In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 14-113V
(to be published)

EVANS JOHNSON, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	Special Master Corcoran Dated: January 6, 2017 Decision; Human Papillomavirus ("HPV") Vaccine; Immune Thrombocytopenic Purpura ("ITP"); Onset; Discovery of Condition.

Joseph M. Pepper, Conway Homer P.C., Boston, MA, for Petitioner.

Heather L. Pearlman, U.S. Dep't of Justice, Washington, DC, for Respondent.

ENTITLEMENT DECISION[1]

On February 7, 2014, Lynn Johnson filed a petition as legal representative of her minor child, E.J., seeking compensation under the National Vaccine Injury Compensation Program ("Vaccine Program"),[2] alleging that the human papillomavirus ("HPV") vaccine received on July 15, 2011, caused E.J. to develop immune thrombocytopenic purpura ("ITP").[3] ECF No. 1. The

[1] Because this decision contains a reasoned explanation for my actions in this case, I will post it on the United States Court of Federal Claims website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the published decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the whole decision will be available to the public. *Id*.

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

[3] ITP is characterized by a decrease in the number of platelets. *Dorland's Medical Dictionary* 1922 (32nd ed. 2012) (hereinafter "*Dorland's*"). As discussed in greater detail herein, the condition used to be known as "idiopathic" thrombocytopenic purpura but is now defined as "immune" thrombocytopenic purpura, because it is generally thought

case caption was subsequently amended on February 12, 2016, to identify Evans Johnson as the Petitioner after she ceased being a minor. ECF No. 29.

An entitlement hearing was held in Washington, DC, on May 25, 2016, and in the months following the parties submitted post-hearing briefs. *See* ECF Nos. 38 and 40. Having completed my review of the parties' filings and the evidentiary record, I hereby **DENY** Petitioner's request for compensation. As discussed in greater detail below, resolution of the claim turns not on whether Petitioner experienced ITP at all, or whether a vaccine could cause the condition, but rather whether her ITP began after she received the HPV vaccine.

I. FACTUAL BACKGROUND

Ms. Johnson was born on December 13, 1997. Petitioner's Exhibit ("Pet'r's Ex.") 1 at 4. The medical records filed in this case do not show that she experienced any significant illnesses or complications for the majority of her adolescence, other than an arteriovenous malformation ("AVM")[4] in her left medial hindfoot. Pet'r's Ex. 4 at 5. Petitioner was diagnosed with the AVM at age three or four and had surgery performed on it in 2007. *Id*. Prior to the vaccination at issue, Petitioner had two blood tests (on April 16 and October 20, 2009, respectively) revealing normal platelet counts of 228,000 and 200,000, based upon a "normal" range of 150,000 to 450,000. Pet'r's Ex. 1 at 22.

Petitioner received the HPV vaccine on July 15, 2011, during her well-child check-up at Mayfair Medical Clinic in Birmingham, Alabama. Pet'r's Ex. 1 at 4, 63. The medical records reveal no subsequent reaction in the immediately-following days and weeks, nor does Petitioner allege she experienced one. A little over one month later, on August 18, 2011, Petitioner was seen in the Department of Radiology at the University of Alabama at Birmingham ("UAB") to evaluate the reoccurrence of the AVM in her left heel. Pet'r's Ex. 4 at 6, 11. Petitioner returned to the UAB Hospital on August 24, 2011, for a scheduled embolization[5] of her AVM. *Id.* at 20, 31. It was then that the first indicator of Petitioner's ITP was discovered, as her pre-surgery lab work revealed a low platelet count of 65,000. *Id.* at 46.

Ms. Johnson's AVM procedure was performed as scheduled. Then, on September 7, 2011, Petitioner was seen for a follow-up after the embolization. Pet'r's Ex. 4 at 45. Petitioner reported no complaints and was asymptomatic, but the records note that she now had a platelet count of 64,000 – slightly lower than that measured in August. Pet'r's Ex. 1 at 21. Petitioner also

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to be caused by an autoimmune process involving activation against platelets that causes them to be eliminated in large amounts from blood. Tr. at 7.

[4] Arteriovenous means both arterial and venous; pertaining to or affecting an artery and a vein. *Dorland's* at 144. Malformation is a morphologic defect resulting from an intrinsically abnormal developmental process. *Id.* at 1098.

[5] Embolization is the therapeutic introduction of a substance into a blood vessel in order to close it. *Dorland's* at 606.

individually recounted to her treater a recent platelet level of 70,000, but he could not corroborate the statement based upon review of existing computer records. Pet'r's Ex. 4 at 46. It was recommended that Ms. Johnson consult with a hematologist about the platelet count if it did not soon return to normal. *Id.*

Dr. Stuart Cramer, a hematologist and oncologist, saw Petitioner at Children's of Alabama Health Center in Birmingham for an evaluation of possible thrombocytopenia on September 12, 2011, and he examined her while also performing a follow-up platelet count test. Pet'r's Ex. 2 at 86-87. Dr. Cramer's written assessment confirmed that Petitioner had experienced no symptoms until her lowered platelet count had been inadvertently discovered in preparation for her AVM procedure. *Id.* at 86. Petitioner's platelet count was now recorded at 86,000, however, which Dr. Cramer deemed an improvement from her lower readings in August and early September. *Id.* Based on these results and his examination, Dr. Cramer proposed that Ms. Johnson had "thrombocytopenia, etiology unclear, however most likely idiopathic in nature," and he opined that intervention was unnecessary due to this improvement in her platelet levels. *Id.*

Ms. Johnson returned to Dr. Cramer for follow-up lab work at the end of September 2011. Pet'r's Ex. 2 at 78-85. Petitioner's anti-nuclear antibody ("ANA") titer[6] was now positive, although her platelet count had risen again, to 93,000. *Id.* at 78, 85. Based upon the ANA titer results coupled with the still relatively low platelet counts (despite the noted improvement), Dr. Cramer referred Petitioner to the rheumatology department at Children's of Alabama Health Center for further evaluation. *Id.* at 87.

On October 19, 2011, Petitioner obtained a consultation with a rheumatologist, Dr. Tim Beukelman, M.D. Petitioner reported no complaints or new symptoms and appeared normal, but Dr. Beukelman nevertheless ordered lab testing in order to evaluate her for lupus. Pet'r's Ex. 2 at 76-77. Dr. Beukelman's recorded assessment noted that Petitioner had asymptomatic ITP that had been determined from an incidental finding, but stated (consistent with Dr. Cramer's assessment) that the ITP appeared to be "resolving spontaneously" given the rising platelet counts. *Id.* at 77. He further noted that there were no other signs suggestive of systemic lupus erythematosus ("SLE"),[7] other than the previously-observed positive ANA titer – a result that was mitigated by a

[6] An antibody is an immunoglobulin molecule that has a specific amino acid sequence by which it interacts only with the antigen that induced its synthesis in cells, or with antigen closely related to it. *Dorland's* at 100. An ANA is an antibody directed against nuclear antigens. ANAs are almost always found in individuals suffering from systemic lupus erythematosus, and frequently in rheumatoid arthritis. *Id.* at 101.

[7] Systemic lupus erythematosus is a chronic, inflammatory, often febrile multisystem disorder of connective tissue that proceeds through remissions and relapses. It may be either acute or insidious in onset and is characterized principally by involvement of the skin, joints, kidneys, and serosal membranes. It can be marked by a wide variety of abnormalities, including thrombocytopenia. *Dorland's* at 1080.

negative ENA panel result.[8] *Id.* at 75, 77. Dr. Beukelman proposed a return to the rheumatology department in 12 months to check again for SLE, and otherwise recommended a repeat in blood testing in the more immediate future. *Id.* at 77.

Petitioner was then seen back at Mayfair Medical Group on November 3, 2011, due to complaints of a sore throat. Pet'r's Ex. 1 at 59. Her platelet count was now measured to be 42,000 – the lowest it had been since the first low-count discovery three months before. *Id.* at 21. Over the next few months, Petitioner was seen every week at Mayfair Medical Group to have her platelet count re-checked at the direction of Dr. Beukelman. *Id.* at 25. Her platelet counts during this time fluctuated but remained low overall, with results (over the course of November and December) of 69,000; 52,000; 57,000; 61,000; 58,000; and 59,000. *Id.* at 20-21.

