servs.*, 746 F.3d 1334, 1339 (Fed. Cir. 2014) (citing *Moberly*, 592 F.3d at 1322). Indeed, the Federal Circuit has “consistently rejected theories that the vaccine only ‘likely caused’ the injury and reiterated that a ‘plausible’ or ‘possible’ causal theory does not satisfy the standard.” *Boatmon v. Sec’y of Health & Hum. Servs.*, 941 F.3d 1351, 1360 (Fed. Cir. 2019) (citing *Moberly*, 592 F.3d at 1322; *LaLonde*, 746 F.3d at 1339). Rather, “[a] petitioner must provide a reputable

medical or scientific explanation that pertains specifically to the petitioner’s case.” *Moberly*, 592 F.3d at 1322. In general, “the statutory standard of preponderance of the evidence requires a petitioner to demonstrate that the vaccine more likely than not caused the condition alleged.” *LaLonde*, 746 F.3d at 1339.

Furthermore, establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of her claim. *Lampe v. Sec’y of Health & Hum. Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). The Supreme Court’s opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993) requires that courts determine the reliability of an expert opinion before it may be considered as evidence. However, in the Vaccine Program, the *Daubert* factors are used in the weighing of the reliability of scientific evidence proffered. *Davis v. Sec’y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66–67 (2010) (“[U]niquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to the persuasiveness of expert testimony already admitted.”); *see also 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).

The *Daubert* factors are “meant to be helpful, not definitive.” *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 151 (1999). The factors do not “constitute a ‘definitive checklist or test’” and may be applied differently depending on the facts of a particular case. *Id.* at 150 (quoting *Daubert*, 509 U.S. at 593).

“In short, the requirement that an expert’s testimony pertain to ‘scientific knowledge’ establish a standard of evidentiary reliability.” *Daubert*, 509 U.S. at 590 (citation omitted). Thus, for Vaccine Act claims, a “special master is entitled to require some indicia of reliability to support the assertion of the expert witness.” *Moberly*, 592 F.3d at 1324. 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.” *Synder v. Sec’y of Health & Hum. Servs.*, 88 Fed. Cl. 706, 743 (2009) (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also D’Tiole v. Sec’y of Health & Hum. Servs.*, No. 15-085V, 2016 WL 7664475, at *24 (Fed. Cl. Spec. Mstr. Nov. 28, 2016) (stating that the Vaccine Act “require[s] a chain of reliable propositions supporting [a] petitioner’s theory[.]”).

Under the second prong of *Althen*, a petitioner must prove that the vaccine actually did cause the alleged injury in a particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1279. The second *Althen* prong requires proof of a logical sequence of cause and effect,

usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; instead, the petitioner "must explain *how* and *why* the injury occurred." *Pafford*, 2004 WL 1717359, at *4 (emphasis in original). The special master in *Pafford* noted petitioners "must prove [] both that her vaccinations were a substantial factor in causing the illness . . . and that the harm would not have occurred in the absence of the vaccination." 2004 WL 1717359, at *4 (citing *Shyface*, 165 F.3d at 1352). A reputable medical or scientific explanation must support this logical sequence of cause and effect. *Hodges v. Sec'y of Health & Hum. Servs.*, 9 F.3d 958, 961 (Fed. Cir. 1993) (citation omitted). Nevertheless, "[r]equiring epidemiologic studies . . . or general acceptance in the scientific or medical communities . . . impermissibly raises a claimant's burden under the Vaccine Act and hinders the system created by Congress" *Capizzano*, 440 F.3d at 1325–26. "[C]lose calls regarding causation are resolved in favor of injured claimants." *Althen* 418 F.3d at 1280.

