



1274 (Fed. Cir. 2005) (“*Althen*”). See *Dobrydneva ex rel. Dobrydnev v. Sec’y of Health & Human Servs.*, 2010 WL 2143481, at \*23 (Fed. Cl. Mar. 12, 2010) (“*Dobrydneva I*”).

On July 30, 2010, the undersigned judge of the United States Court of Federal Claims reversed, holding that the temporal proximity requirement of *Althen* was satisfied and remanded the case for the Special Master’s ruling as to the first and second elements of *Althen*. See *Dobrydneva ex rel. Dobrydnev v. Sec’y of Health & Human Servs.*, 94 Fed. Cl. 134, 149 (2010) (“*Dobrydneva II*”).

On October 27, 2010, the Special Master issued an Entitlement Decision, again denying Petitioners’ claim on the grounds that Petitioners failed to satisfy the first and second elements of *Althen*. See *Dobrydneva ex rel. Dobrydnev v. Sec’y of Health & Human Servs.*, No. 04-1593, slip op. at 18 (Fed. Cl. Oct. 27, 2010) (“*Dobrydneva III*” or “October 27, 2010 Entitlement Decision”).

On November 23, 2010, Petitioners filed a Motion for Review of the Special Master’s October 27, 2010 Entitlement Decision.

## **I. RELEVANT FACTS.<sup>2</sup>**

### **A. Chronic Fatigue Syndrome.**

Chronic Fatigue Syndrome is defined as

Persistent debilitating fatigue lasting longer than six months, with other known medical conditions having been ruled out by clinical diagnosis, accompanied by at least four of the following: significantly impaired short-term memory or concentration, muscle weakness, pain in multiple joints without swelling or redness, sore throat, tender lymph nodes, headaches, unrefreshing sleep, and malaise that lasts more than 24 hours following exertion. The cause is unknown and may be multifactorial; immune dysfunction has been suggested, and viral infection may be associated with it, although no causal relationship has been demonstrated.

DORLAND’S ILLUSTRATED MEDICAL DICTIONARY 1851 (31st ed. 2007) (“DORLAND’S”).

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<sup>2</sup> The relevant facts discussed in *Dobrydneva II*, 94 Fed. Cl. at 136-140, were derived from Petitioners’ Appendix of Exhibits (“Pet. Ex. 1-23”); Petitioners’ Second Filing of Exhibits (“Pet. Ex. 1(a) – 19(a)”); Respondent’s (“Government”) Appendix of Exhibits (“Gov’t Ex. A-CC”); an April 25-26, 2007 evidentiary hearing (“4/25/07 TR 1-449,” “4/26/07 TR 450-740”). Most of that discussion has been repeated here, together with additional facts that were derived from a September 29, 2010 remand hearing (“9/29/10 TR 1000-1198”).

**B. Petitioners’ Medical Records Prior To The November 5, 2001 Vaccination.**

Ilya Dobrydnev was born on April 14, 1991 in Moscow, Russia and moved to the United States when he was 15 months old. *See Dobrydneva II*, 94 Fed. Cl. at 136 (citing 4/25/07 TR at 30). During 1992 and 1993, Ilya received three doses of the hepatitis B vaccine.<sup>3</sup> *Id.* at 136-37 (citing Pet. Ex. 9(a) at 37). Ilya had no adverse reaction to any of these inoculations.<sup>4</sup> *Id.* at 137 (citing Pet. Ex. 19 at 7-8).

In July 1996, Ilya’s mother reported on a kindergarten registration form that Ilya had “frequent colds,” a “frequent sore throat,” and “frequent ear infection[s].” *Id.* (citing Pet. Ex. 7 at 12-13).<sup>5</sup> From October 1996 to October 2000, Ilya was examined by his pediatrician, Dr. Robert Fink, or other pediatricians in Dr. Fink’s office, on thirteen occasions for different complaints, including fever, sore throat, and weakness. *Id.* (citing Pet. Ex. 5 at 43-47; 4/25/07 TR at 143-45).

In 2001, Ilya saw a pediatrician at Pediatric Specialists in Norfolk, Virginia, eight times for upper respiratory issues. *Id.* (citing Pet. Ex. 5 at 39-43). On February 26, 2001, a physician associated with Pediatric Specialists noted that Ilya was in the “convalescent phase” of a “recent

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<sup>3</sup> The records present inconsistent information, as shown in the following chart:

<b>Hepatitis B Vaccination Records for Ilya Dobrydnev</b>			
Source	Dr. Robert Fink	School Records & Dr. Robert Lehman	Virginia Health Department
Citation	Ex. 7 at 17 (dated Jan. 7, 1997)	Ex. 7 at 15; Ex. 9(a) at 37.	Ex. 9 at 3.
<b>First Dose</b>	9/25/92	9/25/92	11/6/92
<b>Second Dose</b>	11/6/92	11/6/92	8/6/93
<b>Third Dose</b>	8/6/92 * [sic] *Should be 8/6/93.	8/6/93	---

Dr. Lehman’s records appear to be the most accurate. *See* Pet. Ex. 9(a) at 37 (Dr. Lehman’s records including vaccination lot numbers).

<sup>4</sup> Although the court previously noted that Ilya had no reaction to the 1992-1993 hepatitis B vaccinations, *see Dobrydneva II*, 94 Fed. Cl. at 136, on further review, Dr. Robert Lehman’s medical records conflict as to whether Ilya had reactions to prior vaccinations. *See* Pet. Ex. 9(a) at 22 (August 12, 1996 medical record indicating that Ilya’s reactions to previous shots were “not severe”), 24 (October 19, 1994 medical record indicating that Ilya had reactions to previous shots), 26 (August 6, 1993 medical record not indicating whether Ilya had reactions to previous shots), 28 (February 19, 1993 medical record indicating no reactions to previous shots), 30 (August 7, 1992 medical record indicating reactions to previous shots)

<sup>5</sup> At the evidentiary hearing, Ilya’s mother did not recall filling out this form. *See Dobrydneva II*, 94 Fed. Cl. at 137 n.2 (citing 4/25/07 TR at 64).

[Epstein-Barr virus or EBV] infection.”<sup>6</sup> *Id.* (citing Pet. Ex. 5 at 39). In January and February 2001, Ilya missed more than twenty days of school. *Id.* (citing Pet. Ex. 7 at 6). During the same period, a report by Dr. Randall Fisher, a pediatric infectious disease specialist at Children’s Hospital of the King’s Daughter (“Children’s Hospital”) in Norfolk, Virginia, indicated that Ilya experienced fatigue. *Id.* (citing Pet. Ex. 6 at 366; 4/25/07 TR at 73).

In March 2001, Ilya was examined by Dr. Thomas Rubio of the Pediatric Infectious Disease Clinic of the Children’s Hospital. *Id.* (citing Pet. Ex. 6 at 358-59). Ilya’s mother informed Dr. Rubio that Ilya was very weak and could not walk. *Id.* (citing Pet. Ex. 6 at 358). When Ilya’s mother was advised of the need to perform medical procedures, Ilya “‘recovered’ all his strength” and “was able to walk normally, jump, and had normal strength in his lower extremities.” *Id.* (citing Pet. Ex. 6 at 358). Nevertheless, Dr. Rubio noted: “I believe that this child is still suffering from some sort of psychological maladjustment perhaps with some fatigue. However, he appear[s] to be safe from suffering from a definite neurological syndrome.” *Id.* (citing Pet. Ex. 6 at 358).

In April 2001, Ilya returned to school. *Id.* (citing Pet. Ex. 7 at 6). On April 23, 2001, Ilya saw Dr. Fink for a sore throat, fever, and fatigue. *Id.* (citing Pet. Ex. 5 at 38). Dr. Fink diagnosed Ilya as having a probable viral illness, but not mononucleosis. *Id.* (citing 4/25/07 TR at 182). Dr. Fink concluded that Ilya was cured of mononucleosis by April or May 2001. *Id.* (citing 4/25/07 TR at 149, 259).

On May 25, 2001, Ilya’s mother called Dr. Fink to report that Ilya was suffering from a fever, headache, white patches on his throat, and hallucinations. *Id.* (citing Pet. Ex. 5 at 38). Dr. Fink recommended that Ilya be admitted to a hospital. *Id.* (citing Pet. Ex. 5 at 38). Ilya’s mother decided not to take him to the hospital, but treated him with “leftover” CEFZIL™.<sup>7</sup> *Id.* at 137-38 (citing Pet. Ex. 5 at 38). On May 30, 2001, Dr. Fink examined Ilya, but warned Ms. Dobrydneva that he had “difficulty [] making a diagnosis with her self-medicating.” *Id.* at 138 (citing Pet. Ex. 5 at 38).

On June 6, 2001, Ilya was seen for a three-day low grade fever and fatigue. *Id.* (citing Pet. Ex. 5 at 37). On June 7, 2001, Ilya had blood tests performed. *Id.* (citing Pet. Ex. 6 at 350-52). Titers<sup>8</sup> for EBV were 37 arbitrary units (“AU”). *Id.* (citing Pet. Ex. 6 at 350). The “EBV Interpretation Chart” indicates that any value exceeding 20 AU is positive for acute infection.

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<sup>6</sup> The Epstein-Barr virus is a “herpes virus that is the causative agent of infectious mononucleosis.” STEDMAN’S MEDICAL DICTIONARY 275 (2007) (“STEDMAN’S”); *see also* 4/26/07 TR at 561-62.

<sup>7</sup> CEFZIL™ is “a trademark for a preparation of cefprozil.” Cefprozil is a “semisynthetic, broad-spectrum, second-generation cephalosporin effective against a wide range of gram-negative and gram-positive organisms, used in the treatment of otitis media and infections of the respiratory and oropharyngeal tracts, skin, and soft tissues[.]” DORLAND’S at 317.

<sup>8</sup> A “titer” is “the quantity of a substance required to produce a reaction with a given volume of another substance[.]” DORLAND’S at 1958.

*Id.* (citing Pet. Ex. 6 at 350). Dr. Fink observed that this test may have shown the presence of a persistent Epstein Barr Virus, but this diagnosis was not confirmed. *Id.* (citing Pet. Ex. 5 at 37; 4/26/07 TR at 717). The test also could have simply reflected a recurrence of EBV. *Id.* (citing Pet. Ex. 5 at 37).

On July 2, 2001, Dr. Fink was informed that Ilya was “fatigued again. At times he has [had] to be carried around.” *Id.* (citing Pet. Ex. 5 at 37). Dr. Fink did not observe fatigue, but referred Ilya to Dr. Cynthia Kelly, an allergist/immunologist at Children’s Hospital for further testing. *Id.* (citing 4/25/07 TR at 184-85).