On January 11, 2012, Petitioner returned to Children's of Alabama Health Center for a check-up with Dr. Beukelman. Pet'r's Ex. 2 at 62-64. Petitioner reported feeling well, with no symptoms. *Id.* at 62. Petitioner's platelet levels were in the 50,000 range at this appointment, and Dr. Beukelman again expressed concern that these low levels might represent an early presentation of lupus. *Id.* He proposed immunoglobulin ("IVIG")[9] treatments to address Ms. Johnson's persistently low platelet counts. *Id.* Dr. Beukelman's notes also reveal that Petitioner's mother stated at the time to Dr. Beukelman that Petitioner had received the HPV vaccine over the summer, and that she had seen reports of "ga[]rdasil with rare se[q] of thrombocytopenia." *Id.* at 62. But the records do not indicate that Dr. Beukelman for his part deemed the vaccine to be related to Ms. Johnson's low platelet count. *Id*.

Petitioner received her first IVIG infusion on February 13, 2012. Pet'r's Ex. 2 at 52-53. The next day, on February 14, 2012, Petitioner presented with complaints of an increasing headache and neck pain, most likely a side effect of the treatment. *Id.* at 45-50. Petitioner was diagnosed with headache secondary to aseptic meningitis and treated with saline before being discharged that same day. *Id.* at 49. Ms. Johnson had no other reaction to the IVIG treatments in the weeks thereafter, nor was her headache attributed to any other cause.

In the ensuing five months, Petitioner's platelet count remained low, although she continued to suffer no obvious ITP-related symptoms. *See, e.g.,* Pet'r's Ex. 1 at 25-26. Dr. Beukelman saw Petitioner for a follow-up visit on July 11, 2012, and noted that though she

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[8] An ENA panel test attempts to measure amounts of the extractable nuclear antigen, a specific kind of antinuclear antibody. ENA panels are often performed after a positive ANA test to help diagnose and distinguish the type of autoimmune disorder detected, and thus help treaters evaluate the meaningfulness of the initial ANA measurements. *See* American Association for Clinical Chemistry, *ENA Panel*, Lab Tests Online, https://labtestsonline.org/understanding/analytes/ena-panel/tab/test (last visited Dec. 19, 2016).

[9] Immunoglobulin is a concentrated preparation containing mostly gamma globulins from a large pool of human donors. It is used for treatment of hypogammaglobulinemia or agammaglobulinemia in immunodeficient patients, and can also be used for passive immunization against measles, hepatitis A, and varicella. *Dorland's* at 785.

presented with ANA and anti-thyroid antibodies, suggestive of early lupus, she still did not meet the other diagnostic criteria for the disease at that time. *Id.* at 25. That same day, Petitioner received her first Rituximab[10] infusion, intended to treat her low platelet count. *Id.* at 23. The following day, Petitioner had a well-child visit at Mayfair Medical Group with Bevelle Worthen, M.D. *Id.* at 16. Petitioner stated that she felt nauseated after her Rituximab infusion, but she otherwise reported no bleeding, bruising, or limitations on her physical activity. *Id.* at 19. Dr. Worthen did note that Petitioner conveyed she no longer wanted to receive HPV vaccinations. *Id.* Petitioner underwent a second Rituximab infusion on July 25, 2012. Pet'r's Ex. 2 at 25.

Petitioner's ITP continued to be monitored over the following months. Thus, at a September 2012 visit to follow up with her ongoing AVM, Ms. Johnson's platelet count was measured at 63,000. Pet'r's Ex. 10 at 2. After a follow-up with Dr. Beukelman on October 17, 2012, Petitioner's platelet count was now recorded at 94,000, a level he termed "borderline normal approximately 3 months after Rituximab." Pet'r's Ex. 2 at 18, 20. On November 5, 2012, Petitioner underwent another surgery to correct her left foot AVM. Pet'r's Ex. 4 at 118, 142. At this time, her platelet count had now risen to 106,500. Pet'r's Ex. 4 at 167. Petitioner continued to be seen for lab work into 2013, with recorded platelet counts in the 110,000 to 140,000 range. Pet'r's Ex. 6 at 28; Pet'r's Ex. 12 at 34.

Dr. Beukelman saw Petitioner again on March 6, 2013, and noted that he was uncertain if her ITP could still be interpreted as a possible SLE indicator, considering that her condition had not changed in the eighteen months since her initial diagnosis. Pet'r's Ex. 2 at 3. He recommended against further treatment unless her platelet count fell below 40,000 or she developed other "features." *Id*. Ms. Johnson again saw Dr. Beukelman on July 9, 2014, for a follow up, where he confirmed the lack of evidence of lupus despite her three-year duration of ITP. Pet'r's Ex. 17 at 17. He also stated that her multiple AVMs were curious, but there was no recognized association between AVMs and ITP. Pet'r's Ex. 18 at 21.

On July 8, 2015, Petitioner was seen at Children's of Alabama Health Center, where it was noted that her platelet count remained stable, between 74,000 and 119,000 over the past year. Pet'r's Ex. 17 at 33; Pet'r's Ex. 18 at 10. Dr. Beukelman also stated at this visit that though there was no diagnosis of lupus, he suspected that eventually Petitioner would develop additional autoimmune manifestations of the disease, based on her positive ANA titer and anti-thyroid Ab. Pet'r's Ex. 18 at 10. No subsequent medical records were filed in the matter.

[10] Rituximab is a chimeric murine/human monoclonal antibody that binds the CD 20 antigen, and is used as an antineoplastic in the treatment of CD20-positive, B-cell non-Hodgkin lymphoma. It is administered intravenously. *Dorland's* at 1650.

II. TESTIMONY PRESENTED AT HEARING

A. Petitioner's Expert – Dr. Paula Goodman Fraenkel

Dr. Fraenkel offered two expert reports, as well as testimony during the entitlement hearing. *See* June 26, 2014 Report, filed on July 30, 2014, as Pet'r's Ex. 13 (ECF No. 16-1) ("First Fraenkel Rep."); March 9, 2015 Report, filed on March 17, 2015, as Pet'r's Ex. 15 (ECF No. 23-1) ("Second Fraenkel Rep."). Dr. Fraenkel testified as an expert in hematology and oncology, opining in favor of Petitioner's theory that Ms. Johnson's ITP was caused by the HPV vaccine. Tr. at 5, 7.

Dr. Fraenkel is a staff physician in the Hematology/Oncology Division at Beth Israel Deaconess Medical Center in Boston, Massachusetts. First Fraenkel Rep. at 1. She graduated from Harvard Medical School in 1995. Tr. at 4; First Fraenkel Rep. at 1. She completed her residency in internal medicine at Tufts New England Medical Center, and thereafter completed a fellowship in hematology and oncology at Beth Israel Deaconess Medical Center. Tr. at 4-5; First Fraenkel Rep. at 1. She then did a post-doctoral fellowship in hematology research at Children's Hospital in Boston, Massachusetts. First Fraenkel Rep. at 1. Dr. Fraenkel currently is on the editorial board of the journal, Blood, and serves as an assistant professor at Harvard Medical School teaching residents, fellows, and medical students. Tr. at 5. She is licensed by the American Board of Internal Medicine and is a registered physician in Massachusetts. First Fraenkel Rep. at 9.

Besides the academic and research experience referenced above, Dr. Fraenkel has ongoing clinical exposure to blood-related illnesses like ITP, although she has not published any articles specifically on that condition. Tr. at 35. Thus, Dr. Fraenkel currently evaluates and treats patients in a hematology clinic, in which she sees eight to ten patients per week and gives general consultations relating to anemia, high or low blood counts, bleeding or clotting problems, and hemochromatosis. First Fraenkel Rep. at 9. She also presently treats patients with ITP, seeing approximately 25 patients each year with this diagnosis (although all are adults). Tr. at 5, 35. She has never had a patient whose ITP was thought to have possibly been induced by the HPV vaccine, as here, though she did clarify that her patients are generally not in the age range of individuals receiving that vaccine. *Id.* at 52, 58.