In Program cases, contemporaneous medical records and the opinions of treating physicians are favored. *Capizzano*, 440 F.3d at 1326 (citing *Althen*, 418 F.3d at 1280). Indeed, when reviewing the record, a special master must consider the opinions of treating physicians. *Capizzano*, 440 F.3d at 1326. This is because "treating physicians are likely to be in the best position to determine whether 'a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury.'" *Id.* In addition, "[m]edical records, in general, warrant consideration as trustworthy evidence. The records contain information supplied to or by health professionals to facilitate diagnosis and treatment of medical conditions. With proper treatment hanging in the balance, accuracy has an extra premium. These records are also generally contemporaneous to the medical events." *Cucuras v. Sec'y of Health & Hum. Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993). However, there is no "presumption that medical records are accurate and complete as to all of the patient's physical conditions." *Kirby v. Sec'y of Health & Hum. Servs.*, 997 F.3d 1378, 1383 (Fed. Cir. 2021) (finding that a special master must consider the context of a medical encounter before concluding that it constitutes evidence regarding the absence of a condition). While a special master must consider these opinions and records, they are not "binding on the special master or court." § 300aa-13(b)(1). Rather, when "evaluating the weight to be afforded to any such . . . [evidence], the special master . . . shall consider the entire record" *Id.*

In determining the accuracy and completeness of medical records, special masters will consider various explanations for inconsistencies between contemporaneously created medical records and later given testimony. The Court of Federal Claims has identified four such explanations for explaining inconsistencies: (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 with testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *LaLonde v. Sec'y of health & Hum. Servs.*, 110 Fed. Cl. 184, 203 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014).

To satisfy the third *Althen* prong, a petitioner must establish a "proximate temporal relationship" between the vaccination and the alleged injury. *Althen*, 418 F.3d at 1281. This

“requires preponderant proof that the onset of symptoms occurred within a timeframe for which, given the medical understanding of the disorder’s etiology, it is medically acceptable to finger causation-in-fact.” *de Bazan v. Sec’y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). Typically, “a petitioner’s failure to satisfy the proximate temporal relationship prong is due to the fact that onset was too late after the administration of a vaccine for the vaccine to be the cause.” *Id.* However, “cases in which onset is too soon” also fail this prong; “in either case, the temporal relationship is not such that it is medically acceptable to conclude that the vaccination and the injury are causally linked.” *Id.*; *see also Locane v. Sec’y of Health & Hum. Servs.*, 685 F.3d 1375, 1381 (Fed. Cir. 2012) (“[If] the illness was present before the vaccine was administered, logically, the vaccine could not have caused the illness.”).

Although a temporal association alone is insufficient to establish causation, under the third prong of *Althen*, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. The special master cannot infer causation from temporal proximity alone. *See Thibaudeau v. Sec’y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403–04 (1991); *see also Grant*, 956 F.2d at 1148 (“[T]he inoculation is not the cause of every event that occurs within the ten[-]day period . . . [w]ithout more, this proximate temporal relationship will not support a finding of causation.” (quoting *Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983))).

A petitioner who satisfies all three prongs of the *Althen* test has established a prima facie showing of causation. *Hammitt v. Sec’y of Health & Hum. Servs.*, 98 Fed. Cl. 719, 726 (2011). A petitioner who demonstrates by a preponderance of the evidence that she suffered an injury caused by vaccination is entitled to compensation unless the respondent can demonstrate by a preponderance of the evidence that the injury was caused by factors unrelated to the vaccination. *See Althen*, 418 F.3d at 1278; *Knudsen*, 35 F.3d at 547. In such a case, the government must not merely prove the existence of an alternative cause, but that such an alternative actually caused the injury. *Kundsen*, 35 F.3d at 549. Consequently, when and if the petitioner establishes a prima facie case, the burden shifts to the government to prove that an alternative cause, unrelated to the administration of the vaccine, was the “sole substantial factor” in causing the alleged injury. *See de Bazan*, 539 F.3d at 1354; *see also Hammitt*, 98 Fed. Cl. at 726 (explaining that respondent’s burden is to show that the “factor unrelated” was the “sole substantial factor” in causing the injury). Additionally, a factor unrelated “may not include ‘any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause, factor, injury, illness or condition.’” § 300aa-13(a)(2); *see also Doe v. Sec’y of Health & Hum. Servs.*, 601 F.3d 1349 (Fed. Cir. 2010) (stating that an idiopathic diagnosis cannot be a “factor unrelated,” as it is idiopathic).

