In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 04-1528V

(E-Filed: December 8, 2009; Re-issued for Publication: December 9, 2009)

SARAH FREEMAN Petitioner, v. SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, Respondent.	TO BE PUBLISHED Respondent's Motion for Judgment on the Record; Hepatitis B Vaccine Series; Alleged Injury of Systemic Lupus Erythematosus; Rashes Consistent with Positive Rechallenge Reactions

Ron Homer, Boston, MA, for petitioner.

Katherine Esposito, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

[1] Because this Ruling contains a reasoned explanation for the special master's action in this case, the special master intends to post this order on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, 116 Stat. 2899, 2913 (Dec. 17, 2002).

Vaccine Rule 18(b) states that all of the decisions of the special masters will be made available to the public unless an issued decision contains trade secrets or commercial or financial information that is privileged or confidential, or the decision contains medical or similar information the disclosure of which clearly would constitute an unwarranted invasion of privacy. When a special master files a decision or substantive order with the Clerk of the Court, each party has 14 days within which to identify and move for the redaction of privileged or confidential information before the document's public disclosure.

On October 7, 2004, Wendy Freeman, filed a petition pursuant to the National Vaccine Injury Compensation Program[2] (Vaccine Program or Program) seeking compensation for rheumatological injuries sustained by her then-minor daughter, Sarah Freeman (Sarah) as a result of the hepatitis B vaccination that she received on October 17, 2001. Petition at 1. After reaching the age of majority, Sarah moved to amend the case caption. See Petitioner's Motion to Amend the Caption. The undersigned granted the motion to amend, and Sarah is now the petitioner in this case.

As petitioner, Sarah relies on a theory of causation in fact to establish her vaccine claim. In particular, she asserts that the hepatitis B vaccination she received in October of 2001 caused her rheumatological injury. In support of her theory of causation, Sarah filed: (1) an affidavit from her mother; (2) her medical records[3]; (3) the expert opinion of Robert Sundel, MD., a rheumatologist; (4) supporting medical literature and (5) a joint stipulation of facts.

For a period of time, the parties engaged in settlement discussions. The parties were not able to resolve the matter, and the case was scheduled for a hearing in Boston, Massachusetts on August 7, 2009. After the conduct of the pre-hearing conference, respondent's counsel requested a cancellation of the hearing and moved for a ruling on the record. See Respondent's Motion for Ruling on the Record and Motion to Cancel the Hearing filed on July 23, 2009 (R's Motion for Ruling). As respondent's counsel noted in the motion, the undersigned had indicated during the pre-hearing conference that she "[was] very interested in respondent's defense [of] [the] case," because "it appear[ed] to the undersigned that petitioner [was] likely to prevail on her claim." R's Motion for Ruling at 1.

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[2] The National Vaccine Injury Compensation Program is set forth in Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. § 300aa-10 et seq. (2006) (Vaccine Act or the Act). All citations in this Ruling to individual sections of the Vaccine Act are to 42 U.S.C. § 300aa.

[3] In addition to the petition, petitioner's counsel filed the following records in support of petitioner's claim: (1) medical records from Victor Valley Dermatology, see Petitioner's Exhibit (P's Ex.) 1; (2) medical records from Weed Army Community Hospital in California, see P's Exs. 2 and 10; (3) medical records from Children's Hospital & Health Center; see P's Exs. 3 and 9; (4) medical records from Retina Consultants of Southern California; see P's Ex. 4; (5) medical records from Mukeshm Patel, M.D., see P's Ex. 5; (6) medical records from Excelsior Education Center, see P's Ex. 6; (7) medical records from Department of Air Force - Pediatric Clinic; see P's Exs. 11 and 14; (8) medical records from National Archives and Records Administration; see P's Exs. 12 and 13; and (9) medical records from Arizona Arthritis & Rheumatology Associates; see P's Ex. 15, 18, 19 and 20.

During the conduct of the status conference and in the July 22, 2009 Order (7/22/09 Order) issued by the undersigned memorializing the discussion during the status conference, the undersigned identified the key factors that appeared to militate in petitioner's favor. See 7/22/09 Order at 2. First, petitioner's treaters have diagnosed her with a lupus-like illness. Second, the parties have stipulated that petitioner developed a rash after each of her received hepatitis B vaccinations. And third, respondent's expert does not dispute that rashes are characteristic of the lupus-type rashes. The undersigned observed that the nature of petitioner's reactions is suggestive evidence of a positive rechallenge. See id. The undersigned observed in her order that as recognized by the Institute of Medicine, the occurrence of an adverse event on rechallenge has "a major impact on the causality assessment." See id. quoting 1994 IOM Report, Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality, at 26, 89.

The undersigned also observed that she found the facts in this case even more supportive of a finding of vaccine-related causation than the facts in the case of Williams v. Sec'y of HHS, 2007 WL 2775190 (Sept. 11, 2007). In the Williams case, the Special Master found that petitioner was entitled to compensation following the administration of the first hepatitis B vaccination and the subsequent development of petitioner's systemic lupus erythematosus (SLE) based in part on petitioner's prior military service in parts of the world where he may have been exposed to the hepatitis B virus. Here, the record indicates that petitioner received a series of three hepatitis B vaccinations and after each vaccination developed the type of rash that occurs in lupus patients.

After cancelling the hearing, the undersigned held a status conference on August 25, 2009. The undersigned encouraged the parties to continue their earlier work on a damages determination while awaiting the issuance of the entitlement ruling because she "anticipated a ruling finding that petitioner's received hepatitis B vaccinations led either to her subsequent development of or to the significant aggravation of her SLE." See August 26, 2009 Order (8/26/09 Order) at 2. The undersigned issued an order indicating that the motion for ruling on the record was under active consideration. See 8/26/09 Order.