Dr. Fraenkel began her testimony by explaining that ITP previously stood for "idiopathic" thrombocytopenic purpura but is now called "immune" thrombocytopenic purpura, because it is thought to be mediated by an autoimmune process involving antibody attacks against platelets. Tr. at 7-8; *see also* D.B. Cines et al., *The ITP Syndrome: Pathogenic and Clinical Diversity*, 113 Blood 26: 6511 (2009) (filed as Pet'r's Ex. 15 Tab E) ("Cines II"). She also highlighted the difference between primary and secondary ITP, noting that primary ITP occurs with no known underlying

cause, while secondary is believed to involve a contributing factor, such as an infection or vaccine. Tr. at 8.

Ms. Johnson, Dr. Fraenkel opined, suffered from ITP secondary to the HPV vaccine. She did not see any evidence in the record of an alternative cause, nor did she understand there to be a medically-recognized association between Petitioner's AVM malformation and the low platelet counts. Tr. at 12. Primary ITP is also more common in young children; 80 percent of primary ITP occurs in children under the age of eight, whereas Petitioner was 14 at the time of her vaccination. *Id.* at 13. In addition, although Petitioner's treating doctors considered her positive ANA titers to be possibly indicative of SLE, Dr. Fraenkel proposed that such evidence corroborated the autoimmune nature of her condition, especially because Ms. Johnson ultimately showed no other signs of lupus. *Id.* at 15, 47.

Dr. Fraenkel submitted several articles and case studies, which she alleged established a causal link between the HPV vaccine and ITP. Tr. at 55-56. One of these articles was L. Grimaldi-Bensouda et al., *Autoimmune Disorders and Quadrivalent Human Papillomavirus Vaccination of Young Female Subjects*, 275 J. Intern. Med. 4:398 (2014) (filed as Pet'r's Ex. 13 Tab C), a case study review of six cases of ITP occurring after a prior HPV vaccination. Tr. at 56. Another article, T. Harris et al., *Adverse Events Following Immunization in Ontario's Female School-Based HPV Program*, 32 Vaccine 1061:1063 (2014) (filed as Pet'r's Ex. 13 Tab B), discussed a single confirmed case of thrombocytopenia that was considered HPV-related. Tr. at 56. A third item filed was a letter to the editor of a scientific vaccine-related journal involving a report of a single case of acute ITP occurring three months after receipt of the Gardasil HPV vaccine. Tr. at 46; G. Pugnet et al., *Immune Thrombocytopenic Purpura Following Human Papillomavirus Vaccination*, Letter to the Editor, 27 Vaccine 3690 (2009) (filed as Pet'r's Ex. 13 Tab A) ("Pugnet").

Although Dr. Fraenkel acknowledged that the case studies she offered did not specifically address causation (or even involve scientific studies exploring or helping to establish the link between the HPV vaccine and ITP)[11] and instead might only be indirect evidence of an association, she emphasized they still merited some weight in consideration of the causal question in this case. Tr. at 59-60. She also admitted that not all vaccines could be associated with ITP (Tr. at 49), although she pointed out that other vaccines (in particular, the measles-mumps-rubella ("MMR")) vaccine, as well as some others not covered under the Vaccine Act) had been so linked to the disease. *Id.* at 58.

Dr. Fraenkel also took issue with several of the epidemiologic studies Respondent cited as disproving any causal relationship between the HPV vaccine and ITP. Tr. at 27. Thus, Dr. Fraenkel

[11] Indeed, the authors of the Pugnet letter themselves acknowledged that the reported ITP instance was insufficient to establish a causal relationship. Pugnet at 3690.

opined that Ms. Johnson would have been excluded from some of them because she was never hospitalized for her ITP. *Id.*; L. Sauvé et al., *Postvaccination Thrombocytopenia in Canada*, 29 Pediatric Infectious Disease J. 6:559 (2010) (filed as Resp't's Ex. L) ("Sauvé"); L. Arnheim-Dahlstrom et al., *Autoimmune, Neurological, and Venous Thromboembolic Adverse Events after Immunisation of Adolescent Girls with Quadrivalent Human Papillomavirus Vaccine in Denmark and Sweden*, 347 BMJ 1:2 (2013) (filed as Resp't's Ex. C) ("Arnheim-Dahlstrom"). Both of these studies focused solely on hospital diagnoses, thereby leaving out individuals like Petitioner, who had (as the medical records show) experienced only a very mild form of the disease. Tr. at 27-28. Other epidemiologic evidence, like Grimaldi-Bensouda, was insufficiently powered[12] to allow any conclusions to be drawn about the overall expected incidence of autoimmune diseases like ITP. Tr. at 28; Grimaldi-Bensouda at 405. She also questioned the reliability of studies involving manufacturer-reported adverse events, which the authors themselves noted did not provide sufficient data to perform a full case review. Tr. at 29; B. Slade et al., *Postlicensure Safety Surveillance for Quadrivalent Human Papillomavirus Recombinant Vaccine*, 302 JAMA 7:750 (2009) (filed as Pet'r's Ex. 15 Tab J). Another such large-scale study, C. Chao et al., *Surveillance of Autoimmune Conditions Following Routine Use of Quadrivalent Human Papillomavirus Vaccine*, 271 J. Intern. Med. 193: 201-02 (2012) (filed as Pet'r's Ex. 15 Tab K) ("Chao"), was in her opinion similarly flawed, both for methodologic reasons as well as its possible bias, given that the source of its funding was a pharmaceutical company with an economic interest in its determinations. Tr. at 29; Chao at 202.

For a scientific mechanism by which the autoimmune process necessary to cause ITP after receipt of the HPV vaccination could theoretically occur, Dr. Fraenkel proposed molecular mimicry. She described molecular mimicry as an immune response to an infection or a vaccination resulting in an unintended immune response against proteins on the platelets, causing platelet destruction. Tr. at 8; Second Fraenkel Rep. at 2-3 (explaining the "phenomenon" thought to occur during vaccine-associated ITP). In support, she offered two pieces of scientific literature discussing the biologic process by which ITP was believed to occur following vaccination. Tr. at 8-10; Cines II at 6511; C. Perricone et al., *Immune Thrombocytopenic Purpura (ITP) Associated with Vaccinations: A Review of Reported Cases*, 60 Immunology Res. 226:227 (2014) (filed as Pet'r's Ex. 15 Tab L) ("molecular mimicry is considered the classic pathogenic mechanism responsible for ITP development after vaccinations").[13]

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[12] "The power of an epidemiologic study is the probability of finding a statistically significant association of a given magnitude (if it exists) in light of the sample sizes used." Michael D. Green et al., "Reference Guide on Epidemiology," in *Reference Manual on Scientific Evidence* 549, 582 (Federal Judicial Center, 3d ed. 2011). A study with a greater sample size, and therefore sufficient statistical power, can more persuasively support a determination as to whether a causal link exists. *Id*.

[13] Dr. Fraenkel admitted, however, that she had not identified or offered any particular literature discussing the exact protein sequences that would demonstrate homology (meaning a correspondence in structure, position, origin, etc. (*see Dorland's* at 868)) between components of the HPV vaccine and the blood platelets. Tr. at 68. She was also unable to produce any studies that examined antibodies produced by the HPV vaccine against platelets, and there were no reports identifying an antibody against a specific platelet antigen following HPV vaccination. Tr. at 48. And in any

At the hearing, much of Dr. Fraenkel's testimony was devoted to addressing the differences between the presentation and symptoms of "chronic" versus "acute" ITP – a matter that Respondent's expert (as discussed in more detail below) deemed highly relevant to whether Ms. Johnson's ITP could be considered vaccine-induced. Tr. at 11. Dr. Fraenkel admitted that there were some differences in the presentation of both. *Id.* at 11-12. Dr. Fraenkel characterized the acute form of ITP as more commonly experienced by children (and also more consistently linked to vaccines). *Id.* This version of the disease tended to have a very short duration and spontaneously cease, whereas older children and adults were more likely to experience a longer, chronic form requiring repeated courses of treatment. *Id.* at 12.