On July 23, 2001, Ilya saw Dr. Kelly. *Id.* (citing Pet. Ex. 6 at 340-41). Dr. Kelly reported that Ilya’s mother told her that “Ilya has been sick with infectious mononucleosis since December.” *Id.* (citing Pet. Ex. 6 at 340). Dr. Kelly recommended that blood tests be taken. *Id.* at 341. Ilya’s mother objected. *Id.* (citing Pet. Ex. 6 at 341; 4/25/07 TR at 186-87).

During the summer of 2001, Ilya attended a summer camp for academically gifted children where he played tennis and swam. *Id.* (citing 4/25/07 TR at 40-41).

In the fall of 2001, Ilya started the fifth grade. *Id.* (citing 4/25/07 TR at 43). Ilya missed school on October 1 to October 4, 2001. *Id.* (citing Pet. Ex. 7 at 5).

### **C. Petitioners’ Medical Records Following The November 5, 2001 Vaccination.**

On November 5, 2001, Ilya received a fourth dose of the hepatitis B vaccine. *See Dobrydneva II*, 94 Fed. Cl. at 138 (citing Pet. Ex. 9 at 3). Thereafter, according to Ilya’s mother, he experienced malaise, fever, sore throat, lymph node swelling, and marked pallor. *Id.* (citing 4/25/07 TR at 47; Pet. Ex. 3 at 1-2). Ilya missed school on November 6 and 7, 2001. *Id.* (citing Pet. Ex. 7 at 5; 4/25/07 TR at 48).

On November 19, 2001, Ilya saw Dr. Fink for a “2-3 day history of low grade temperature elevation along with a sore throat,” and “some degree of nasal congestion with minimal cough.” *Id.* (citing Pet. Ex. 5 at 36). Dr. Fink diagnosed Ilya as having “febrile viral illness/viral pharyngitis.” *Id.* (citing Pet. Ex. 5 at 36).

By November 26, 2001, Ilya had a yellow nasal discharge and a frontal headache. *Id.* (citing Pet. Ex. 5 at 36). Dr. Fink’s diagnosis was sinusitis and AUGMENTIN<sup>9</sup> 500 was prescribed for 10 days. *Id.* (citing Pet. Ex. 5 at 36; 4/25/07 TR at 189-90).<sup>10</sup>

On November 29, 2001, Ilya was diagnosed with a sore throat. *Id.* (citing Pet. Ex. 5 at 35).

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<sup>9</sup> AUGMENTIN<sup>TM</sup> is a trademark for a “combination preparations of amoxicillin and clavulanate potassium.” DORLAND’S at 181.

<sup>10</sup> Dr. Fink also noted that Ilya’s mother was using an “immunomodulator/stimulant that is made in France.” *Dobrydneva II*, 94 Fed. Cl. at 138 n.9 (citing Pet. Ex. 5 at 36).

On November 30, 2001, Ilya experienced severe dizziness, nausea, and vomiting. *Id.* (citing Pet. Ex. 10 at 1). Ilya arrived at Children’s Hospital via ambulance, where he was diagnosed with vestibular neuronitis.<sup>11</sup> *Id.* (citing Pet. Ex. 11 at 2). One of the physicians noted that “the most likely cause of injury is herpes virus.” *Id.* (citing Pet. Ex. 11 at 2). Ilya was given prescriptions for Scopolamine<sup>12</sup> and Acyclovir,<sup>13</sup> and discharged. *Id.* (citing 4/25/07 TR at 49-51).

On December 3, 2001, Ilya saw Dr. Fink who noted that Ilya should continue using Meclizine,<sup>14</sup> Acyclovir, and a Transderm Scopolamine patch. *Id.* at 139 (citing Pet. Ex. 5 at 35-36). On December 6, 2001, Ilya again visited the doctor for evaluation of a sore throat. *Id.* (citing Pet. Ex. 5 at 35). On December 10, 2001, Ilya saw Dr. Fink for a sore throat and “white patches” on his throat. *Id.* (citing Pet. Ex. 5 at 35). Ilya’s mother told Dr. Fink that she had been giving Ilya CEFZIL™, that Dr. Fink had not prescribed. *Id.* (citing Pet. Ex. 5 at 35). Dr. Fink believed that Ilya had tonsillitis. *Id.* (citing Pet. Ex. 5 at 35). On December 26, 2001, Ilya’s mother called Dr. Fink to report that Ilya had puss on his tonsils. *Id.* (citing Pet. Ex. 5 at 55). On December 27, 2001, blood was drawn. *Id.* (citing Pet. Ex. 6 at 325). Tests confirmed that the IgM<sup>15</sup> titers for EBV were elevated (22 AU). *Id.* (citing Pet. Ex. 6 at 325).

On January 2, 2002, Ilya saw Dr. Jennifer Holland, Dr. Fink’s partner. *Id.* (citing Pet. Ex. 5 at 34-35). Dr. Holland recorded that Ilya had “no real fevers.” *Id.* (citing Pet. Ex. 5 at 34). Dr. Holland noted that Ilya had blood work done on December 27, 2001 and his mother was still concerned about Ilya continuing to be tired. *Id.* (citing Pet. Ex. 5 at 34). On this date, Ilya’s mother first mentioned that Ilya began to get sick “two weeks after” his November 5, 2001 hepatitis B vaccination and asked whether that could be the cause of his health problems. *Id.* (citing Pet. Ex. 5 at 34). On January 9, 2002, Ilya again saw Dr. Holland, who recorded that, although Ilya’s mother reported that Ilya’s condition worsened since January 2, 2002, he was

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<sup>11</sup> Vestibular neuritis “causes a self-limited episode of vertigo, presumably due to inflammation of the vestibular division of the 8th cranial nerve; some vestibular dysfunction may persist.” THE MERCK MANUAL 795 (18th ed. 2006) (“MERCK MANUAL”).

<sup>12</sup> Scopolamine is an “anticholinergic alkaloid, derived from several solanaceous plants, including *Atropa belladonna*, *Hyscyamus niger*, *Datura* species, and *Scoplia* species . . . has effects on the autoimmune system similar to those of atropine.” DORLAND’S at 1707. Scopolamine is used as an antiemetic, particularly in motion sickness. *Id.*

<sup>13</sup> Acyclovir is a “synthetic acyclic purine nucleoside analog . . . used . . . in the treatment of infections.” STEADMAN’S at 15. Epstein-Barr virus is a “herpes virus.” *Id.* at 275.

<sup>14</sup> Meclizine hydrochloride is “an antihistamine used in the management of nausea, vomiting, and dizziness associated with motion sickness and of vertigo associated with disease affecting the vestibular system.” DORLAND’S at 1134.

<sup>15</sup> IgM is one of five classes of immunoglobulin that are “structurally related glycoproteins that function as antibodies.” DORLAND’S at 933.

“better today.” *Id.* (citing Pet. Ex. 5 at 32-33). On January 14, 2002, Ilya saw a pediatrician at Dr. Fink’s practice. *Id.* (citing Pet. Ex. 5 at 32). This doctor reported that Ilya had “not been able to lie down completely at all because he gets dizzy.” *Id.* (citing Pet. Ex. 5 at 32). The doctor made the following note: “recent [EBV] with possible recurrence versus exacerbation,” was referred to Dr. Cynthia Kelly and Dr. Doug Mitchell. *Id.* (citing Pet. Ex. 5 at 32). On January 17, 2002, Ilya was tested for Epstein-Barr Virus using polymerase<sup>16</sup> chain reaction (“PCR”). *Id.* (citing Pet. Ex. 6 at 309). This test did not detect the presence of the EBV. *Id.* (citing Pet. Ex. 6 at 309). On January 23, 2002, Ilya saw Dr. Kelly. *Id.* (citing Pet. Ex. 6 at 276-77). Dr. Kelly recorded that Ilya’s mother again stated that she believed that the hepatitis B vaccine was the cause of Ilya’s problems; Dr. Kelly only noted that “Ilya does look allergic to me.” *Id.* (citing Pet. Ex. 6 at 276). Ilya’s mother also did not want a prick skin test. *Id.* (citing Pet. Ex. 6 at 276). Dr. Kelly proposed examining Ilya’s B-cell function.<sup>17</sup> *Id.* (citing Pet. Ex. 6 at 276).

On February 11, 2002, Ilya saw Dr. Douglas Mitchell, an infectious disease specialist. *Id.* (citing Pet. Ex. 6 at 283). Dr. Mitchell recommended that Ilya’s mother stop administering Acyclovir. *Id.* (citing Pet. Ex. 6 at 287.)<sup>18</sup>

On February 19, 2002, Ilya again saw Dr. Kelly, who noted that “many of [Ilya’s] vestibular complaints have improve[d] [but] . . . He still fatigues easily and has been maintained on homebound [schooling].” *Id.* (citing Pet. Ex. 6 at 278). Dr. Kelly also noted that Ilya’s mother “attribute[d] the improvement in [Ilya’s] symptoms to a dose of Acyclovir at 400 mg q.i.d.,” but Ilya also was taking AUGMENTIN™. *Id.* (citing Pet. Ex. 6 at 278). Based on laboratory tests, Dr. Kelly determined that Ilya’s B-cells functioned reasonably well. *Id.* (citing Pet. Ex. 6 at 278). Dr. Kelly wanted, however, to see whether Ilya’s T-cell system functioned normally and whether Ilya had any allergies. *Id.* (citing Pet. Ex. 6 at 278-79). Ilya’s mother objected. *Id.* (citing Pet. Ex. 6 at 278-79).

On March 20, 2002, Ilya saw Dr. Mitchell for a follow-up appointment. *Id.* (citing Pet. Ex. 6 at 250-51). Dr. Mitchell reported that “the majority of [Ilya’s] symptoms are achy legs. He is very fatigued and tired.” *Id.* (citing Pet. Ex. 6 at 250). Dr. Mitchell also was concerned about whether “there is a behavioral psychological component contributing to this continued subjective fatigue and possibly school avoidance.” *Id.* (citing Pet. Ex. 6 at 251). Nevertheless, he noted: “Chronic fatigue syndrome itself may be considered in this child.” *Id.* (citing Pet. Ex. 6 at 251). Dr. Mitchell recommended Ilya’s care be coordinated with Dr. Fink.<sup>19</sup> *Id.* at 140 (citing Pet. Ex. 6 at 251).

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<sup>16</sup> A “polymerase” is “any enzyme that catalyzes polymerization, especially of nucleotides to polynucleotides.” DORLAND’S at 1512.

<sup>17</sup> B-cells are a component of the immune system. MERCK MANUAL at 1322-24.

<sup>18</sup> At some point, Ilya’s mother stopped giving Ilya Acyclovir for a period, but then restarted the medication. *Dobrydneva II*, 94 Fed. Cl. at 139 n.17 (citing 4/25/07 TR at 203).