VI. Analysis

A. Symptom Onset

The parties agree that A.R. suffered from VEO-IBD, but they dispute whether her symptoms likely occurred before or after vaccination. A.R.’s medical records from her one-month well-baby visit in January 2017 indicate she was healthy with no noted symptoms, while her two-month well-baby visit on February 8, 2017, the date of her rotavirus vaccination, noted that she suffered from occasional reflux with no other symptoms. Although there is an acknowledgement between the parties that A.R.’s February 11, 2017 ED records list incorrect dates regarding

Petitioner's reported onset of A.R.'s symptoms, the parties agree that A.R. began experiencing diarrhea the day following vaccination.

However, the parties disagree as to whether A.R.'s note of "occasional reflux" constitutes vomiting and disagree as to whether A.R.'s reflux/vomiting was a symptom of her VEO-IBD. Petitioner contends that A.R.'s note of reflux is inconsequential, and that A.R.'s treating physician did not appear to be urgently concerned with A.R.'s symptoms. Respondent contends that "reflux" was a diagnosis given by A.R.'s physician to describe her vomiting, which was later reported at her February 11, 2017 ED visit. The parties also disagree as to whether A.R.'s weight trends indicate she suffered from FTT prior to vaccination. Petitioner contends that A.R.'s weight-to-length trends track her as maintaining growth in the 50th percentile, and thus is not indicative of FTT. Conversely, Respondent contends that A.R.'s weight-to-age trends from January 2017 to February 2017 show her crossing below two percentile lines, which he argues is indicative of FTT and attributes to her having IBD prior to vaccination.

After reviewing the relevant evidence in the record, I find there is preponderant evidence that A.R.'s VEO-IBD symptoms began after her February 8, 2017 rotavirus vaccination. A.R. had no noted gastrointestinal issues prior to February 8, 2017, other than a singular note of occasional reflux. Vomiting in a child A.R.'s age would be a cause for extreme concern, and it is notable that NP Huie did not indicate an appropriate treatment plan when making her notes for this visit. This lack of urgency was also acknowledged by Respondent's experts at the hearing. Further, NP Huie did not believe A.R.'s symptoms to be so severe as to withhold her vaccinations, as one might expect with a young child experiencing severe signs of an acute infection such as vomiting. Additionally, I find it persuasive that the most significant of A.R.'s symptoms began the day following vaccination, to include severe vomiting and diarrhea, and that this onset date was consistently noted by A.R.'s treating physicians throughout her medical record.

Respondent's contention that A.R. suffered from FTT prior to vaccination and therefore was suffering from VEO-IBD prior to vaccination is also belied by an absence of any such notation in her treater's recommendations and notes; and I find Petitioner's arguments that A.R. was not in fact behind on her growth curve to be more persuasive. As noted by Dr. Sferra at the hearing, the literature filed by Dr. Romberg in support of his use of weight charts directly note that single metrics had "a low positive predictive value," and instead recommended the use of weight-for-length charts. Resp't's Ex. D, Tab 7. When using the weight-to-length chart for girls provided by the CDC, A.R.'s metrics consistently track along the 50th percentile without strong deviations. *See* Pet'r's Ex. 92 at 1. It is also noted at A.R.'s two-month well-baby visit that Petitioners had changed A.R.'s feeding schedule to have shorter lengths and no overnight feeds, which may be an explanation for her reduced weight gain between January and February. This theory is supported by NP Huie's lack of concern over A.R.'s presentation at this visit and her recommendation to decrease feeding intervals and continue overnight feeds.

Accordingly, there is preponderant evidence that A.R.'s symptoms began after vaccination, and I find Respondent's arguments to the contrary to be unpersuasive.