Dr. Fraenkel acknowledged that Petitioner did not fit the description of the acute presentation in young children, as described in Cines II. Tr. at 36-37; Cines II at 6513. Indeed – Dr. Fraenkel was largely compelled at hearing to admit that, if anything, Ms. Johnson's form of the condition appeared far more like the chronic version. Thus, in her direct testimony, Dr. Fraenkel initially attempted to classify Ms. Johnson's ITP as having resolved within 12 months of onset, therefore meeting a clinical definition of acute. Tr. at 20. Petitioner's primary treating doctor, Dr. Beukelman, however, had diagnosed her ITP as chronic very recently (*see, e.g.,* Pet'r's Ex. 17 at 33 (July 2015 record)), and there was record evidence that Petitioner's platelet count continued to fluctuate even more than a year from the time her low platelet count was first discovered. When such facts were pointed out to Dr. Fraenkel on cross-examination, she modified her position to be that Petitioner was merely on the "borderline" between acute and chronic ITP. Tr. at 21, 44-45.

However, Dr. Fraenkel insisted that Ms. Johnson's ITP could still have been vaccine-caused, whether acute or chronic in form. Tr. at 12, 44-45. In so arguing, she disputed Dr. Gill's assertion that ITP following vaccination presents most often in the acute form of the disease. On the contrary – she argued that ITP presentations are inherently heterogeneous, depending on the individual involved and their physiologic status or makeup. *Id.* at 18.[14] She attributed the apparent association between the acute form of ITP and vaccination to the fact that young children most commonly receive the MMR vaccine (the vaccine most closely associated with ITP and with acute symptoms). *Id*. By contrast, teenage girls (who have different immune systems and different risks

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event, she is not an immunologist and does not study molecular mimicry on a regular basis, and thus lacked the specific professional expertise to opine on the topic that narrowly. *Id.* at 67.

[14] As further proof for the heterogeneity of ITP's presentation, Dr. Fraenkel offered K. Heitink-Pollé, *Clinical and Laboratory Predictors of Chronic Immune Thrombocytopenia in Children: A Systematic Review and Meta-Analysis*, 124 Blood 22:3295 (2014) (filed as Pet'r's Ex. 15 Tab H) ("Heitink-Pollé"). Tr. at 22-23. Factors relevant to whether ITP presented in acute or chronic form, she maintained, include gender, age (with differences evident at equal to or over 11 years), preceding infection or vaccination, insidious onset, and higher platelet counts at presentation (over 20,000), or the presence of positive ANA – many of which were evident in Petitioner's presentation. *Id.* at 23, 25.

for ITP) are the more likely recipients of the HPV vaccine and would therefore inherently present with different symptoms. *Id.* at 19. She also stated that vaccines are designed to initiate a long-lasting immune response, so it is plausible that an autoimmune reaction resulting in ITP would last for many months, if not years, even if mild in form. *Id.* at 21.

With respect to the temporal development of Petitioner's ITP after vaccination, Dr. Fraenkel contended that it had occurred within a medically appropriate timeframe. For support, she relied on criteria from the World Health Organization ("WHO"). Tr. at 18; *see* Uppsala Monitoring Centre, *The Use of the WHO-UMC System for Standardised Case Causality Assessment* (last visited Dec. 23, 2016), *available at* who-umc.org/Graphics/24734.pdf (filed as Pet'r's Ex. 20) ("WHO Criteria"). The WHO criteria provide a practical tool for assessing case reports in order to detect unexpected adverse reactions, in the form of general definitions of probable associations between a drug and an adverse event. Tr. at 52; WHO Criteria at 2. Applying these standards, Dr. Fraenkel opined that the timing of Petitioner's alleged onset of ITP following the vaccination (based on discovery of her low platelet count on August 24, 2011) was appropriate, coming 40 days after the HPV vaccine had been administered. Tr. at 18, 38. She also considered the timing appropriate when compared to MMR-associated ITP, which is recognized by reliable science to develop within 42 days of vaccination. Tr. at 21; Cines II at 6513.

The timing issue, however, highlighted a deficiency in Petitioner's case in light of undisputed record evidence. Petitioner, as noted above, never presented with any symptoms of ITP. Rather, she displayed a *sign* of the condition: her low platelet count, which was itself only incidentally discovered. When asked when the onset was for Petitioner's ITP, Dr. Fraenkel testified that "I believe that the condition began close to the time that it was discovered." Tr. at 39. To support this contention, however, Dr. Fraenkel could state only (and in circular fashion) that it was "because of the timing after the – after the vaccination," admitting that "**[w]e don't know exactly when her platelet count declined**." *Id.* (emphasis added). Thus, she observed that Ms. Johnson's prior, normal platelet counts were based on blood tests performed two years before vaccination, making it impossible to ascertain when the platelet count had first dropped. In fact, Dr. Fraenkel admitted, onset could have been two, three, or up to eight weeks prior to discovery of the low count in August 2011 (which would place onset *before* the vaccine was administered). *Id.* at 39-40.

Despite such admissions, Dr. Fraenkel maintained her opinion that the platelet decline had most likely begun after vaccination. Tr. at 41. For support, she referenced the trend in Petitioner's platelet counts decline (based on measurements taken in August 2011 and thereafter) as suggesting that, if in fact onset began pre-vaccination, Ms. Johnson would have been more symptomatic and the platelet counts would have continued to decline sooner and more precipitously. *Id.* at 40. Dr. Fraenkel did not believe Ms. Johnson could have gone two years without clinically presenting other symptoms of such a low platelet count, like bleeding or bruising. *Id.* at 41. Thus, the fact that

this did not occur, and that the arc of Petitioner's platelet decline extended into 2012, all made it in her opinion unlikely that Petitioner's ITP began earlier than July 2011. *Id.* at 13.[15]

B. Respondent's Expert – Dr. Joan Cox Gill

Dr. Gill testified for Respondent as an expert in pediatric hematology. Tr. at 72; *see* Resp't's Ex. B at 1-2 ("Dr. Gill's Curriculum Vitae"). Respondent also submitted one expert report from Dr. Gill. *See* December 14, 2014 Report, filed on December 18, 2014, as Resp't's Ex. A (ECF No. 21-1) ("Gill Rep.").

Dr. Gill is a medical director in the Hemophilia and Bleeding Disorders Center at the Children's Hospital of Wisconsin, as well as a professor of medicine, pediatrics, and population health at the Medical College of Wisconsin. Dr. Gill's Curriculum Vitae at 2. Dr. Gill graduated from medical school at the Medical College of Wisconsin, followed by a pediatric internship and residency at Milwaukee Children's Hospital in Wisconsin. Tr. at 70. She then completed a pediatric hematology/oncology fellowship at the Medical College of Wisconsin. *Id*. She is board certified in pediatric hematology and oncology, and is a member of the American Society of Hematology and the Hemostasis and Thrombosis Research Society. *Id*. at 71. She has been in clinical practice for almost 40 years and has both treated and diagnosed many patients with ITP – the majority of whom were children. *Id.* at 70-71. Though she performed basic laboratory research regarding the etiology of acute ITP in her fellowship, she has not published any papers on ITP, or studied the condition, since that time. *Id.* at 72.