<sup>19</sup> During February and March of 2002, Ilya also saw Dr. Fink several times. *See Dobrydneva II*, 94 Fed. Cl. at 139 n.17 (citing Pet. Ex. 5 at 27-30). These visits provide

On April 1, 2002, Ilya saw Dr. Fink. *Id.* (citing Pet. Ex. 5 at 27). Dr. Fink’s assessment concluded “[p]ossible chronic fatigue secondary to chronic EBV or HSV, though doubt.”<sup>20</sup> *Id.* (citing Pet. Ex. 5 at 27). In May 2002, Ilya’s doctors continued to record that he was fatigued and weak. *Id.* (citing Pet. Ex. 5 at 17-18, 20, 25-26; *see also* Pet. Ex. 6 at 112-13). Pet. Ex. 13(a) at 102-104. Some doctors suggested that Ilya’s problems were psychological.<sup>21</sup> *Id.* (citing Pet. Ex. 5 at 25-26; Pet. Ex. 6 at 69-70, 112-13).

On May 6, 2004, Dr. Fink filed a Vaccine Adverse Event Reporting System (“VAERS”) Report indicating that as a result of the November 11, 2001 hepatitis B vaccination, Ilya “had an episode of vestibular neuronitis requiring an [emergency room visit on November 30, 2001.] [H]e has had chronic fatigue since.” Pet. Ex. 13(a) at 103. Dr. Fink indicated that the vaccination “Required [an] emergency room/doctor visit” and “Resulted in permanent disability.” *Id.*

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At the time of the April 25-26, 2007 evidentiary hearing, Ilya was not taking any medications, but his mother testified that “He doesn’t walk far or he doesn’t walk a lot . . . . He is homebound and he is schooled through the Norfolk Public Schools that provides [a] homebound teacher that instructs him . . . . However, in the past several months, he was able to return to school part time for one class, two, maximum three times a week . . . . I do not know whether this improvement is going to last.” *Id.* (citing 4/25/07 TR at 60-61).

As of the September 29, 2010 remand hearing, Ilya continued to tire easily. 9/29/10 TR at 1010. He currently is a sophomore at Old Dominion University, where he takes approximately one and a half hours of classes each day. 9/29/10 TR at 1010. The school allows Ilya to record lectures and make up missed classes, and provides extra time for exams in a “distraction-reduced setting,” because “he is still easily distracted.” 9/29/10 TR at 1010-12.

## II. PROCEDURAL HISTORY.

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relatively few details other than what was presented by Dr. Kelly and Dr. Mitchell. *Id.* (citing Pet. Ex. 6 at 278).

<sup>20</sup> It is not clear from the text of Dr. Fink’s April 1, 2002 notes whether his doubts were about the presence of Chronic Fatigue Syndrome or chronic EBV or HSV, or both. *See Dobrydneva II*, 94 Fed. Cl. at 140 (citing Pet. Ex. 5 at 27).

<sup>21</sup> On June 10, 2003, Dr. Randall Fisher, a specialist in pediatric infectious diseases, observed that Ilya’s mother’s behavior “borders on Munchausen’s syndrome by proxy or factitious disorder by proxy.” *Dobrydneva II*, 94 Fed. Cl. at 140 (citing Pet. Ex. 6 at 43 (reflecting that Child Protective Services (“CPS”) investigated and found any concern about child abuse to be “unfounded – lack of evidence.” CPS Investigation Report, issued September 30, 2003, at 16)).

On October 25, 2004, Ilya and his parents filed a petition for compensation in the United States Court of Federal Claims, alleging that Ilya developed Chronic Fatigue Syndrome as a result of the cumulative effects of a fourth hepatitis B vaccination. The matter was assigned to then Special Master Edwards.

On March 30, 2007, the Petitioners filed prehearing submissions, including a CD with approximately 50 medical articles.

On April 25-26, 2007, an evidentiary hearing was conducted (“4/25/07 TR 1-449”; “4/26/07 TR 450-740”) wherein Special Master Edwards heard the testimony of Ilya’s mother, his treating physician, Dr. Robert Fink, and experts Dr. David Bell, and Dr. James Oleske. The Government presented the expert testimony of Dr. Raoul Wientzen, Jr. and Dr. Alan Brenner.

On August 1, 2008, Special Master Edwards resigned and this case was reassigned to Special Master Christian J. Moran. On March 12, 2010, Special Master Moran issued an Entitlement Decision, determining that Petitioners failed to establish “a showing of a proximate temporal relationship between vaccination and injury,” under the third element of *Althen*. See *Dobrydneva I*, at 18. On April 12, 2010, Petitioners filed a timely Motion for Review. On May 18, 2010, the Government filed a Response.

On July 30, 2010, the undersigned issued a Memorandum Opinion and Order vacating the Special Master’s March 12, 2010 Entitlement Decision and remanding for a ruling as to the first and second elements of *Althen* and an award of interim expert fees. See *Dobrydneva II*, 94 Fed. Cl. at 149. The Special Master was instructed to reconvene an evidentiary hearing, if requested by the parties. *Id.*

On September 29, 2010, a supplemental evidentiary hearing was held where Dr. Fink, Dr. Oleske, and Dr. Bell testified for Petitioners (“9/29/10 TR 1000-1196”). The Government called no witnesses. 9/29/10 TR at 1179. On September 30, 2010, the Special Master issued an order, instructing the parties to submit briefs as to the first two elements of *Althen* and requesting argument as to “how the proposed sequence of cause and effect in Ilya’s case compares to the evidence offered in *Moberly ex [r]el[.] Moberly v. Sec’y of Health & Human Servs.*, 592 F.3d 1315, 1323 (Fed. Cir. 2010).”

On October 12, 2010 Petitioners filed a Response to the Special Master’s September 30, 2010 Order, together with an attached medical article: Oscar-Danilo Otega-Hernandez & Yehuda Shoenfeld, *Infection, Vaccination and Autoantibodies in Chronic Fatigue Syndrome, Causes or Coincidence*, 203 ANNALS OF NEW YORK ACAD. OF SCIENCES 600 (2009) (“2009 NEW YORK ACADEMY OF SCIENCES ARTICLE”).

On October 18, 2010, the Government filed a Post Hearing Brief. On October 22, 2010, Petitioners filed a Post Hearing Brief. On October 27, 2010, the Special Master issued a second Entitlement Decision, determining that Petitioners had established neither a medical theory casually connecting the vaccination and the injury nor a logical sequence of cause and effect showing that the vaccination was the reason for the injury. See *Dobrydneva III*.

On November 23, 2010, Petitioners filed a timely Motion for Review of the October 27, 2010 Entitlement Decision. On December 22, 2010, the Government filed a Response.

### **III. DISCUSSION.**

#### **A. Standard of Review.**

Congress authorized the United States Court of Federal Claims to set aside any decision of a special master, if findings of fact or conclusions of law are found to be “arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.” 42 U.S.C. § 300aa-12(e)(2)(B) (2006). Findings of fact are reviewed under an “arbitrary and capricious” standard; conclusions of law are reviewed *de novo*. See *Munn v. Sec’y of Health & Human Servs.*, 970 F.2d 863, 870 n.10 (Fed. Cir. 1992).

#### **B. Burden of Proof in Vaccine Act Cases.**

The Vaccine Act provides that a petitioner may receive compensation and other relief under the Vaccine Injury Compensation Program (“Vaccine Program”), if injury can be established either by causation in law or causation in fact. Causation in law is established if one of the vaccines listed in the Vaccine Injury Table at 42 U.S.C. § 300aa-14(a) (2006) (“Vaccine Table”) was administered to a petitioner and the “first symptom or manifestation of onset or of the significant aggravation of such injuries, disabilities, illnesses, conditions, and deaths” of specific adverse medical conditions associated with the use of each vaccine occurred within a time period specified in the Vaccine Table. See 42 U.S.C. § 300aa-14(a); 42 C.F.R. § 100.3(a) (2010). The Vaccine Table is to be read and interpreted by reference to “Qualifications and aids to interpretation,” that define the key terms used therein. *Id.*

Congress also afforded a petitioner the opportunity to receive relief under the Vaccine Program, even if the time period for the first symptom or manifestation of a specified injury is not listed in the Vaccine Table. See 42 U.S.C. §§ 300aa-11(c)(1)(C)(ii), 300aa-13(a)(1) (2006). Under these circumstances, a petitioner must establish causation in fact, *i.e.*, first, by establishing a *prima facie* case offering evidence of sufficient facts to establish each element of the claim and then by meeting a burden of proof as to each element of the claim by a “preponderance of the evidence” standard. See 42 U.S.C §§ 300aa-13(a)(1)(A). Accordingly, a non-Vaccine Table petitioner must proffer at least some evidence as to each element of the claim and sufficient evidence to persuade the special master or court by a preponderance of evidence. *Id.*

In *Capizzano v. Sec’y of Health & Human Servs.*, 440 F.3d 1317 (Fed. Cir. 2006), the United States Court of Appeals for the Federal Circuit re-affirmed the three-part test for determining causation in fact in non-Vaccine Table cases, established in *Althen*, requiring that a petitioner:

show by preponderant evidence that the vaccination brought about [the] injury by providing:

- (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.

*Capizzano*, 440 F.3d at 1324 (quoting *Althen*, 418 F.3d at 1278).

If a petitioner is able to establish causation in fact, then the burden of proof shifts to the Government to establish that a factor unrelated to the vaccine was the actual cause of the petitioner's injury. *See* 42 U.S.C. § 300aa-13(a)(1)(B); *see also Althen*, 418 F.3d at 1278.

Two recent decisions by the United States Court of Appeals for the Federal Circuit discuss *Althen*. In *Andreu ex rel. Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1377 (Fed. Cir. 2010), our appellate court held that the Special Master “erred in requiring . . . conclusive evidence in the medical literature linking the DPT vaccine [to the petitioner’s injury],” because doing so would increase a claimant’s burden under the Vaccine Act. Although the Special Master had correctly recited the *Althen* test, the Federal Circuit found that the Special Master had attempted to “cloak the application of an erroneous legal standard in the guise of a credibility determination, and thereby shield it from appellate review.” *Id.* at 1379. The Special Master was instructed that “[m]edical literature and epidemiological evidence must be 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. This standard requires only a “simple preponderance of evidence” and “not scientific certainty.” *Id.* Thus, while medical literature tends to not attribute causation “until a level of very near certainty—perhaps 95% probability—is achieved,” under the Vaccine Act, causation in fact is determined on a much lower standard, *i.e.*, whether causation is “logical” and “legally probable.” *Id.*

In *Moberly*, the United States Court of Appeals for the Federal Circuit held that the Special Master did not err in refusing to credit expert witness opinion where the petitioners were unable to establish any support for their expert’s theory and petitioners’ expert acknowledged that the theory propounded had not been tested. *See Moberly*, 592 F.3d at 1324. In reconciling this case with *Andreu*, the appellate court explained, “Although a Vaccine Act claimant is not required to present proof of causation to the level of scientific certainty, the special master is entitled to require some indicia of reliability to support the assertion of the expert witness.” *Id.* Although “conclusive evidence in the medical literature” is not required to find causation, the appellate court recognized that

Finders of fact are entitled—indeed expected—to make credibility determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of persons presenting that evidence. *What Andreu prohibited was for the finder of fact to reject evidence based on an unduly stringent legal test while characterizing the rejection as based on the reliability of particular evidence or the credibility of a particular witness.*

*Id.* at 1326.