B. *Althen* Prong One

Under *Althen* prong one, Petitioner must set forth a medical theory explaining how the received vaccine could have caused or sustained injury. *Andreu*, 569 F.3d at 1375; *Pafford*, 451 F.3d at 1355–56. Petitioner’s theory of causation need not be medically or scientifically certain, but it must be informed by a “sound and reliable” medical or scientific explanation. *Boatmon*, 941 F.3d at 1359; *see also Knudsen*, 35 F.3c at 548; *Veryzer v. Sec’y of Health & Hum. Servs.*, 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both “relevant” and “reliable”), *aff’d* 475 F. App’x 765 (Fed. Cir. 2012). If Petitioner relies upon a medical opinion to support her theory, the basis for the opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. *See Broekelschen v. Sec’y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (“The special master’s decision oftentimes is based on the credibility of the experts and the relative persuasiveness of their competing theories”); *Perriera v. Sec’y of Health & Hum. Servs.*, 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an “expert opinion is no better than the soundness of the reasons supporting it” (citing *Fehrs v. United States*, 620 F.2d 255 (Ct. Cl. 1980))).

Dr. Sferra proposed three potential biologic mechanisms for how A.R.’s receipt of the rotavirus vaccine may have caused her VEO-IBD: dysregulation and disruption of the intestinal mucosal barrier due to the rotavirus infection, bystander activation, and molecular mimicry.³³ At the hearing, Dr. Sferra testified that all of his medical theories relied on A.R. having sustained an acute rotavirus infection as a result of the rotavirus vaccine, which then caused A.R.’s symptoms, and not that the vaccine itself directly caused A.R.’s symptoms. Tr. 224:12–25, 225:1–7. Both parties admit that the role enteric viruses play in the development of IBD is unclear at best, and that it is possible for a live rotavirus vaccine to cause a rotavirus infection. *See* Tr. 207:12–19.

With regard to Dr. Santoro’s and Dr. Sferra’s theory of disruption of the mucosal barrier, the medical literature indicates that viruses may play some role in the development and exacerbation of IBD.³⁴ Khor et al. presented a detailed review of known causal factors in the etiology of IBD. The article noted that non-genetic factors play a substantially larger role than genetic factors in the development of IBD, and that both the innate and adaptive immune systems were crucial for intestinal homeostasis. Specifically, the article noted that the integrity of intestinal epithelial cells are critical for the development of IBD, and that breakdowns could lead to pathological intestinal inflammation through a weakening of the mucosal barrier. Because these cells perform both barrier and signal functions, maintaining the functional equilibrium of the microbiome within the mucosa is essential, as perturbations contribute to the pathophysiology of many gastrointestinal disorders, including IBD. The article also found that the specific deletion of intestinal epithelial cells in animal models did not always result in the development of spontaneous

³³ Although Dr. Sferra mentioned both bystander activation and molecular mimicry as possible mechanisms for A.R.’s injury, he did not file any medical literature relating to either of these processes and did not discuss either at length in his testimony or expert reports. Accordingly, I will not address these theories in depth.

³⁴ This is similar to the theory posited in *Morgan v. Sec’y of Health & Hum. Servs.*, where the special master found by preponderant evidence that the petitioner’s HPV vaccine caused her ulcerative colitis, a form of IBD. No. 13-529V, 2015 WL 9694667 (Fed. Cl. Spec. Mstr. Dec. 10, 2015).

colitis, suggesting that further environmental triggers are required for disease onset in addition to genetic susceptibility. The article's emphasis on a combination of genetic and environmental factors is particularly persuasive in the case of A.R., who was shown to have a genetic defect of unknown significance and an active rotavirus infection prior to her VEO-IBD diagnosis, in contrast to Dr. Liacouras' and Dr. Romberg's assertions that A.R.'s VEO-IBD was solely monogenic.