Dr. Gill began by clarifying the differences between primary and secondary ITP, in a manner largely consistent with Dr. Fraenkel's testimony. Primary ITP, in her description, is generally a diagnosis reached after ruling out other potential causes, therefore permitting the conclusion that the ITP's cause could only be idiopathic. Tr. at 99. Secondary ITP involves thrombocytopenia occurring in response to some prior condition, such as a viral infection, autoimmune disorder, or certain vaccines like the MMR vaccine. *Id.* at 76. In most cases of childhood ITP, the development of the disease is usually preceded by infection, and then followed by evidence of antibodies cross-reacting with viral antigens on the surface of platelets in an autoimmune process producing antibodies that mistakenly attack as "foreign" those same platelets via molecular mimicry. *Id*. at 75. Dr. Gill admitted that secondary ITP could be vaccine-caused as well – although she denied that there was sufficient scientific support to conclude that antibodies produced by a cross-reaction between components of the HPV vaccine (or virus for that matter) and platelets could cause ITP. *Id.* at 78. Dr. Gill opined that Ms. Johnson's ITP was primary, noting

[15] Dr. Fraenkel also asserted during the hearing that the prompt treatment of Ms. Johnson's declining platelet count prevented the development of more obvious ITP symptoms that would otherwise have manifested. Tr. at 41. However, under cross-examination she admitted that in fact, Petitioner's treaters hesitated for six months before aggressively treating the ITP. *Id.* at 42.

a lack of other plausible and recognized explanations, as well as the fact that the HPV vaccine had not been identified as a possible cause by any of her treaters. *Id.* at 84.

Dr. Gill also spent considerable time testifying on the differences between acute and chronic ITP. Tr. at 73, 95-96, 101. In acute ITP, patients (male and female in equal numbers) generally present with sudden onset symptoms (petechiae,[16] bruising, or nosebleeds) within a few days or weeks after an infectious illness, and have very low platelet counts under 20,000. *Id.* at 74. Children under the age of five were more likely to present with acute ITP symptoms, while adolescents and young adults would typically display clinical indicia characteristic of chronic ITP. *Id.* at 74-75; D. Cines et al., *Immune Thrombocytopenic Purpura*, 345 N. Engl. J. Med 13:995 (2002) (filed as Resp't's Ex. F) ("Cines I"). Childhood, acute-form ITP usually resolves within six months in more than 70 percent of affected children. Cines I at 995.

Patients with chronic ITP, by contrast, are generally teenagers or older children and more often female than male. Cines I at 995. Chronic ITP is also usually characterized by higher platelet counts (over 20,000) and an "insidious" onset, meaning that the low count is generally discovered incidentally, as occurred here. *Id.* It also tends to persist for more than six months. Tr. at 86; Cines I at 995; K. Heitink-Pollé, *Clinical and Laboratory Predictors of Chronic Immune Thrombocytopenia in Children: A Systematic Review and Meta-Analysis*, 124 Blood 22:3295 (2014) (Resp't's Ex. I) ("Heitink-Pollé"). And individuals with chronic ITP will, in Dr. Gill's view, more likely have positive ANA screenings as well. Tr. at 86; Heitink-Pollé at 3295. However, Dr. Gill did not explain in her report or at hearing why this was the case.

Based upon all of the above, Dr. Gill proposed that the record in this case best supported the conclusion that Petitioner's presentation was chronic in nature. Tr. at 77, 82. At the time her low platelet count was discovered, Ms. Johnson (a female) was over 11 with no known or recorded preceding infection. *Id.* at 86. Dr. Gill also cited the lengthy and slow course of the development of her symptoms, which never devolved into any classic indicia like bleeding or bruising, as further underscoring its chronic character. *Id.* at 73-74, 77. Because of the chronic and mild nature of Petitioner's ITP, Dr. Gill stated that (consistent with what Petitioner's treaters actually did) she would have hesitated to treat it too quickly, given the known deleterious side effects of treatment. *Id.* at 94-95. She nevertheless concurred with Dr. Fraenkel's view that it is hard for treaters to judge the likely course of ITP at the moment it first presents. *Id.*

But Dr. Gill took the further step of asserting that the chronic form of ITP was not likely vaccine-related, since the existing scientific and medical evidence only linked vaccines of any kind to the acute form of the disease. Tr. at 88; Sauvé at 559. Sauvé observed that out of 107 reported cases of secondary ITP caused by a vaccine, 96 percent were symptomatic upon admission, and

[16] Petechiae are pinpoint, non-raised, perfectly round, purplish-red spots caused by intradermal or submucous hemorrhages. *Dorland's* at 1422.

on discharge 26 percent of the children were approaching "normal" platelet counts. Sauvé at 560. Of the remaining patients for which follow-up information was available, about 92 percent had returned to normal platelet counts within three months after treatment – suggesting that a vaccine-caused form of ITP would most likely be acute in its presentation. *Id.* at 559-60. Here, by contrast, Petitioner's presentation was consistent only with the chronic form of ITP. Tr. at 77. Dr. Gill acknowledged, however, that Sauvé did not include in its studied population more mild cases of ITP; because Ms. Johnson was never hospitalized for her symptoms, she would not have been part of that study's population, reducing its relevance to the present case. *Id.* at 105.

Dr. Gill also cited the Cines II article to further describe the different causes associated with acute ITP, including vaccines. Tr. at 83-84. Cines II noted that the MMR vaccine was the most studied vaccine associated with ITP, but also stated that there was developing evidence showing as well that ITP was associated with the pneumococcus, Haemophilus influenza B, hepatitis B, and varicella-zoster vaccines. Cines II at 6513. Cines II did not mention the HPV vaccine, however. Cines II's authors also stated that although most vaccine-associated cases were acute, less than 10 percent ever evolved into chronic ITP, further diminishing the likelihood that the HPV vaccine could cause ITP. *Id*. She noted that out of the data presented in Cines II, nothing implicated the HPV vaccine specifically, and thus ITP was more likely related to the MMR vaccine. Tr. at 84.

Dr. Gill next referenced several epidemiologic studies as bulwarking her assertion that there was no causal link between ITP and the HPV vaccine. *See* Arnheim-Dahlstrom at 5. The Arnheim-Dahlstrom study examined hospital diagnoses for a variety of autoimmune and neurological events up to 180 days after adolescent girls received the quadrivalent HPV vaccine in Denmark and Sweden, and up to 90 days after vaccination for venous thromboembolism events. *Id.* at 1, 3. Out of more than 296,000 women vaccinated with the HPV vaccine, no evidence was found that exposure to the vaccine caused any of these serious adverse events. *Id.* at 4; Tr. at 79. Dr. Gill did admit that there were three autoimmune events observed in Arnheim-Dahlstrom, but argued that they were weak, not temporally related to vaccine exposure, and not actual instances of ITP. Tr. at 79-80. She also pointed out the importance of considering the background incidence of ITP (about two to six per 100,000), as set forth in D. Terrell et al., *The Incidence of Immune Thrombocytopenic Purpura in Children and Adults: A Critical Review of Published Reports*, 85 Am. J. Hematology 174: 174 (2009) (filed as Resp't's Ex. M). Tr. at 79. In the Arnheim-Dahlstrom study, almost 700,000 doses of the HPV vaccine were given, and only 20 to 23 autoimmune events occurred. *Id*. at 80. This was less than the background incidence of ITP, which led Dr. Gill to conclude that those cases were coincidental rather than causative. *Id.* She stressed that an association of an event happening after the vaccine is not necessarily proof that it is causative. *Id.*

Dr. Gill also discussed the findings from a Canadian epidemiologic study that Dr. Fraenkel had discussed in her testimony, Harris. Tr. at 85; Harris at 1061. Harris examined a school-based

HPV vaccination program for 13-year-old girls implemented in Ontario, Canada, looking specifically at reports of post-vaccination adverse events. Harris at 1061. Out of 700,000 HPV vaccine doses received, only 133 adverse events were reported, with only one case of thrombocytopenia between 2007 and 2011 – far fewer than the expected incidence rate. Tr. at 85; Harris at 1062. Dr. Gill admitted, however, that the reporting rates of incidences in this particular study were less than incidences reported in the United States.[17] Tr. at 112.

Dr. Gill went on to consider an even bigger study involving the number of ITP cases observed from a population of 1.8 million children receiving various vaccinations. Tr. at 87; S. O'Leary et al., *The Risk of Immune Thrombocytopenic Purpura after Vaccination in Children and Adolescents*, 129 Pediatrics 248:1-6 (2012) (filed as Resp't's Ex. J) ("O'Leary"). O'Leary observed an elevated risk of ITP after receipt of only certain vaccines, such as hepatitis A, varicella, and the diphtheria-tetanus-acellular pertussis vaccines, and only in certain age categories. Tr. at 87; O'Leary at 3-4. The study also stated that ITP was unlikely after early childhood vaccines other than the MMR vaccine. Tr. at 87; O'Leary at 6. Out of the entire O'Leary study, only one case of ITP after the HPV vaccine was identified – not enough to be statistically significant.[18] Tr. at 87; O'Leary at 5.