**C. The Record In This Case.**

**1. Petitioners' Medical Expert Testimony: Dr. David Bell and Dr. James Oleske.**

**a. Dr. David Bell.**

Petitioners' first expert, Dr. David Bell, received an undergraduate degree from Harvard and attended medical school at Boston University. 4/25/07 TR at 231. He is an Advisor to the National Institute of Health on Chronic Fatigue Syndrome and a Member of the Chronic Fatigue Syndrome Program of the Center for Disease Control, that develops criteria for diagnosing children with Chronic Fatigue Syndrome. 4/25/07 TR at 232. In addition, Dr. Bell served for three years as the Chairman of the Department of Health and Human Services Advisory Committee For Chronic Fatigue Syndrome. 4/25/07 TR at 233. Dr. Bell has examined thousands of patients with Chronic Fatigue Syndrome and was recognized by Special Master Edwards as an expert "in the field of Chronic Fatigue Syndrome, and pediatric treatment of the same." 4/25/07 TR at 235. Dr. Bell is the only expert witness that actually examined Ilya. 4/25/07 TR at 238.

Dr. Bell's October 11, 2004 Report stated:

The current thinking is that global central nervous system injury and antigenic stimuli<sup>[22]</sup> are the direct causes of Chronic Fatigue Syndrome. Antigenic stimuli would be defined as any stimulus that would cause the body to generate an immune response, and examples of antigenic stimuli would include infection or immunization. A unifying hypothesis suggests that the disorder underlying Chronic Fatigue Syndrome may actually be a dysfunction of the immune system that responds to different stimuli with a *sustained inappropriate cytokine release*<sup>[23]</sup> (interferons, interleukins) *resulting in the fatigue, myalgias, and neurological complaints of [Chronic Fatigue Syndrome]*.

Pet. Ex. 17 at 2 (citations omitted) (emphasis added).

Dr. Bell's Report acknowledged, however, that

The mechanism whereby hepatitis B vaccine could cause neurologic injury and subsequent Chronic Fatigue Syndrome has not been proven. However, I feel that

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<sup>22</sup> An antigen is "any substance capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response, that is, with specific antibody or specifically sensitized T lymphocytes, or both." DORLAND'S at 104. Forms of hepatitis B are identified as antigens. *Id.* at 106.

<sup>23</sup> 'Cytokine' is "a generic term for nonantibody proteins released by one cell population . . . on contact with specific antigen, which acts as intercellular mediators, as in the generation of an immune response." DORLAND'S at 473.

is *reasonable to assume* that the hepatitis B vaccine initiated an immune response in Ilya Dobrydnev. *This response then caused Chronic Fatigue Syndrome by either initiating an encephalitis either through an autoimmune response or sustained cytokine activity.* I felt that the temporal relationship between the administration of the vaccine as well as *what is known about antigenic stimuli causing Chronic Fatigue Syndrome* creates a *definitive link* between the vaccine administration and the illness.

Pet. Ex. 17 at 4 (emphasis added).

During his testimony, Dr. Bell explained that approximately 75% of Chronic Fatigue Syndrome cases commence with an infectious agent, such as the Epstein-Barr virus, Lyme disease, parvovirus, Z fever, the Ross River virus, and five or six other infectious agents. 4/25/07 TR at 262. In the remaining 25% cases, this condition commences with something “other than a clear-cut infection,” *i.e.*, “any kind of antigenic challenge.” 4/25/07 TR at 263. The antigenic challenge causes a “cascade” of cytokines “which is the body’s attempt to remove or treat the infection.” 4/25/07 TR at 263. For individuals suffering from Chronic Fatigue Syndrome, the “cytokine cascade is abnormal, and as a result those symptoms persist indefinitely.” 4/25/07 TR at 263.

Specifically, Dr. Bell testified that the hepatitis B vaccine can cause Chronic Fatigue Syndrome, because it is designed as an antigenic challenge. *See* Pet. Ex. 17 at 3 (“Hepatitis B vaccine will stimulate an antigenic response, and as such can be assumed to cause Chronic Fatigue Syndrome, just as any antigenic stimulus can. It is well known that hepatitis B vaccine can cause neurologic injury and rheumatic disease. The possibility that hepatitis B vaccination can cause Chronic Fatigue Syndrome has been debated but not proven.” (citations omitted)). In other words, one of the properties of the hepatitis B vaccine is that it stimulates an immune response that, in turn, can trigger the production of cytokines within a matter of hours. 9/29/10 TR at 1144.

As to a logical sequence of cause and effect, Dr. Bell testified that Ilya appears to have a “predisposing vulnerable condition”<sup>24</sup> that would make him more susceptible to an antigenic stimulus that a hepatitis B vaccination can trigger. 9/29/10 TR at 1129-30. The existence of this condition helps explain why, on November 5, 2001, the day Ilya received a fourth hepatitis B vaccination, he experienced a fever and developed a persistent sore throat shortly thereafter that did not resolve without antibiotics.<sup>25</sup> Instead, within 25 days after the fourth hepatitis vaccination, Ilya developed vestibular neuritis, indicating inflammation of the vestibular division of the 8<sup>th</sup> cranial nerve. 4/25/07 TR at 261, *see also* 9/29/10 TR at 1131-32; MERCK MANUAL at

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<sup>24</sup> Ilya’s father may have had Chronic Variable Immune Deficiency. Pet. Mot. at 3, n.3; *see also* 9/29/10 TR at 4 and note 5 (reflecting that Dr. Bell took a family medical history when he examined Ilya).

<sup>25</sup> Dr. Bell also testified that although sore throat is not an expected consequence of hepatitis B vaccination, the “immunologic effect” of cytokines could cause sore throat. 9/29/10 TR at 1145, 1150.

795. Dr. Bell further testified that vestibular neuritis was “impressive evidence that [Ilya] had a process going on in his central nervous system.” 4/25/07 TR at 314. Dr. Bell considered this to be significant because, patients who develop Chronic Fatigue Syndrome also exhibit central (not peripheral) vestibular problems. 4/25/07 TR at 247.

**b. Dr. James Oleske.**

Petitioners’ second expert, Dr. James Oleske, received a medical degree from the New Jersey Medical School and a Masters in Public Health in Epidemiology from Columbia University. 4/26/07 TR at 455-56. Dr. Oleske is the Francis Xavier Bagnoud Professor of Pediatrics at the New Jersey Medical School, where he directs the Allergy, Immunology, and Infectious Diseases Division of the Department of Pediatrics and the Center for Children. 4/26/07 TR at 463. Dr. Oleske has published approximately 200 peer-reviewed articles in the fields of allergy, immunology, and infectious disease, and has conducted research on children and adolescents with Chronic Fatigue Syndrome. 4/26/07 TR at 457. Dr. Oleske has treated over 1,000 patients with “chronic fatigue-like syndromes.” *Id.* He is also involved in the Brighton Collaborative Group, a part of the Center for Disease Control that seeks to standardize diagnostic criteria for adverse reactions to immunizations. *Id.* Dr. Oleske became the Chairman of the Department of Health and Human Services Advisory Committee For Chronic Fatigue Syndrome after Dr. Bell’s tenure. 4/25/07 TR at 233; 4/26/07 TR at 458. Dr. Oleske was recognized by Special Master Edwards as an expert in pediatric immunology and pediatric infectious disease. 4/26/07 TR at 464.

Dr. Oleske concurred with Dr. Bell’s medical theory, which he explained in this way:

[T]he general principle is to stimulate the immune system [in such a way] that mimics as much as possible the natural consequence of infection without obviously having infection . . . . To accomplish that, besides carefully selecting antigens prepared from the organism you want to develop your vaccine from, people have in the past added what we call adjuvants or immune stimulants to the vaccines to make them more effective in stimulating a specific response. . . . Hepatitis B vaccine is made under these principles. There is no risk of becoming infected with hepatitis B from the vaccine, however, it’s produced in a way that it stimulates the immune system in a broad enough fashion that it results in the development of antibody and as well cell mediated immune responses.

4/26/07 TR at 475-76.

In addition, Dr. Oleske testified that the hepatitis B vaccine contains hepatitis B antigens and adjuvants<sup>26</sup> that serve to boost the immune response and vestibular dysfunction is “an unusual but known complication of hepatitis B vaccination.” 4/26/07 TR at 467. In short, the immune reaction “doesn’t turn off as we normally would expect. It results in the cascade of

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<sup>26</sup> An adjuvant, as used in the context of immunology, is a “nonspecific stimulator of the immune response.” DORLAND’S at 33.

inflammatory mediators [called] cytokines.” 4/26/07 TR at 477. In Ilya’s case, he may have an “abnormal functioning immune system” that “may very well be a potentiating factor” making him “more susceptible” to a cytokine cascade. 4/26/07 TR at 469.

Dr. Oleske’s views about the effect of Ilya’s fourth, and unnecessary, hepatitis B vaccination and subsequent manifestation of Chronic Fatigue Syndrome were reinforced by the fact that Dr. Fink, Ilya’s treating physician, identified the relationship between Ilya’s fourth hepatitis B vaccination, vestibular neuritis, and Chronic Fatigue Syndrome in a May 6, 2004 VAERS Report. 4/26/07 TR at 474, 478.

## **2. Medical Literature Regarding Chronic Fatigue Syndrome.**

The theory that Chronic Fatigue Syndrome has a “multi-factorial etiology” is supported by several articles proffered by Petitioner, discussed herein in chronological order and in brief.