The article further discussed the role of pro-inflammatory cytokines, macrophages, and dendritic cells as crucial players in the tolerance of commensal bacteria in the intestinal lumen, which promote digestion, and the response to pathogens that breach the mucosal barrier stimulating an inflammatory response. The authors noted "[i]mmune stimulatory effects of the microbiota are important to promote an effective response against potential pathogens, although dysregulated interactions, which might arise from perturbations in host, microbial or environmental factors, could lead to a loss of tolerance and promote intestinal inflammation." Pet'r's Ex. 39 at 9. "Viral infections are common, and key studies highlight their potential to exert important immune modulatory effects. Acute and/or chronic viral infections could interact with host-susceptibility factors in a manner that leaves either the cell or the cellular milieu poised to promote pathological intestinal inflammation after subsequent triggering events." *Id.* Ultimately, the article concluded that more research is needed to fully understand the effects of exogenous or environmental factors in promoting IBD but discussed the important role of both the innate and adaptive immune systems in causing IBD. These findings are consistent with A.R.'s medical history of an acute rotavirus infection and subsequent development of VEO-IBD, taken in the context of a potential genetic susceptibility from her WDFY4 defect. These conditions, taken separately, may not have resulted in the eventual development of A.R.'s VEO-IBD, however, Dr. Santoro and Dr. Sferra both explain the process of how A.R.'s acute infection and symptoms of diarrhea would result in the depletion of intestinal epithelial cells, allowing a weakened mucosal barrier to be permeated by a live rotavirus infection in a genetically susceptible environment, thereby prolonging an already ongoing inflammatory response into the development of VEO-IBD.

Benn et al. focused on the non-specific effects of vaccines and explained that T cells are the most likely immunomodulators causing non-specific autoimmune responses. Particularly, the article stated "[i]n other scenarios detrimental heterologous (non-specific) immunity can lead to severe immunopathology." Pet'r's Ex. 34 at 4. The article discussed lymphocytic choriomeningitis virus-immune mice developing severe panniculitis in the form of inflammation and necrosis of visceral fat tissue. *Id.* It further observed that subcutaneous fat pathology, erythema nodosum, had been seen in humans after vaccination with vaccinia virus, human papillomavirus, and hepatitis B virus. *Id.* Although these references do not create direct proof, they do show a logical sequence of events to explain why a susceptible individual could get a chronic inflammatory condition from a vaccination.

Taken together, these studies, in addition to Dr. Sferra's reliance on Tarris et al. and Hummel & Cadwell, explain how an individual in A.R.'s position could develop VEO-IBD from a rotavirus infection that resulted from the receipt of a live rotavirus vaccine. Respondent's experts Dr. Liacouras and Dr. Romberg disputed Dr. Sferra's proposed theories on the basis that they were not based on epidemiologic studies, that there was no direct link between rotavirus and IBD. It has been reiterated countless times within the Program that petitioners' standard for the first *Althen* prong does not require them to provide "epidemiologic studies, rechallenge[] the presence of

pathological markers or genetic disposition, or [show] general acceptance in the scientific or medical communities.” *Capizzano*, 440 F.3d at 1325 (quoting *Althen*, 418 F.3d at 1280). Instead, as explained above, “[a] petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner’s case.” *Moberly*, 592 F.3d at 1322. Respondent’s experts additionally assert that A.R.’s symptoms began before vaccination, and therefore the theories could not be applicable. As noted above, there is preponderant evidence that A.R.’s symptoms of VEO-IBD began after her vaccination and I find the theory presented by Dr. Santoro and Dr. Sferra to be persuasive. *See, e.g., Morgan*, 2015 WL 9694667. In general, “the statutory standard of preponderance of the evidence requires a petitioner to demonstrate that the vaccine more likely than not caused the condition alleged.” *LaLonde*, 746 F.3d at 1339. Accordingly, for the above reasons, I find that Petitioner has presented a sound and reliable medical theory that the rotavirus vaccine could cause a rotavirus infection, which could lead to a disruptive inflammatory process in the intestine and result in the development of IBD, and therefore, Petitioner has satisfied the first *Althen* prong.