As noted above, Dr. Fraenkel raised several objections to such epidemiologic evidence, pointing in particular to either methodologic deficiencies in the various studies cited by Respondent or questions about the representativeness of the studied sample groups in comparison to Ms. Johnson (given the mildness of her symptoms). In response, Dr. Gill maintained that the studies were still relevant and probative, since they generally revealed no real-world evidence linking the HPV vaccine to ITP, making it more likely that Petitioner's particular case was only a coincidence. Tr. at 118-19.

Besides such epidemiologic evidence, Dr. Gill discussed some articles looking at evidence culled from the Vaccine Adverse Event Reporting System "(VAERS").[19] Tr. at 81; N. Borja-Hart

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[17] Harris's authors also noted that the reason for this lower reporting rate might be due to the fact that the study did not include any adverse events occurring outside the school-based program or outside the demographic of the tested group (12-15 year old females). Tr. at 112; Harris at 1062.

[18] In her direct testimony, Dr. Fraenkel argued that in fact, O'Leary actually *established* an increased risk for ITP following HPV. Tr. at 30. Although O'Leary's authors had stated that there were not enough cases in the baseline population of older children to make a stable estimate of the relative risk, in Dr. Fraenkel's reading O'Leary nevertheless supported a causal link between HPV and ITP in older children. *Id.* at 31. The higher "P value" (the estimate of the probability of having an incorrect result) – 7 out of 100 – was, in her understanding, the product of having a smaller number of cases to study, and did not contradict the evidence she proposed established a link. Tr. at 32. O'Leary's authors did note that the HPV incident rate ratio approached statistical significance in older children, but this was a less stable estimate due to the fewer cases of ITP on which to perform an analysis. O'Leary at 4.

[19] VAERS is a national vaccine safety surveillance program co-sponsored by the Centers for Disease Control and Prevention and the Food and Drug Administration, and allows individuals who believe they may have experienced a vaccine reaction to make a report of the incident. *See* https://vaers.hhs.gov/index (last visited Dec. 22, 2016). As Dr.

et al., *Human Papillomavirus Vaccine Safety in Pediatric Patients: An Evaluation of the Vaccine Adverse Event Reporting System*, 43 Ann. of Pharmacology 356 (2009) (filed as Resp't's Ex. D) ("Borja-Hart"). Borja-Hart examined reported adverse events after receipt of the HPV vaccine in children, finding no instances in which ITP was attributed to the vaccine. Tr. at 81. She relied on another similar article in which no instances of ITP were reported in 51 examined VAERS reports. *Id.* at 87-88; Slade at 750.

Dr. Gill also offered an opinion on the date of onset for Petitioner's ITP. From review of the medical record, Dr. Gill could not determine when Ms. Johnson's ITP began, and thus maintained it could not be concluded that the disease was vaccine-associated. Tr. at 86, 91. She rejected Dr. Fraenkel's testimony that onset was most likely after the vaccine because Petitioner's platelet counts declined in that temporal period, pointing out that the record revealed that (at least in the fall of 2011) Petitioner's counts were actually *increasing* for a period post-vaccination. *Id.* at 91; *see also* Pet'r's Ex. 2 at 86. Dr. Gill also stressed that the date of discovery of the low platelet count could not, as a general rule, be conflated with date of onset, and thus did not inform the question of when Petitioner's ITP began. Tr. at 92. Rather, the very fact that it was difficult to determine when Ms. Johnson's low platelet count started made it far more likely that the timing of discovery was coincidental to the vaccination. *Id.* at 122-23. Dr. Gill otherwise agreed that if the HPV vaccine could cause ITP, approximately 40 days post-vaccination would be a temporally appropriate timeframe for onset. *Id.* at 107.

III. PROCEDURAL HISTORY

As noted above, the Petition was filed in February 2014. *See* Petition at 1 (ECF No. 1). Thereafter, Respondent filed her Rule 4(c) Report on April 18, 2014, detailing why she believed Petitioner should be denied compensation and identifying certain deficiencies in the record. ECF No. 9. Petitioner filed a response to the Rule 4(c) Report and the requested missing medical records on April 30, 2014. ECF Nos. 10 and 11. Then, on July 30, 2014, Petitioner filed her expert report from Dr. Fraenkel, along with Dr. Fraenkel's curriculum vitae and four medical articles. ECF No. 16.

Respondent was required to file an expert report on or before October 17, 2014. Respondent filed an unopposed Motion for an Extension of Time until December 15, 2014, which was granted. ECF No. 19. Respondent thereafter requested a few additional days to file the responsive expert report (ECF No. 20), and ultimately filed an expert medical report from Dr. Gill, along with her curriculum vitae and eleven medical articles. ECF No. 21. Petitioner thereafter filed

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Gill clarified, because it is a passive reporting system, VAERS database findings that a number of individuals have complained of a supposed adverse effect from a particular vaccine does not *imply* causation, but such evidence can still be used as a means to find potential signals of causation. Tr. at 81.

a supplemental expert report on March 17, 2015, after an unopposed extension of time. ECF No. 23.

Petitioner filed her pre-hearing submissions on February 12, 2016 (ECF No. 31), and Respondent filed her pre-hearing submissions on March 11, 2016. ECF No. 32. The entitlement hearing took place on May 25, 2016, in Washington, DC, and I thereafter set the schedule for the parties' post-trial briefings. ECF No. 35. Petitioner and Respondent both filed post-hearing briefs on August 5, 2016. ECF Nos. 38 and 40.

The issue of entitlement is now ripe for a decision.

IV. APPLICABLE LEGAL STANDARDS

A. Petitioner's Overall Burden in Vaccine Program Cases

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury" – *i.e.*, an injury falling within the Vaccine Injury Table – corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[20] In this case, Petitioner does not assert a Table claim.

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

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

rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen*: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury." *Althen*, 418 F.3d at 1278.

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

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Human Servs.*, 121 Fed. Cl. 230, 245 (2015) ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)), *vacated on other grounds*, No. 2015-5097 (Fed. Cir. Jan. 3, 2017). But this does not negate or reduce a petitioner's ultimate burden to establish his overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).[21]

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*,

[21] There is ample contrary authority for the more straightforward proposition that the first *Althen* prong, like the overall test itself, simply applies a preponderance standard when evaluating if a reliable and plausible causal theory has been established. *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1350 (Fed. Cir. 2010). For purposes of the present analysis, I am stressing those cases focusing on the *plausibility* of the causal theory proposed, as opposed to whether preponderant evidence supports it, in order to avoid imposing on Petitioner a greater evidentiary burden than the law requires. This does not, however, change the fact that the theory's plausibility is properly analyzed by subjecting its components to the *Daubert* tests for scientific reliability. *Terran v. Sec'y of Health & Human Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999).

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

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct – that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record – including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Dept. of Health & Human Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 Fed. App'x 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 2013 WL 1896173 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Law Governing Analysis of Fact Evidence

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

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd*, *Rickett v. Sec'y of Health & Human Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Human Servs.*, No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Human Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms. It is equally unlikely that pediatric neurologists, who are trained in taking medical histories concerning the onset of neurologically significant symptoms, would consistently but erroneously report the onset of seizures a week after they in fact occurred").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Human Servs*., No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony – especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528;

see also Murphy v. Sec'y of Health & Human Servs., 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), *cert. den'd*, *Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, there are situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Human Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Human Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

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

C. Analysis of Expert Testimony

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

reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial for a (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Human Servs*., 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742-45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of her own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs*., 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 91997)); *see also Isaac v. Sec'y of Health & Human Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 Fed. App'x 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Human Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. Consideration of Medical Literature

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

ANALYSIS

The parties largely do not disagree as to the nature of Ms. Johnson's illness. The record itself strongly establishes that Ms. Johnson experienced a very mild case of ITP that better fits the definition of chronic than acute, given its temporal course and overall absence of typical symptoms. Rather, the parties dispute whether Petitioner's ITP was primary or secondary – a conflict that ultimately goes to the role of the HPV vaccine in development of the condition. However, the case turns on a simpler issue: *when* Petitioner's ITP began. Based on consideration of the record as a whole and the testimony of both side's experts, I conclude that Petitioner has not carried her burden under the Federal Circuit's test for non-Table causation claims established in *Althen*. I address the relevant *Althen* prongs in order of their significance to my determination.