The first article is a study of two patients who “experienced neurological symptoms and signs with evidence of central-nervous-system demyelination, 6 weeks after administration of recombinant hepatitis B vaccine.” L. Herroelen et al., *Central-Nervous-System Demyelination After immunization With Recombinant Hepatitis B Vaccine*, 338 THE LANCET 1174, 1175 (1991). This study did not establish causation between the hepatitis B vaccination and demyelination, but observed that “the pathogenetic process . . . is probably immune mediated; postvaccinal acute disseminated encephalomyelitis or, respectively, relapse and the onset of multiple sclerosis are two possible explanations.” *Id.*

A second article suggested that “the disorder underlying Chronic Fatigue Syndrome may actually be a dysfunction of the immune system that responds to different stimuli with a sustained inappropriate cytokine release,” because “the adverse effects of therapeutically administered interferon and/or interleukin-2 [two types of cytokines] resemble the clinical picture of Chronic Fatigue Syndrome.” G. Valesini et al., *Chronic Fatigue Syndrome: What Factors Trigger It Off?*, 12 CLINICAL AND EXPERIMENTAL RHEUMATOLOGY 473, 473-74 (1996). Although this article does not discuss vaccines in particular, it identified viral, bacterial, fungal, and protozoan infections, allergies, drugs, and silicone, as agents believed to induce Chronic Fatigue Syndrome. *Id.* at 475; *see also id.* (“Whatever the stimulus . . . , immune activation seems to play a pivotal role. The broadening spectrum of potential triggering agents strengthens the hypothesis of a multi-factorial etiology for Chronic Fatigue Syndrome[.]”).

A third medical article reported chronic immune activation in Chronic Fatigue Syndrome patients, observing that “a state of immune activation could lead to the production of cytokines that disrupt neuro-transmitter function and result in the symptoms of Chronic Fatigue Syndrome, but that hypothesis remains unproven.” A. L. Komaroff & D. S. Buchwald, *Chronic Fatigue Syndrome: An Update*, 49 ANNUAL REV. MED. 1, 13 (1998).

A fourth medical study reported that four individuals who received hepatitis B vaccinations suffered from “polyarthralgia and myalgia” following vaccination; three of whom also suffered from fatigue. *See* J. F. Maillefert et al., *Rheumatic Disorders Developed After Hepatitis B Vaccination*, 30 RHEUMATOLOGY 978, 979 (1999). This study showed that of 22

cases reporting injury following hepatitis B vaccination, eight developed symptoms after the first dose, five after the second, three after a third dose, and six after a booster. *Id.* at 979. Patients also reported rheumatoid arthritis, post-vaccinal arthritis, vasculitis, and miscellaneous other symptoms after having a hepatitis B vaccination. *Id.* Complaints of fatigue persisted in the individuals from 2 months to one year. *Id.*

A fifth medical article reported associative data linking the hepatitis B vaccine to central demyelination disease, but concluded that the risk of harm is outweighed by the benefits provided by the vaccine. See Daniel Lévy-Bruhl, *Central Demyelinating Disorders and Hepatitis B Vaccination: A Risk-Benefit Approach For Pre-Adolescent Vaccination in France*. 20 VACCINE 2065, 2065-71 (2002).

Finally, an article discussed further herein, reported that both the hepatitis B virus and hepatitis B vaccine have been “suggested [in French medical literature] to be associated with Chronic Fatigue Syndrome onset,” but at present there is insufficient evidence to conclude, as medical fact, that either the virus or vaccine “causes” Chronic Fatigue Syndrome. See 2009 NEW YORK ACADEMY OF SCIENCES at 600-01.

### **3. The Government’s Experts: Dr. Alan Brenner and Dr. Raoul Wientzen, Jr.**

#### **a. Dr. Alan Brenner.**

Dr. Alan Brenner received a medical degree from the University of Cincinnati, and performed a two-year rheumatology fellowship at Boston University. 4/26/07 TR at 555. He is a member of the American College of Rheumatology, American College of Physicians, the New York Academy of Sciences, and the Massachusetts Medical Society. 4/26/07 TR at 556. His primary experience with Chronic Fatigue Syndrome comes from treating “thousands” of patients with Chronic Fatigue Syndrome. 4/26/07 TR at 557. Dr. Brenner also has published a number of articles, including articles about the anthrax vaccine. 4/26/07 TR at 557-58. He is a certified as an expert in Rheumatology. 4/26/07 TR at 558.

Dr. Brenner testified that no link has been established between the hepatitis B vaccine and vestibular neuritis or encephalitis. 4/26/07 TR at 568. Dr. Brenner further explained that there was no evidence of encephalitis in Ilya. 4/26/07 TR at 573. One method of testing for encephalitis is by “lumbar puncture and an analysis of spinal fluid,” a procedure that Ilya did not undergo. 4/26/07 TR at 573. Another method is through an MRI, a test that Ilya did receive, but it showed no abnormality. 4/26/07 TR at 574. Although a SPECT study found abnormality, this test was unreliable, because of a “position artifact that makes it very difficult to interpret one way or the other.” 4/26/07 TR at 575. Dr. Brenner also testified that the most common antecedent in patients who develop vestibular neuritis is upper respiratory infection. 4/26/07 TR at 576. Although Dr. Brenner agreed that vestibular problems in Chronic Fatigue Syndrome patients are usually in the central nervous system, he noted that Ilya’s hospital physician believed that his vestibular neuritis was peripheral, suggesting that Ilya did not have Chronic Fatigue Syndrome at the time of his November 30, 2001 hospitalization. 4/26/07 TR at 598.

In addition, Dr Brenner testified that the hepatitis B vaccine was an unlikely cause of a cytokine cascade, because the vaccine is created from a “sub-unit particle” made of “a piece of the hepatitis B surface antigen” that does not create a strong immune response, “hence the requirement for three doses.” 4/26/07 TR at 569-71. Moreover, the “reactogenicity of hepatitis vaccine” goes down with the second and third doses and there is some evidence that this is also true for the fourth dose. 4/26/07 TR at 571-72. Dr. Brenner disagreed that cytokine production is related to Chronic Fatigue Syndrome. 4/26/07 TR at 581-82. Instead, Dr Brenner testified that Chronic Fatigue Syndrome is predominantly caused by viral infection and, in this case, the Epstein-Barr virus is a primary suspect. 4/26/07 TR at 567-68. Dr. Brenner testified that Ilya’s Mononucleosis/Epstein-Barr virus was active throughout the summer of 2001, suggesting that one of these was the most likely cause of Chronic Fatigue Syndrome. 4/26/07 TR at 561-65.<sup>27</sup>

**b. Dr. Raoul Wientzen.**

Dr. Raoul Wientzen received his medical degree from Georgetown Medical School, where he also served as a faculty member from 1977-2002, the last two years of which he was the Associate Dean and Vice Chairman for the Department of Pediatrics. 4/26/07 TR at 631-32. Dr. Wientzen is a member of the Pediatric Infectious Disease Society and conducts research concerning bacterial infection in children and “the evolutionary immune response to normal oral flora.” 4/26/07 TR at 633. Since 2002, Dr. Wientzen continues to work part time at Georgetown, while serving as Medical Director at the Vishnevskaya-Rostropovich Foundation, an organization that creates and manages health programs for children in “Russia and the newly independent states,” including a program vaccinating 2 million children against hepatitis B. 4/26/07 TR at 632-33. Dr. Wientzen has examined approximately 10-12 Chronic Fatigue Syndrome patients per year over the past thirty years. 4/26/07 TR at 634. Dr. Wientzen is certified as an expert in pediatrics and pediatric infectious disease. 4/26/07 TR at 636.

Dr. Wientzen testified that Ilya does not have Chronic Fatigue Syndrome and his condition cannot be accurately diagnosed without evaluation of psychological, social, and cultural factors. 4/26/07 TR at 647-48, 681-98. Dr. Wientzen suggested that if Ilya has Chronic Fatigue Syndrome, then it probably occurred much earlier in the year, at the same time as his mononucleosis. 4/26/07 TR at 654. According to Dr. Wientzen, the most likely cause of Ilya’s vestibular neuritis was a viral illness. 4/26/07 TR at 645. In Dr. Wientzen’s experience, he has never heard a report of Chronic Fatigue Syndrome resulting from a vaccination. 4/26/07 TR at 698-99.

**D. The Special Master’s October 27, 2010 Entitlement Decision On Remand.**

In analyzing the first element of *Althen*, the Special Master determined that, although the exact cause and causal mechanism of Chronic Fatigue Syndrome are unknown, one medical theory is that Chronic Fatigue Syndrome is caused when “a foreign substance, known as an antigen, stimulates a person’s immune system to produce an overabundance of cytokines.” *Dobrydneva III*, at 7-8. The Special Master characterized the validity of the “cytokine theory”

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<sup>27</sup> Dr. Oleske disagreed: “by the time [Ilya] was immunized, [the Epstein-Barr virus] was in a very latent form.” 9/29/10 TR at 1033.

was a “close call,” but one “that should be resolved in favor of petitioners.” *Id.* at 8. Nevertheless, the Special Master determined that Petitioners did not meet their burden of proof to causally connect Ilya’s hepatitis B vaccinations to Chronic Fatigue Syndrome, because they failed to “explain why, based upon reliable scientific evidence” the “hepatitis B vaccine is one type of antigen [that] can cause chronic fatigue syndrome” or why their cytokine cascade theory is “plausible.” *Id.* at 9.

In reaching this conclusion, the Special Master discounted the opinions of Petitioners’ experts as unsupported by “reliable evidence,” referring to two medical articles proffered by the parties. *Id.* at 8, 10-12. The first article, submitted by the Government and cited by Dr. Brenner, reported that there was “no biologic evidence to support the hypothesis that hepatitis B vaccine can cause [Chronic Fatigue Syndrome].” *Id.* at 10 (quoting Gilles Dillage et al., *Report of the Working Group on the Possible Relationship between Hepatitis B Vaccination and the Chronic Fatigue Syndrome*, 149(3) CAN. MED. ASSOC. J. 314, 315 (1993) (“1993 CANADIAN STUDY”)). The second, the 2009 NEW YORK ACAD. OF SCIENCES ARTICLE, proffered by Petitioners reported only “uncertainty” on this issue. *See Dobrydneva III*, at 10-11. The Special Master determined that neither of these articles established that the hepatitis B vaccine causes Chronic Fatigue Syndrome. *See Dobrydneva III*, at 10-11.

As to the second element on *Althen*, the Special Master’s analysis began by dismissing the Epstein-Barr virus as a potential cause of Chronic Fatigue Syndrome, because it was dormant at the time that Ilya’s Chronic Fatigue Syndrome manifested. *See Dobrydneva III*, at 14-15. The Special Master also ruled out Ilya’s November 2001 infection as a cause, because the Special Master thought that the court previously ruled that that Ilya’s Chronic Fatigue Syndrome manifested prior to that time. *Id.* at 17 (citing *Dobrydneva II*, 94 Fed. Cl. at 146). In any event, the Special Master determined that the second element of *Althen*, *i.e.*, a logical sequence of cause and effect, was not satisfied, because none of Petitioners’ treating physicians identified Ilya’s hepatitis B vaccinations as the cause of Ilya’s Chronic Fatigue Syndrome. *Dobrydneva III*, at 17-18 (citing *Capizzano*, 440 F.3d at 1326 (“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.’”)).