C. *Althen* Prong Two

Under *Althen* prong two, Petitioner must prove by a preponderance of the evidence that there is a “logical sequence of cause and effect showing that the vaccination was the reason for the injury.” *Capizzano*, 440 F.3d at 1324 (quoting *Althen*, 418 F.3d at 1278). “Petitioner must show that the vaccine was the ‘but for’ cause of the harm . . . or in other words, that the vaccine was the ‘reason for the injury.’” *Pafford*, 451 F.3d at 1356 (internal citations omitted). This includes instances where an action is “a substantial factor in bringing about the harm, and that the harm would not have occurred but for that action.” *Shyface*, 165 F.3d at 1365 (internal citations omitted). The Federal Circuit has explained that in such cases, “while the vaccination must be a substantial factor in the [injury], it need not be the sole factor or even the predominate factor.” *Pafford*, 451 F.3d at 1357.

In evaluating whether this prong is satisfied, the opinions and views of the vaccinee’s treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 (“[M]edical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a ‘logical sequence of cause-and-effect show[s] that the vaccination was the reason for the injury.’” (quoting *Althen*, 418 F.3d at 1280)). Medical records are generally viewed as trustworthy evidence, since they are created contemporaneously with the treatment of the vaccinee. *Curcuras*, 993 F.2d at 1528. Petitioner need not make a specific type of evidentiary showing, i.e., “epidemiologic studies, rechallenge, the presence of pathological markers or genetic predisposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect.” *Capizzano*, 400 F.3d at 1325. Instead, Petitioner may satisfy her burden by presenting circumstantial evidence and reliable medical opinions. *Id.* at 1325–26.

There is preponderant evidence in the record to support a logical sequence of cause and effect showing the February 8, 2017 rotavirus vaccination was a substantial factor in causing A.R.'s VEO-IBD. As discussed above, I do not find preponderant evidence that A.R.'s reflux and weight trends are indicative of IBD symptom onset prior to vaccination. Following vaccination, A.R. experienced significant diarrhea, dehydration, and tested positive for rotavirus in her stool. Although Dr. Romberg testified that "everybody sheds rotavirus after rotavirus vaccination," and thus did not believe this to be indicative of a rotavirus infection, Yen et al. found that only 21% of samples collected following rotavirus vaccination were positive for rotavirus. Resp't's Ex. A, Tab 16. Further, until A.R.'s eventual diagnosis of VEO-IBD, her treating physicians consistently noted her diagnosis to be rotavirus enteritis. *See* Pet'r's Ex. 10 at 4532 (Dr. Lewis noting A.R.'s diagnosis to be "villous atrophy secondary to rotavirus enteritis" on February 22, 2017); 4533 (endocrinology noting that A.R.'s diagnosis was "pseudohypoaldosteronism secondary to her severe case of rotavirus enteritis"). Additionally, once diagnosed with VEO-IBD, A.R.'s physicians opined that her VEO-IBD may have been exacerbated by her rotavirus vaccine. *See* Pet'r's Ex. 10 at 4373 (Dr. Lewis noting that original positive rotavirus test was due to the vaccine, and that A.R.'s symptoms were likely the result of "a significant and severe intestinal inflammatory condition"); *but see* Pet'r's Ex. 10 at 5265 (noting A.R.'s diagnosis as "immune disorder leading to infantile onset IBD like picture perhaps expedited by rotavirus"); *see also* Pet'r's Ex. 11 at 1427 (noting that "[a]ccording to [the gastrointestinal department], assumption is that she has an immune disorder leading to infantile onset IBD perhaps expediated by rotavirus infection"). I also find it persuasive that A.R.'s treating physicians also relate A.R.'s rotavirus infection to the onset of her VEO-IBD.

Further, I find it persuasive that A.R.'s pathology meets Dr. Romberg's own explanation of an infected patient shedding rotavirus as opposed to asymptomatic shedding following vaccination. Dr. Romberg testified that the primary difference between shedding rotavirus following vaccination and an acute enteritis would be the existence of symptoms explaining the enteritis. *See* Tr. 208:3–4. At the time of A.R.'s initial positive stool samples, she was experiencing several symptoms, including vomiting, diarrhea, and dehydration. Although Respondent attributes these symptoms to A.R.'s VEO-IBD by claiming they began prior to vaccination, as noted above, there is preponderant evidence to show that these symptoms began *after* vaccination, and thus could not be explained away as pre-existing.