I. Petitioner Has Not Shown that Onset of Her ITP Began after Vaccination.

As set forth above, establishing the third *Althen* prong requires preponderant evidence of a medically-acceptable temporal relationship between a vaccination and alleged illness. *Althen*, 418 F.3d at 1281. But a mere temporal association between the two, without more, does not carry a petitioner's burden of proof for a non-Table claim. *Grant*, 956 F.2d at 1148. Fundamentally, a Vaccine Act claim must establish that the injury in question did not precede the relevant vaccine's administration. *See, e.g., Shalala v. Whitecotton*, 514 U.S. 268, 273-274 (1995). Thus, onset of an injury (or the significant aggravation of a preceding injury)[22] must be shown to have occurred after the date of vaccination.

[22] Petitioner has not alleged that her ITP preceded the HPV vaccine but was significantly aggravated by it, and the record does not support such an allegation.

Both side's experts agreed that (assuming the HPV vaccine could cause ITP), a reasonable timeframe in which the proposed autoimmune process would occur and result in ITP would be within 42 days of vaccination. Tr. at 18, 107. Thus, because Ms. Johnson's ITP was discovered about 40 days from her receipt of the HPV vaccine, Petitioner maintains that she has met the third *Althen* prong. The deficiency in Ms. Johnson's claim, however, lies in her inability to establish that *onset* of her chronic ITP (as opposed to when it was discovered) began after vaccination. The record is silent on this issue – the sole indication that Petitioner had ITP resulted from an incidental discovery that occurred temporally after receipt of the HPV vaccine. Although the platelet count provided a sign to treaters that Ms. Johnson had some form of ITP, she never experienced any symptoms of the condition at all, in the weeks immediately before or after. Nor is there any record proof that would corroborate the existence of ITP, such as some other presenting sign or symptom, in the period between July 17, 2011, and August 24, 2011. There is no way to conclude from the record alone that onset was post-vaccination, unless I simply assume that Petitioner's ITP "had" to have begun around the time it was discovered – an assumption that is rooted in the sort of "mere temporal association" that case law says is not a basis for an entitlement finding.

Dr. Fraenkel's testimony did not successfully fill this evidentiary hole. She admitted that the temporal association was her primary grounds for finding the existence of a causal relationship under these circumstances. Tr. at 39-40. She could not say when Petitioner's ITP actually began, and pointed to nothing from the treatment history that supported her supposition, other than the absence of any other explanation to her (an assertion that might have weight if *other* evidence of ITP existed in the period between vaccination and discovery of the low platelet count). At best, Dr. Fraenkel proposed that the course of Petitioner's platelet loss, coupled with her successful treatment in 2012, suggested post-vaccination onset, because otherwise her symptoms would have been worse and/or more dramatic at an earlier point in time. *Id.* at 40-42. But this aspect of her opinion was rooted in unsupported assumptions about the disease's progression not reflected in the actual medical history (which showed some variation in platelet loss over a lengthy period of time, and even a brief increase, but no real symptoms of the condition). Indeed – because Ms. Johnson's ITP was chronic, it likely never would have presented with severe symptoms in any event, and therefore it cannot be assumed from this fact pattern that the slow progression of her ITP suggests it had to have begun post-vaccination.[23]

Although I deem Dr. Fraenkel a qualified and competent witness on the topic of hematology generally, her expertise did not compel acceptance of her testimony about onset. Her opinion on this specific aspect of Petitioner's claim was unmoored from identifiable scientific or record support, and instead reflected conclusory reasoning that did not merit great weight merely on account of her status as an expert. *Cedillo*, 617 F.3d at 1339 ("a Special Master need not credit

[23] Thus, although Dr. Fraenkel attempted to characterize the eventual IVIG and Rituximab treatment that Ms. Johnson received as aggressive and timely, she admitted that it was in fact delayed for six months from the time of the ITP's discovery – undercutting the suggestion that the immediate timing of treatment supported Petitioner's onset argument. Tr. at 41-42.

expert opinion testimony that is connected to the existing data or methodology 'only by the *ipse dixit* of the expert,'") (quoting *General Electric Co. v. Joiner,* 522 U.S. 136, 146 (1997)). I do not accept her conclusion that Petitioner's illness must have begun after the receipt of the HPV vaccine simply because she so testified. Instead, I have looked for *some* objective evidence of onset beyond the *sign* of ITP provided by the low platelet counts – evidence that is lacking, and which Dr. Fraenkel could not otherwise persuasively identify.

To a large extent, Petitioner's evidentiary failure in identifying onset is the product of confusing *discovery* of an illness's existence (here from inadvertence) with onset of allegedly vaccine-related symptoms. The burden of establishing onset of a vaccine injury is subject to the same preponderant evidence test that the overall *Althen* test requires. *de Bazan*, 539 F.3d at 1352. Special masters have dismissed claims under similar circumstances, finding that the post-vaccination discovery of an illness does not prove when it began. *Tarsell v. Sec'y of Health & Human Servs.,* No. 10-251V, 2016 WL 880223, at *7-8 (Fed. Cl. Spec. Mstr. Feb. 16, 2016) (petitioner failed to establish when onset of her arrhythmia began – either before or after vaccination), *mot. for review filed*, Mar. 16, 2016 (Fed. Cl.); *Doyle v. Sec'y of Health & Human Servs.,* No. 05-605V, 2009 WL 2973106 (Fed. Cl. Spec. Mstr. Aug. 28, 2009) (petitioner failed to establish proximate temporal relationship between vaccination and child's development of ITP), *mot. for review den'd,* 92 Fed. Cl. 1 (2010).

Doyle provides a useful comparison for the present analysis. There, the petitioner alleged that her one-year-old daughter experienced chronic ITP after receiving the MMR vaccine (which both experts in this case agreed is associated with ITP for purposes of establishing causation) in October 2002. *Doyle,* 2009 WL 2973106, at *1. Bruising on the child's skin was subsequently discovered sometime between April and July 2003, and ITP was confirmed after a blood test revealed an extremely low platelet count. *Id.* There was no other record evidence of any post-vaccination symptoms, however, and the bruising was discerned well after the six-week post-vaccination onset period that both side's experts accepted as medically acceptable for the condition to develop. *Id.* at *6. Accordingly, the special master responsible for the case dismissed the claim, largely because the evidence of ITP (bruising) from April 2003 at the earliest was too long after the October 2002 vaccination. *Id.* at *15.

Despite the above, the petitioner's expert proposed that the child had experienced an "insidious onset" that likely began a few weeks after vaccination, but which remained subacute and hence undetected. *Id.* at *2-3. In so doing, he admitted that "you cannot pinpoint exactly when the ITP started," but that "looking retrospectively at the historical events [in the medical record] symptoms of ITP are recognized that previously were not considered." *Id.* at *10. The special master presiding over the case attempted to have the expert more specifically propose a date of onset based on the record, but the expert could not do so, making it impossible to even determine if the ITP had begun after vaccination. *Id.* at *13. Thus, a failure to offer evidence establishing

onset consistent with the petitioner's theory – as here – was an element in the special master's decision to deny entitlement.

As noted, *Doyle* was upheld on review, by the late Judge Allegra of the Court of Federal Claims. *Doyle,* 92 Fed. Cl. 1. In affirming the decision, Judge Allegra noted that the petitioner's expert "had essentially admitted that if there was an insidious onset – that [the child's] ITP was percolating below the surface without evidence of bruising – [the expert] could not say whether the ITP began prior to the immunization." *Id*. at 4. As a result, the expert "was unable to establish, under his causation theory, whether the insidious onset of the chronic ITP began before or after the MMR vaccination," thereby failing to meet the third *Althen* prong. *Id.* at 7. Here, as in *Doyle,* Petitioner's expert can point to nothing in the record to support her proposed onset other than her own unsupported supposition, and indeed cannot persuasively establish that onset could not have occurred prior to immunization. As a result, onset cannot be assumed to have occurred at the time Petitioner's ITP was discovered.