**E. The Special Master Erred In Determining That Petitioners Did Not Establish, By A Preponderance Of Evidence, A Medical Theory Causally Connecting A Fourth, And Unnecessary, Hepatitis B Vaccination With Chronic Fatigue Syndrome.**

**1. Petitioners' Arguments.**

Petitioners argue that the first element of *Althen*, *i.e.*, a medical theory causally connecting vaccination and injury, was established by Petitioners' experts, Dr. Bell and Dr. Oleske. Pet. Mot. at 7. Nevertheless, the Special Master discounted their medical opinions articulating "the logical autoimmune reaction in a detailed biological mechanism of the immune system"; other medical articles submitted by Petitioners; and the fact that hepatitis B antigen-containing vaccines are known to be the cause of anaphylaxis and anaphylactic shock, as evidenced in the Vaccine Injury Table. Pet. Mot. at 14-15 (citing 42 C.F.R. § 100.3 (2010)).

In addition, the Special Master's reliance on *Moberly* was misplaced, because in that case no medical expert was able to articulate a medical theory that explained the cause of the injury. Pet. Mot. at 11-12 (citing *Moberly*, 592 F.3d at 1326). In this case, however, Petitioners' experts identified a medical theory connecting Ilya's fourth hepatitis B vaccination and subsequent development of Chronic Fatigue Syndrome. Pet. Mot. at 11-12.

**2. The Government's Response.**

The Government responds that Petitioners' medical theory did not satisfy the first element of *Althen*, because the theory must be "specific to petitioners' case and supported by a reputable (*i.e.*, reliable) scientific or medical explanation." Gov't Mot. at 10 (citing *Moberly*, 592 F.3d at 1322 (holding that a "petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case")); *see also Althen*, 418 F.3d at 1278 ("A persuasive medical theory is demonstrated by 'proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury[,] the logical sequence being supported by 'reputable medical or scientific explanation . . .'" (citations omitted); *Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994) (petitioners' theory of causation must be supported by a "sound and reliable medical or scientific explanation").

The Government further argues that the special master's role is to determine whether expert testimony is reliable, either under *Daubert v. Merrell Dow Pharms.*, 509 U.S. 579, 593-94 (1993) or another reliability standard developed by the special master. *See Kumho Tire Co. Ltd v. Carmichael*, 526 U.S. 137, 151 (1999) ("Thus, whether *Daubert's* specific factors are, or are not, reasonable measures of reliability in a particular case is a matter that the law grants the trial judge broad latitude to determine."); *see also Kumho Tire*, 526 U.S. at 158-59 (observing that it "is not discretion to abandon the gatekeeping function") (Scalia, J., concurring). In this case, the Special Master properly concluded that the Petitioners' medical theory lacked scientific support: Petitioners "provide[d] scant information as to the causal theory connecting the hepatitis B vaccine to Chronic Fatigue Syndrome." Gov't Mot. at 13 (quoting *Dobrydneva III*, at 8). Instead, the Special Master properly noted that Petitioners' experts made multiple assumptions

and the medical literature proffered was contrary to Petitioners' medical theory. *See Dobrydneva III*, at 9-11.

Determinations as to the persuasiveness of a witness “and overall reliability of the evidence presented, [are] wholly within the province of the Special Master.” Gov’t Mot. at 17. These determinations are “virtually unreviewable on appeal so long as the Special Master ‘has considered the relevant evidence of record, drawn plausible inferences and articulated a rational basis for the decision.’” Gov’t Mot. at 17 (citing *Moberly*, 592 F.3d at 1325 (“Weighing the persuasiveness of particular evidence often requires a finder of fact to assess the reliability of testimony, including expert testimony, and we have made clear that the special masters have that responsibility in Vaccine Act cases.”)); *see also Lampe v. Sec’y of Health & Human Servs.*, 219 F.3d 1357, 1360 (Fed. Cir. 2000) (“[W]e do not sit to reweigh the evidence. Since the special master’s conclusion was based on evidence in the record that was not wholly implausible, we are compelled to uphold that finding as not being arbitrary or capricious.”).

### 3. The Court’s Resolution.

As to the first element of *Althen*, the Special Master erred in finding that Dr. Bell and Dr. Oleske failed “to explain why, based upon reliable scientific evidence [their cytokine cascade] theory is plausible.” *Dobrydneva III*, at 9. As a threshold matter, the United States Court of Appeals for the Federal Circuit has held that a “medical theory” in Vaccine Act cases can be established *either* by “reputable medical *or* scientific explanation, *i.e.*, evidence in the form of scientific studies *or* expert medical testimony.” *Althen*, 418 F.3d at 1278 (emphasis added; internal quotation marks omitted). In addition, by discounting the expert medical testimony of Dr. Bell and Dr. Oleske<sup>28</sup> as “*ipse dixit*” the Special Master misapplied *Daubert* and its progeny.<sup>29</sup> *See Dobrydneva III*, at 8. Although the United States Court of Appeals for the

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<sup>28</sup> The only expert testimony from Petitioners that the Special Master appears to have deemed relevant is a sentence from Dr. Bell on cross examination. Dr. Bell was asked: “Isn’t it true that any type of *infectious agent* can cause chronic fatigue?” 4/25/07 TR at 298 (emphasis added). Dr. Bell responded: “The current thinking is that there is a relatively restricted list of things that can cause [Chronic Fatigue Syndrome].” 4/25/07 TR at 298. On this basis, the Special Master concluded that Dr. Bell’s testimony contained a “gap,” because he did not explain why the hepatitis B vaccine belongs on this “relatively restricted list.” *Dobrydneva III*, at 9. During the hearing, the Special Master made no inquiry about this “gap,” although he frequently engaged in questioning the experts. *See, e.g.*, 9/29/10 TR at 1156-76. Nevertheless, a careful reading of Dr. Bell’s exact testimony shows that the Special Master took Dr. Bell’s statement out of context. On cross examination, Dr. Bell was only repeating his direct testimony: there are only a limited number of *infectious agents* that can cause Chronic Fatigue Syndrome. 4/25/07 TR at 262-63. Dr. Bell never suggested that the hepatitis B vaccine is an “infectious agent”; instead, he testified that 25% of Chronic Fatigue Syndrome cases begin with a variety of non-infectious “antigenic challenges” and that the hepatitis B vaccination is specifically designed to be an antigenic challenge. *Id.*

<sup>29</sup> The United States Supreme Court has posited five factors to determine the admissibility of scientific evidence in a jury trial: (1) whether the theory has or can be tested; (2) whether the theory has been subjected to publication and peer review; (3) whether there are

Federal Circuit has held that it is not reversible error for a special master to evaluate medical expert opinion by considering *Daubert* factors, our appellate court appropriately has not required a *Daubert* inquiry in Vaccine Act cases, because a special master is the fact finder, not a jury—so that “gatekeeping” concerns are not relevant. See *Cedillo v. Sec’y of Health & Human Servs.*, 617 F.3d 1328, 1339 (2010). Our appellate court, however, has emphasized that “the focus of [any] *Daubert* inquiry must generally be ‘on principles and methodology, not the conclusions they generate.’” *Id.* at 1339 (quoting *Daubert*, 509 U.S. at 595). Principles and methodology are not relevant to “plausibility,” but to how scientific facts are established. *Id.* The Special Master made no inquiry at the initial or remand hearings about the principles or methodology of the cytokine cascade theory, but instead, in the October 27, 2010 Entitlement Decision, launched into a wholesale critique of Dr. Bell for not supporting this theory with “reliable scientific evidence.” *Dobrydneva III*, at 9. Not only is “reliable scientific evidence” not required in Vaccine Act cases (*Althen*, 418 F.3d at 1278), but a medical theory propounded by medical experts with highly relevant academic credentials and specific field expertise, such as those presented by Dr. Bell and Dr. Oleske, is *prima facie* evidence of biologic plausibility, unless their lack of credibility or bias is established or current scientific evidence is proffered to the contrary, none of which happened here. See *Andreu*, 569 F.3d at 1375 (“The first prong [of *Althen*] was satisfied because [the petitioner’s medical expert] presented a ‘biologically plausible’ theory[.]”); see also *Campbell v. Sec’y of Health & Human Servs.*, No. 07-465V, 2011 WL 1289064, at \*8 (Fed. Cl. March 22, 2011) (“Notably, what is at issue respecting the first prong of *Althen* is a ‘theory,’ which, by definition, can be a hypothesis that is offered, propounded, or accepted as accounting for the known facts.” (internal citations omitted)). Of course, causation requires more than a “bare theory,” an issue to which the court now turns.

The Special Master also concluded that “the opinions of Dr. Oleske and Dr. Bell are less than unsupported[,] because their theory has been tested and found not valid in the Canadian Study.” *Dobrydneva III*, at 12. Again, as a threshold matter, the United States Court of Appeals for the Federal Circuit does not require a petitioner in a Vaccine Act case to proffer supporting medical literature to establish an expert’s medical theory. See *Andreu*, 569 F.3d at 1378 (“Requiring 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, in which close calls regarding causation are resolved in favor of injured claimants.” (internal quotation marks omitted)); see also *Capizzano*, 440 F.3d at 1326 (“[R]equiring either epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities . . . is contrary to what we said in *Althen*[.]”). This error was compounded by the fact that the Special Master misunderstood the import of the 1993 CANADIAN STUDY, that he touted as the “most relevant” article. *Dobrydneva III*, at 11. Specifically, the 1993 CANADIAN STUDY concludes that “there was no evidence justifying the allocation of funds for research projects on the possible relationship between Chronic Fatigue Syndrome and hepatitis B vaccination.” Gilles Dillage et al., *Report of the Working Group on the Possible Relationship Between Hepatitis B Vaccination*

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known or potential error rates applicable to the theory; (4) whether there are established standards applicable to the theory and whether those standards were followed; and (5) whether the theory has achieved general acceptance in the appropriate scientific community. See *Daubert*, 509 U.S. at 593-94.