The relation of these symptoms in the medical record is also consistent with the theory proposed by Dr. Santoro and Dr. Sferra that an acute rotavirus infection resulting from A.R.'s receipt of the rotavirus vaccine triggered her VEO-IBD. Dr. Sferra specifically testified that the unique composition of her gut microbiome due to her pre-existing genetic susceptibility was then aggravated by A.R.'s receipt of the rotavirus vaccine. Although Respondent continuously argues that A.R.'s VEO-IBD was monogenic, and therefore would have developed regardless of whether she received the rotavirus vaccine, I find this argument generally unpersuasive given the heavy

reliance on speculation by Respondent and the fact that A.R.'s treating physicians did not appear to relate her symptoms directly to a monogenic cause. Instead, A.R.'s physicians noted the complex causes of VEO-IBD and suggested that her genetic defect may have played a role in her susceptibility towards VEO-IBD, which was then exacerbated by A.R.'s rotavirus infection. I also find Petitioner's explanation of A.R.'s symptoms persuasive given that Respondent's experts concede the possibility that a live rotavirus vaccine can cause a rotavirus infection, and that Petitioner's physicians appear to relate her VEO-IBD towards a combination of a vaccine-induced infection and genetic susceptibility. Contrary to Respondent's assertions, this case appears to be the illustration of a potential genetic defect that is confronted by a live virus, creating an environment which would allow for the development of symptoms such as with A.R.

Accordingly, Petitioners have presented preponderant evidence consistent with the mechanism to show a logical sequence of cause and effect that the rotavirus vaccine was a substantial factor in the development of A.R.'s VEO-IBD and satisfies the second *Althen* prong.

D. *Althen* Prong Three

Althen prong three requires Petitioner to establish a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been defined as a "medically acceptable temporal relationships." *Id.* Petitioner must offer "preponderant proof that the onset of symptoms occurred within a time frame for which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." *de Bazan*, 539 F.3d at 1352. The explanation for what is a medically acceptable time frame must also coincide with the theory of how the relevant vaccine can cause the injury alleged (under *Althen* prong one). *Id.*; *Koehn v. Sec'y of Health & Hum. Servs.*, 773 F.3d at 1239, 1243 (Fed. Cir. 2014); *Shapiro*, 101 Fed. Cl. at 542; *see Pafford*, 451 F.3d at 1358. A temporal relationship between a vaccine and an injury, standing alone, does constitute preponderant evidence of vaccine causation. *See, e.g., Veryzer*, 100 Fed. Cl. at 356 (explaining that "a temporal relationship alone will not demonstrate the requisite causal link and that [P]etitioner must posit a medical theory causally connecting the vaccine and injury").

As stated above, I find by preponderant evidence that the onset of A.R.'s VEO-IBD symptoms began after vaccination. However, Dr. Liacouras and Dr. Romberg contend that the onset of A.R.'s diarrhea was too soon after vaccination to be reasonably attributed to a rotavirus infection resulting from the vaccine. Dr. Sferra opined that A.R.'s symptoms were consistent with the medical literature, as the onset for a wildtype rotavirus infection typically occurs between one to three days; however, he also admitted that if A.R.'s symptoms began within 24 hours of vaccination that it would be too soon to attribute to her receipt of the rotavirus vaccine.

Dr. Sferra relied on Blacklow & Greenberg to show the incubation period for a rotavirus infection to be between one and three days. Dr. Liacouras relied on Lee et al. to rebut this assertion, as that article found that onset of symptoms in 25% of cases occurred at 1.6 days, with a 95% confidence interval of 1.1 to 1.9 days. Resp't's Ex. A, Tab 15 at 7. However, Dr. Liacouras testified that A.R.'s symptoms would only be consistent with the article if it could be shown that she began

experiencing diarrhea at exactly 1.6 days after vaccination or greater, which he argued could not be proven. Tr. 130:8–13. Given that both articles filed show symptoms occurring on or about one day following vaccination, and that A.R.’s reported history consistently notes the onset of symptoms the day following vaccination, I find by preponderant evidence that this timing is consistent with a proximate temporal relationship between vaccination and injury. *See Althen*, 418 F.3d at 1278. Thus, Petitioner has satisfied the third *Althen* prong.