Petitioner also argues that her inability to precisely propose a date of onset reflects not a failure of proof, but a situation in which the proof is in equipoise – since it is (according to Dr. Fraenkel) as equally likely that onset occurred before as after Ms. Johnson received the HPV vaccine. Therefore, she argues that I am required to resolve the matter in Petitioner's favor. Petitioner's Post-Hearing Brief at 20, *citing Knudsen,* 35 F.3d at 550.[24]

As Respondent points out, however, for the evidentiary record to be in equipoise, there must first be *evidence*. Respondent's Post-Hearing Brief at 16. Here, Petitioner (who bears the initial burden of production of proof) has offered little to establish onset beyond her expert's *ipse dixit*. Both experts in fact agree they *cannot* pinpoint onset of Ms. Johnson's ITP given the lack of such evidence – an admission different from the experts agreeing that it is equally likely that onset occurred before or after vaccination. Tr. at 39-40, 91. In fact, Dr. Gill rejected the conclusion that the date of discovery of ITP was congruent with its onset. *Id.* at 92. And to the extent Petitioner hoped to leverage Dr. Fraenkel's expertise to opine to the contrary, that opinion was not only unsupported with evidence itself but was contradicted by her admissions about the impossibility of identifying onset.

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[24] Petitioner's citation to *Knudsen* on this point is somewhat misplaced. In *Knudsen*, the Federal Circuit stated that "[i]f the evidence is seen in equipoise, *then the government has failed in its burden of persuasion* and compensation must be awarded." *Knudsen,* 35 F.3d at 550 (emphasis added). As the full cite makes clear, the Federal Circuit was merely finding that an evidentiary "tie" favored a claimant where *Respondent* bore the burden of proof (on establishing an alternative cause in the *Knudsen* case), but had failed to carry it (as the balance in evidence revealed). Here, by contrast, Petitioner's burden (to establish onset) is at issue.

Of course, the Federal Circuit has also noted that "close calls" regarding causation should be resolved in petitioners' favor. *Althen,* 418 F.3d at 1280 (*citing Knudsen*, 35 F.3d at 549). But that concept is broader and applies more globally to a petitioner's overall burden and the kinds of evidence that can be marshalled in favor of a vaccine injury claim. It does <u>not</u> mean that on specific and fundamental aspects of a petitioner's case, such as establishing onset, a petitioner should not be required to offer persuasive evidence to establish a fact as "more likely than not."

Vaccine Act petitioners must offer preponderant evidence that an allegedly vaccine-caused illness began after receipt of the vaccination to demonstrate entitlement to damages. Ms. Johnson has not done so here.

II. *Althen* Prongs One and Two

Even though I am not finding in favor of Petitioner on a critical element of proof, and therefore need not complete my analysis under *Althen,* I note that she was successful in establishing at least one of the other two *Althen* prongs.

Althen 1 – As Dr. Gill's testimony established, most vaccine-related ITP cases are acute. *See* Tr. at 88, 121-22; O'Leary at 3. However, Petitioner and her expert convincingly established that ITP is heterogeneous – some acute cases develop into chronic cases, and it is difficult for treaters to discern what kind of ITP is presented in its early stages. In addition, there is evidentiary support for the conclusion that, even if acute ITP is more commonly associated with vaccines, the chronic form can be as well. *See, e.g.,* O'Leary at 3 (documenting chronic cases of vaccine-associated ITP). And Petitioner also proposed a mechanism (molecular mimicry) that has repeatedly been embraced in Program cases as applicable to immune-mediated conditions, and which would persuasively and plausibly explain the genesis of ITP. *See, e.g., Tompkins v. Sec'y of Health & Human Servs.*, No. 10-261V, 2013 WL 3498652, at *22 (Fed. Cl. Spec. Mstr. June 21, 2013) ("[t]he molecular mimicry theory is the one most widely accepted for the agents most frequently accepted as causal"), *mot. for review den'd*, 117 Fed. Cl. 713 (2014); *Ebenstein v. Sec'y of Health & Human Servs.*, No. 06-573V, 2010 WL 5113185, at *21 (Fed. Cl. Spec. Mstr. Sept. 1, 2010) (accepting that molecular mimicry could plausibly link the MMR vaccine and ITP).[25] Although most of the evidence presented in this case involved other vaccines, I find that it offers some reasonable and reliable circumstantial proof supporting Petitioner's causation theory regardless.

Petitioner did provide some case study evidence in an effort to link specifically the HPV vaccine to ITP. Although case studies are not probative of causation *per se,* they have been deemed to have some evidentiary value. *See, e.g., Lampe*, 219 F.3d at 1366. In response, Respondent referenced a number of much larger epidemiologic studies in an effort to show that the HPV vaccine is not credibly linked to an autoimmune condition like ITP. I generally find that such evidence can be relevant in rebutting a petitioner's arguments about the causal natures of different

[25] Petitioner did not show exactly which antigen would be involved in the proposed cross-reactivity process, nor did she offer any studies showing molecular mimicry could happen between ITP and HPV. But to require Petitioner to have done so amounts to heightening the burden of proof beyond what a claimant need offer. *See, e.g., Knudsen*, 35 F.3d at 548-49; *Salmins v. Sec'y of Health & Human Servs.*, No. 11-140V, 2014 WL 1569478 (Fed. Cl. Spec. Mstr. Mar. 31, 2014).

vaccines. *See, e.g., D'Tiole v. Sec'y of Health & Human Servs.,* No. 15-085V, slip op. at *29 (Fed. Cl. Spec. Mstr. Nov. 28, 2016), *mot. for review filed*, Dec. 28, 2016 (Fed. Cl.); *Blackburn v. Sec'y of Health & Human Servs.*, No. 10-410V, 2015 WL 425935, at *28-30 (Spec. Mstr. Jan. 9, 2015). I am also, however, mindful of the fact that petitioners need not offer such evidence in the first place, and I cannot require it in reaching my conclusions, since by definition a vaccine injury is a rare event that cannot be disproved merely because a vaccine does not usually produce the claimed injury in the general population. *See Harris v. Sec'y of Health & Human Servs.*, No. 10-322V, 2014 WL 3159377, at *11 (Fed. Cl. Spec. Mstr. June 10, 2014) (epidemiologic studies cannot absolutely refute causal connections, because it is possible that a larger study could always detect an increased risk).

Here, I give such epidemiologic evidence less weight than I would in other contexts. The combination of evidence linking other vaccines (especially MMR) to ITP, coupled with some case study proof, is enough to suggest that Petitioner's theory is sufficiently plausible to have carried her burden of proof on the first *Althen* prong. Moreover, Petitioner persuasively pointed out that many of the studies referenced herein by Respondent did not bear on Petitioner, since her particularly mild form of ITP would not have been included at all in several of the studies, thus reducing the probative strength of studies vouching for the safety of the HPV vaccine. Tr. at 104-05, 114-15.

Althen 2 – As noted, the evidence establishes that Ms. Johnson suffered from a chronic, mild form of ITP, with no symptoms, and with the only physical distress stemming from her treatment rather than the disease directly. However, my findings with respect to timing of onset make it impossible for me to conclude that Petitioner successfully established a logical cause-and-effect sequence – that in this case the HPV vaccine "did cause" Ms. Johnson's ITP, as reflected in the record before me. Without being able to establish onset after vaccination, Petitioner cannot show that the vaccine more likely than not caused her ITP, and therefore the reliability of her overall theory does not aid her claim.

CONCLUSION

In this case, the character of the illness is not disputed, and Petitioner was largely successful in proposing a causation theory. But her inability to establish post-vaccination onset of her ITP is fatal to her claim.

IT IS SO ORDERED.

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