*and the Chronic Fatigue Syndrome*, 149(3) CAN. MED. ASSOC. J. 314, 316 (1993). The fact that there was insufficient medical evidence to justify funding research almost 20 years ago is not relevant to whether a petitioner in a Vaccine Act case today has established a medical theory casually connecting a vaccination to injury—by any standard of proof, much less once of a preponderance of evidence.<sup>30</sup> The more recent 2009 NEW YORK ACADEMY OF SCIENCES ARTICLE surveyed a number of epidemiological articles, including the CANADIAN STUDY, and specifically identified the hepatitis B virus as an “infectious agent associated with Chronic Fatigue Syndrome” and Chronic Fatigue Syndrome onset as a “risk” of the hepatitis B vaccination. 2009 NEW YORK ACADEMY OF SCIENCES ARTICLE at 602-03. Therefore, even the most cursory review of these articles shows that they do not support the Special Master’s conclusion that the hepatitis B vaccine cannot cause Chronic Fatigue Syndrome, only that the medical data is inconclusive. As Dr. Oleske testified:

On the information that [the CANADIAN STUDY] had I would make that same conclusion. I think that there’s no evidence in the studies that were looked at that shows *a conclusive link* between chronic fatigue and hepatitis B. *What that doesn’t say is that . . . patients can’t have chronic fatigue as an adverse event to the immunization.*

4/26/07 TR at 517 (emphasis added).

In a similar vein, the Special Master did not bother to acknowledge, much less discuss, any of the other medical literature proffered by Petitioner and cited by the court herein.

To be sure, medical literature is probative as to the persuasiveness of a medical theory (*see Moberly*, 592 F.3d at 1325), but medical literature is not required to establish a medical theory connecting a vaccine to a petitioner’s injury under a preponderance standard. *See Andreu*, 569 F.3d at 1379 (holding that “‘in a field bereft of complete and direct proof of how vaccines affect the human body,’ *a paucity of medical literature supporting a particular theory of causation cannot serve as a bar to recovery.*” (emphasis added) (quoting *Althen*, 418 F.3d at 1280)); *see also id.* (stating that a special master is required to assess medical literature and epidemiological evidence “not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act’s preponderant evidence standard.”); *see also Althen*, 418 F.3d at 1280 (requiring concurring medical literature contravenes the Vaccine Act’s “allowance of medical opinion as proof”). In this case, however, medical literature lends credence to the expert medical opinions of Dr. Bell and Dr. Oleske, albeit not to a level of medical certainty.

The Special Master also erred in relying on *Moberly* to deflect attention from his failure to follow *Andreu* and *Althen*. *See Dobrydneva III*, at 11. *Moberly* stands for the proposition

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<sup>30</sup> This is not the first time that the Special Master has misconstrued medical literature. *See Campbell v. Sec’y of Health & Human Servs.*, No. 07-465V, 2011 WL 1289064, at \*17 (Fed. Cl. March 22, 2011) (determining that the Special Master’s finding that the medical literature in that case weighs against causation was “wrong as a matter of logic,” because the articles cited “cannot reasonably be said to stand for the proposition that influenza vaccination does not cause rheumatoid arthritis”).

that, as the fact finder, a special master may consider the lack of support in medical literature as a factor in determining whether a petitioner has established a *prima facie* case of causation under a preponderance of evidence standard. See *Moberly*, 592 F.3d at 1324. In this case, however, supporting medical literature was proffered, providing the required “indicia of reliability.” *Id.*

For these reasons, the court has determined that the Special Master erred in finding that Petitioners failed to meet their burden of proof regarding the first element of *Althen*. See *Dobrydneva III*, at 12, 18. The court has determined that, as a matter of law, Petitioners have established a medical theory by “expert medical testimony.” *Althen*, 418 F.3d at 1278.

**F. The Special Master Erred In Determining That Petitioners Did Not Establish, By A Preponderance Of Evidence, A Logical Sequence Of Cause And Effect Showing That A Fourth, And Unnecessary, Hepatitis B Vaccination Was The Reason For Petitioner’s Chronic Fatigue Syndrome.**

**1. Petitioners’ Arguments.**

Petitioners argue that the Special Master erred in failing to consider that Dr. Bell and Dr. Oleske’s testimony, in combination with this court’s findings in *Dobrydneva II*, 94 Fed. Cl. at 137-141, 146-49, established a logical sequence of cause and effect between Ilya’s hepatitis B vaccinations and Chronic Fatigue Syndrome. Pet. Mot. at 8, 19.

**2. The Government’s Response.**

The Government responds that the Special Master correctly found that “neither a showing of a proximate temporal relationship between vaccine and injury, nor a simplistic elimination of other potential causes of the injury suffices, without more to meet the burden of showing actual causation.” *Dobrydneva III*, at 17 (quoting *Moberly*, 592 F.3d at 1323). Specifically, the Government contends that Petitioners did not establish “something more,” because no treating physician attributed Ilya’s chronic fatigue syndrome to his hepatitis B vaccinations. Gov’t Mot. at 14-16. Moreover, the theories proffered by Petitioners’ expert witnesses have not been scientifically tested and are not supported by medical records. Gov’t Mot. at 17 (citing *Dobrydneva III*, at 17; *Moberly*, 592 F.3d at 1323).

**3. The Court’s Resolution.**

Regarding the second element of *Althen*, the Special Master erred when he concluded that Petitioners “have not identified any treating doctor who opined that the hepatitis B vaccine caused Ilya’s chronic fatigue syndrome.” *Dobrydneva III*, at 17.<sup>31</sup> Notably, the Special Master failed to mention that Dr. Fink, Ilya’s long-time treating physician, filed a May 6, 2004 Vaccine Adverse Event Reporting System (“VAERS”) Report that noted an “adverse event” from Ilya’s fourth hepatitis B vaccination on November 5, 2001: “an episode of vestibular neuronitis

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<sup>31</sup> Contrary to the Government’s argument, no precedent requires that a treating physician testify that a vaccination actually caused injury. The testimony of treating physicians is considered “probative,” but “not required in Vaccine Act cases.” *Moberly*, 592 F.3d at 1325.

requiring an [emergency room] visit [on November 30, 2001]—he has had chronic fatigue since.” Pet. Ex. 13(a) at 102-104; *see also* 4/26/07 TR at 478. Specifically, the VAERS Report submitted by Dr. Fink states: “Required emergency room/doctor visit,” and “Resulted in permanent disability.” Pet. Ex. 13(a) at 103.<sup>32</sup> The VAERS program is voluntary; Dr. Fink was not required to submit a report. 4/26/07 TR at 524-27. Either the Special Master did not carefully review the record<sup>33</sup> or purposefully neglected to discuss highly relevant evidence from Ilya’s primary treating physician. In addition, the Special Master failed to afford Dr. Bell’s opinion any deference, even though he was the only expert witness who examined Ilya. 4/25/07 TR at 238. Instead, the Special Master neglected to acknowledge, much less weigh this probative evidence, despite the fact that the United States Court of Appeals for the Federal Circuit has recognized that treating physicians are 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.” *Andreu*, 569 F.3d at 1375; *see also Moberly*, 592 F.3d at 1325 (“treating physician evidence . . . [can] support the claim of causation”).

Second, as the United States Court of Appeals for the Federal Circuit has held, a petitioner in a Vaccine Act case can meet the requirements of one element of *Althen* with another element:

We see no reason why evidence used to satisfy one of the *Althen III* prongs cannot overlap to satisfy another prong. In other words, if close temporal proximity, combined with the finding that hepatitis B vaccine can cause [an injury], demonstrates that it is logical to conclude that the vaccine was the cause of the [injury], then *medical opinions* to this effect are quite probative.

*Capizzano*, 440 F.3d at 1236 (emphasis added).

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<sup>32</sup> The fact that no treating doctor specifically linked Ilya’s fourth hepatitis B vaccination on November 5, 2001 to Chronic Fatigue Syndrome when he was hospitalized on November 30, 2001 is not surprising since this condition requires that six months pass before a diagnosis can be made. *See DORLAND’S* at 1851 (describing Chronic Fatigue Syndrome as a “*persistent debilitating fatigue lasting longer than six months*, with other known medical conditions having been ruled out by clinical diagnosis accompanied by at least four of the following: significantly impaired short term memory or concentration; muscle weakness, pain in multiple joints without swelling or redness, sore throat, tender lymph nodes, headaches, unrefreshing sleep, and malaise that lasts more than 24 hours following exertion”) (emphasis added).

<sup>33</sup> Apparently, the Special Master was not alone in failing to identify the existence of the VAERS Report in the record. As Dr. Wientzen testified: “I have not seen the VAERS [R]eport. I don’t know if that’s considered in the evidence or not, but that’s one thing I would love to review. I have not seen it.” 4/26/07 TR at 637. Of course, the court does not know whether the existence and substance of the VAERS Report would have changed Dr. Wientzen’s testimony.

Therefore, the expert medical opinions of Dr. Bell and Dr. Oleske as to the logical progression of Ilya's fever and persistent sore throat<sup>34</sup> to vestibular neuritis and Chronic Fatigue Syndrome, following his fourth, and unnecessary, hepatitis B vaccination satisfied Petitioners' burden as to the second element of *Althen*. In addition, since the court previously has determined that Petitioners met their burden regarding the third element of *Althen* as to temporal proximity,<sup>35</sup> this determination can be credited towards Petitioners burden to satisfy the "logical sequence of cause and effect" element.

Finally, the Special Master did not consider whether any plausible inferences as to "a logical sequence of cause and effect" were warranted in light of unchallenged medical records that show:

[O]n November 5, 2001, Ilya received an unnecessary and 'excessive' fourth dose of the hepatitis B vaccine. Pet. Ex. 9 at 3; Pet. Ex. 23 at 1. Ilya was absent from school on November 6, 7, 19, 20, 21, and 26. Pet. Ex. 7 at 5. On November 19, 2001, Ilya was diagnosed with 'some degree of nasal congestion with minimal cough.' Pet. Ex. 5 at 36. Within a week, by November 26, 2001, Ilya had developed a yellow nasal discharge and frontal headaches diagnosed as sinusitis and Augmentin™ 500 was prescribed for ten days. *Id.* On December 27, 2001, blood tests indicated that Ilya had abnormal immunoglobulin levels, indicating an immune response. Pet. Ex. 6 at 326. On January 2, 2002, Ilya experienced a sore throat and fatigue. *Id.* at 34 (emphasis added).<sup>36</sup> On January 2, 2002, Ilya's physician's assessment was 'muscle weakness.' Pet. Ex. 11(a) at 113 (emphasis added). On January 23, 2002, Ilya had 'difficulty lying supine because of some neck stiffness[.]' Pet. Ex. 6 at 276. On March 18, 2002, 'persistent atypical lymphocytes'<sup>37</sup> were noted. Pet. Ex. 5 at 28. On March 20, 2002, one of the

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<sup>34</sup> Although sore throat is not a usual complication from the hepatitis B vaccine, Dr. Oleske stated that Ilya's sore throat on the night after he received the vaccination may have been a part of Ilya's "severe rare" immunological reaction to the vaccine. 9/29/10 TR at 1057; *see also* 9/29/10 TR at 1145, 1150 (Dr. Bell) (same).