E. Alternative Causation

Because I conclude that Petitioner has established a prima facie case, Petitioner is entitled to compensation unless Respondent can put forth preponderant evidence “that [Petitioner’s] injury was in fact caused by factors unrelated to the vaccine.” *Whitecotton v. Sec’y of Health & Hum. Servs.*, 17 F.3d 374, 376 (Fed. Cir. 1994), *rev’d on other grounds sub nom., Shalala v. Whitecotton*, 514 U.S. 268 (1995); *see also Walther v. Sec’y of Health & Hum. Servs.*, 485 F.3d 1146, 1151 (Fed. Cir. 2007). Here, Respondent contends that A.R.’s VEO-IBD is the result of her WDFY4 genetic mutation rather than her receipt of the rotavirus vaccine. Respondent’s experts, Dr. Liacouras and Dr. Romberg, rely significantly on the notes of Dr. Chandrakasan, who diagnosed A.R. with a suspect biallelic defect in WDFY4 and VEO-IBD with IPEX-like gastrointestinal biopsy phenotype. They argued that the usage of a bone marrow transplant as a treatment option for A.R. likely would not have been undertaken if Dr. Chandrakasan did not believe that A.R. suffered from a genetic disorder as such treatments can be curative for monogenic forms of IBD.

Although Dr. Liacouras focused more on early-symptom onset to support a theory of monogenic IBD, which I addressed above, Dr. Romberg focused on A.R.’s genetic testing and WDFY4 genetic variant of unknown significance. He acknowledged that WDFY4 was not a gene mutation associated with IBD in any of the filed medical literature and argued that more studies may have been conducted since the filing of the literature which may have found that variant to be associated with IBD. He based his argument on the study by Uhlig et al. which found that monogenic causes can be identified in up to 41% of VEO-IBD cases. Resp’t’s Ex. D, Tab 3. However, I do not find this speculation to be sufficient to satisfy the preponderant evidence standard. It was repeatedly acknowledged by A.R.’s treating physicians that her genetic defect was not associated with VEO-IBD and was instead a variant of unknown significance. Further, Dr. Romberg, like Dr. Liacouras, relied on the manifestation of symptoms prior to vaccination to support a theory that A.R.’s VEO-IBD must have been monogenic, in addition to her existing genetic defect. However, as noted above, there is not preponderant evidence that A.R.’s symptoms began pre vaccination. Furthermore, the presence of a genetic defect which cannot explain A.R.’s condition beyond mere speculation is insufficient to satisfy Respondent’s burden for alternative causation. Dr. Romberg also opined that A.R. could have suffered from a somatic, or acquired, genetic mutation, but he admitted on cross-examination that there was no such evidence in the medical record to support such a theory. Tr. 190:1–2. It is also notable that Respondent and his experts levied accusations of speculative medical theories at Petitioners and their experts, citing a lack of epidemiologic studies, only for Dr. Liacouras and Dr. Romberg assert opinions and theories of genetic causation based on speculation. Importantly, the employing medical institution of both Dr. Liacouras and Dr. Romberg, CHOP, considers monogenic forms of VEO-IBD to be “very rare,” and “very often” they instead identify multiple potential causes for a patients VEO-IBD. Pet’r’s Ex. 93. Given that Respondent’s arguments in support of alternative causation rely on pure speculation, I find that they have failed to show that it is more likely than not that an alternative

cause was the sole cause of A.R.'s injury. Thus, Respondent did not prove by a preponderance of the evidence that Petitioner's injury is "due to factors unrelated to the administration of the vaccine." § 13(a)(1)(B).

VII. Conclusion

For the reasons discussed above, I find that Petitioners have established by preponderant evidence that A.R.'s rotavirus vaccine caused her VEO-IBD. Therefore, Petitioners are entitled to compensation. A separate damages order will issue.

IT IS SO ORDERED.

s/Herbrina D. S. Young
Herbrina D. S. Young
Special Master