<sup>35</sup> *See Dobryднеva II*, 94 Fed. Cl. at 145-46 (holding that "Petitioners produced preponderant evidence that the onset of Chronic Fatigue Syndrome occurred after the November 5, 2001 vaccine and manifested symptoms well within the time period accepted and expected by the medical community").

<sup>36</sup> On January 2, 2002, Ilya's mother first asked whether the hepatitis B shot "could be playing a role in this." Pet. Ex. 6 at 34. Since Petitioners' Complaint was not filed until October 25, 2004, it is difficult to discern any litigation-driven motivation for this inquiry, particularly in light of her related medical training.

<sup>37</sup> A "lymphocyte" is a "mononuclear nonphagocytic leukocyte [ ], found in the blood, lymph, and lymphoid tissues, that are the body's immunologically competent cells and their precursors." DORLAND'S at 1110.

examining physicians observed ‘Chronic [F]atigue [S]yndrome itself may be considered in this child.’ Pet. Ex. 6 at 250 (emphasis added).

Therefore, within three months of Ilya's unnecessary and ‘excessive’ fourth dose of the hepatitis B vaccine, headaches, sore throat, malaise, muscle weakness, and ‘atypical’ lymph cells were observed by Ilya's doctors and documented in medical records, and an initial diagnosis of possible ‘Chronic Fatigue Syndrome’ was suggested -- completely independent of Ilya's mother's testimony and other proffered information from her.

*Dobrydneva II*, 94 Fed. Cl. at 146 (footnotes in original).

In addition, the Special Master did not consider whether any plausible inferences as to “a logical sequence of cause and effect” were warranted in light of Petitioners’ supporting medical theory and opinion that

- the hepatitis B vaccine is a recognized antigen designed to illicit an immune response;<sup>38</sup>
- 25% of Chronic Fatigue Syndrome cases begin with an antigenic challenge as opposed to an infectious agent;<sup>39</sup>
- the effect of a fourth, and unnecessary, dose of the hepatitis B vaccine can cause a cytokine cascade;<sup>40</sup>
- a cytokine cascade can cause vestibular neuritis;<sup>41</sup>

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<sup>38</sup> See Pet. Ex. 17 at 3 (Dr. Bell testifying that “hepatitis B vaccine will stimulate an antigenic response”); 9/29/10 TR at 1144 (Dr. Bell testifying that “one of the properties of the hepatitis B vaccine is that it stimulates an immune response.”); 4/26/07 TR at 467 (Dr. Oleske); see also 4/26/07 TR at 569-71 (Dr. Brenner agreeing that the hepatitis B vaccine is an antigen).

<sup>39</sup> See 4/27/07 TR at 263 (Dr. Bell testifying that “[25%] of patients with Chronic Fatigue Syndrome will start with . . . an antigenic challenge”).

<sup>40</sup> See 4/25/07 TR at 263 (Dr. Bell testifying that the hepatitis B vaccine can “trigger the production of cytokines within a matter of hours.”); 4/26/07 TR at 467 (Dr. Oleske testifying that “we give vaccines . . . to stimulate the immune system . . . . In the process of developing that immunological memory and response a number of cascading events occur in the immune system in response to the antigen.”). In addition, Dr. Oleske testified that Ilya’s fourth vaccination was “an excessive and unnecessary dose.” 4/26/07 TR at 477. No other expert witness, including the Government’s witnesses, contradicted this obvious point.

<sup>41</sup> Compare Pet. Ex. 17 at 2 (Dr. Bell testifying that one theory of the causation of Chronic Fatigue Syndrome is that the body responds to antigenic stimulus with “sustained inappropriate cytokine release . . . resulting in fatigue, myalgias, and neurological complaints”), and 4/26/07 TR at 467 (Dr. Oleske testifying that vestibular dysfunction is “an unusual, but known complication of hepatitis B vaccination”), with 4/26/07 TR at 568 (Dr. Brenner only testifying that the hepatitis B vaccine has not been linked to vestibular neuritis).

- patients with Chronic Fatigue Syndrome exhibit central vestibular problems.<sup>42</sup>

The Government's experts challenged this expert medical opinion evidence of a sequence of cause and effect by arguing that two alternate causes were the source of Ilya's Chronic Fatigue Syndrome: the Epstein-Barr virus, and an infection occurring in November of 2001. 4/26/07 TR at 561-62, 567-68 (Dr. Brenner); 4/26/07 TR at 645 (Dr. Wientzen). The Special Master rejected both of these theories. *See Dobrydneva III* at 14-17.

The Government's experts also testified to other reasons why a logical sequence of cause and effect was not plausible. First, Dr. Brenner testified that a fourth dose of hepatitis B was unlikely to cause chronic fatigue, because the vaccine is produced in a way that it is less reactogenic "than the original plasma derived vaccine . . . hence the requirement for three doses." 4/26/07 TR at 571. Dr. Brenner also testified that the reactogenicity of the hepatitis B vaccine goes down with subsequent doses, and there is some suggestion that this is true for booster shots. 4/26/07 TR at 572. This testimony, however, is inconsistent with the purpose of the hepatitis B vaccine: to create an immune response. Furthermore, at least one medical article, proffered by Petitioners, but not mentioned by the Special Master, reported that a greater number of individuals report adverse reactions to fourth doses of the hepatitis B than to the third dose of the vaccine. *See J. F. Maillefert, et al., Rheumatic Disorders Developed After Hepatitis B Vaccination*, 30 RHEUMATOLOGY 978, 979 (1999).

Second, Dr. Brenner tried to cast doubt on the connection between Ilya's November 30, 2001 vestibular neuritis episode and later diagnosis of Chronic Fatigue Syndrome by pointing out that the hospital neurologist diagnosed Ilya with peripheral vestibular neuritis. 4/26/07 TR at 576-78. The significance is that individuals suffering from Chronic Fatigue Syndrome do not exhibit peripheral symptoms, but do experience vestibular problems in their central nervous system. *Id.* The court, however, does not view the November 30, 2001 diagnosis as inconsistent with a logical sequence of cause and effect, because the hospital neurologist was not aware that Ilya was experiencing other symptoms that later would be diagnosed as Chronic Fatigue Syndrome. As Dr. Bell's un rebutted testimony states:

In practice, however, it is very common for a person who has [central nervous system disturbance] to go to the emergency room and be told that they have a vestibular [neuritis], implying a problem in just the external mechanism. And so in practice, because those sophisticated tests [for determining whether the disturbance is central or peripheral] cannot be done, it is frequently said to be an external vestibular neuritis, when in fact it is a symptom which is reflective of more encephalitis-like problems.

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<sup>42</sup> *See* 4/25/07 TR at 246-48, 314 (Dr. Bell testifying that a 1985 study by the Massachusetts Eye and Ear Infirmary concluded that "all of the patients with Chronic Fatigue Syndrome and vestibular symptoms have central disease and not peripheral disease."); 4/26/07 TR at 474, 478 (Dr. Oleske observing that the link between a hepatitis B vaccine, vestibular neuritis, and Chronic Fatigue Syndrome was noted by Dr. Fink's May 6, 2004 VAERS Report); *see also* 4/26/07 TR at 598 (Dr. Brenner agreeing that Chronic Fatigue Syndrome patients usually display vestibular problems in the central nervous system).

9/29/10 TR at 1133.

Dr. Bell also offered un rebutted testimony that it is extremely difficult to test whether vestibular problems are central or peripheral, because of the physical requirements that must be in place in the testing facility. 4/25/07 TR at 248. Moreover, Dr. Bell's testimony that a diagnosis of vestibular neuritis is consistent with a logical sequence of cause and effect was based on his experience treating thousands of patients suffering from Chronic Fatigue Syndrome.<sup>43</sup> 4/25/07 TR at 247.

Dr. Wientzen raised a last issue requiring comment, *i.e.*, in cases of vestibular neuritis, it is "routine for there to be a preceding viral illness." 4/26/07 TR at 646. As Ilya's medical records indicate, he experienced a number of viral infections prior to November 5, 2001. None of these infections, including the Epstein-Barr virus episode, was followed by a diagnosis of vestibular neuritis, until after Ilya had a fourth, and unnecessary, hepatitis B vaccination.

The United States Court of Appeals for the Federal Circuit has stated that "reversible error is extremely difficult to demonstrate if the special master has considered the relevant evidence of record, drawn plausible inferences and articulated a rational basis for the decision." *Lampe v. Sec'y of Health & Human Servs.*, 219 F.3d 1357, 1360 (Fed. Cir. 2000) (internal quotation marks omitted). Where a special master does not consider highly relevant evidence, such as a VAERS Report submitted by the primary treating physician, and fails to draw plausible inferences in favor of the Petitioners from unchallenged medical records and supporting medical opinion, the United States Court of Federal Claims has been authorized by Congress to correct such errors. *See* 42 U.S.C. § 300aa-12(e)(2)(B) (the United States Court of Federal Claims may set aside the decision of a special master if findings of fact or conclusions of law are found to be "arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law.").

The court has determined that the Special Master erred in finding that Petitioners failed to meet their burden of proof regarding the second element of *Althen*. In addition, the court has determined that, as a matter of law, Petitioners have established through medical records and medical opinion a logical sequence of cause and effect showing that a fourth, and unnecessary, hepatitis B vaccine was the reason for Petitioner's Chronic Fatigue Syndrome. *See Althen*, 418 F.3d at 1278.

#### IV. CONCLUSION.

For the reasons stated herein, the Special Master's October 27, 2010 Entitlement Decision is reversed, vacated, and replaced by the court's own findings of fact and conclusions of law. Based on the totality of the record, the court has determined that entitlement has been established as to all three elements of *Althen*. Accordingly, this case is remanded for a

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<sup>43</sup> Although Dr. Brenner has also seen thousands of patients with Chronic Fatigue Syndrome, it was in his capacity as a rheumatologist. 4/26/07 TR at 555-58. Dr. Bell, however, served as Chairman of the Department of Health and Human Services Advisory Committee For Chronic Fatigue Syndrome and is the only expert witness who was admitted as an expert in the field of Chronic Fatigue Syndrome. 4/25/07 TR at 231-35. In addition, Dr. Brenner has never examined children who suffer from Chronic Fatigue Syndrome. 4/26/07 TR at 585.

determination by the Special Master of the compensation due to Petitioners. In accord with 42 U.S.C. § 300aa-12(e)(2), the court allows the maximum permissible time, 90 days, for the completion of these additional proceedings on remand.

**IT IS SO ORDERED.**

s/Susan G. Braden  
**SUSAN G. BRADEN**  
**Judge**