Respondent's motion for a decision on the record is now ripe for decision.

I. Factual Background

The parties do not dispute the underlying facts in this case and filed a Joint Stipulation of Facts (Joint Stipulation) on May 7, 2008. The parties have stipulated that Sarah suffered intermittent hives for a period of approximately two weeks following each of her three hepatitis B vaccines. See Joint Stipulation at 1-2. In addition, the parties

have stipulated that a few weeks after the administration of her third hepatitis B vaccine, Sarah began to experience pain in the upper part of her legs that worsened over the following months. See id. at 2.

A. Pre-Vaccination Medical History

Sarah was born on February 26, 1989. Affidavit of Wendy Freeman (Affidavit) at 1. According to her mother's affidavit, Sarah was "extremely healthy all through her early childhood" and "often received recognition for perfect attendance at school." Id. Sarah had chickenpox when she was three years old. P's Ex. 10 at 13. An avid golfer, Sarah played regularly. Her medical history prior to her receipt of the hepatitis B vaccination series is notable only for the appearance of a rash on her right lower leg and left knee pain prior to her receipt of the hepatitis B vaccination series. Petitioner's Exhibit (P's Ex.) 2, 19-21; Affidavit at 1.

B. Receipt of the Vaccinations at Issue

On February 22, 2001, at age twelve, Sarah received her first hepatitis B vaccination. Joint Stipulation at 1. Id. Mrs. Freeman stated in her affidavit that at the same time that Sarah received her first hepatitis B vaccine, she was treated for a sore knee and given ibuprofen for pain relief. See Affidavit at 2. As stipulated, Sarah developed hives after the vaccination that appeared intermittently over a two week period of time. Mrs. Freeman initially associated the development of Sarah's hives with an allergic response to the pain medication.

On April 20, 2001, Sarah received her second hepatitis B vaccination and a tetanus booster. Id. at 2. Following her receipt of the second hepatitis vaccine, Sarah again broke out in hives that appeared on and off for about two weeks. See id.

Four months later, on July 1, 2001, Sarah was examined for a vesicular rash that extended from the right of her sternum to her back and that appeared to be spreading. P's Ex. 2 at 17. The rash was described as burning, sore, nonpruiritic, and accompanied by a fever. Id. Sarah's mother stated that Sarah had developed a similar rash in the same area three years prior but had not sought medical attention for it. Id. Sarah's mother also suggested that the rash could have been due to an allergic reaction to something used while at the beach, but Sarah denied using any new products. Id. Sarah was diagnosed as having herpes zoster and was treated with Zovirax, an antiviral drug, and Motrin for pain relief. Id.

On October 17, 2001, Sarah received her third hepatitis B vaccine. Id. at 3.

Following the third administration of the hepatitis B vaccine, Sarah again developed hives and then developed "pain in her upper legs a few weeks later, which grew increasingly worse over the following months." See id. Mrs. Freeman described Sarah as going from "a girl who could carry a 30-pound set of golf clubs quite easily for 18 holes to one who could not even walk across the room without grimacing." See id. at 3.

C. Seeking Medical Treatment

The record contains no documented medical consultations from the date of the third vaccination on October 17, 2001, until February 13, 2003, when Sarah saw Dr. Mitchell Howo at the Weed Army Community Hospital in California, for bilateral leg pain and arm soreness. P's Ex. 2 at 14. During the visit with Dr. Howo in February 2003, Sarah reported pain in her thighs that she had endured over the course of nine months. Id. The pain lessened with prolonged sitting but returned when she stood up, and it resolved with walking. Id. Dr. Howo noted that Sarah's examination was normal except for the presence of tight hamstrings. Id. Dr. Howo noted that Sarah's complete blood count ("CBC") was normal, and that her erythrocyte sedimentation rate ("ESR") was elevated.[4] Id. Dr. Howo diagnosed Sarah as having a bilateral thigh musculoskeletal strain and recommended that she take Motrin for pain. Id.

Sarah returned to Dr. Howo on May 15, 2003, nearly three weeks later, complaining of leg and calf pain and lumps in her wrists. P's Ex. 2 at 12. Dr. Howo noted that Sarah had no joint pain. However, an examination showed tenderness in her bicep tendons. Id. Dr. Howo's impression was that Sarah's thigh pain was due to overuse and that the tendonitis in her wrists was due to her golfing. Id. Dr. Howo recommended a stretching program and Motrin for pain. Id. A repeat of lab testing showed an elevated ESR, a positive antinuclear antibody ("ANA") test,[5] and low hemoglobin. P's Ex. 11 at 13-16, 23. Sarah's rheumatoid factor was reported as

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[4] Erythrocyte Sedimentation Rate (ESR) is a measurement of the rate at which the red blood cells (RBCs) settle in saline solution or plasma over a specified time period. It is a nonspecific test and therefore not diagnostic for any particular injury. However, because inflammatory diseases increase the protein content of the plasma, RBCs tend to stack up on one another, increasing their weight and causing them to descend faster. See Mosby's Manual of Diagnostic and Laboratory Tests at 233 (3d ed. 2006).

[5] Antinuclear Antibodies are used to diagnose SLE and other autoimmune diseases. Because almost all patients with SLE develop autoantibodies, a negative ANA excludes the diagnosis. If the ANA test is positive, other antibody studies must be done to corroborate the diagnosis. Mosby's at 91.

negative. P's Ex. 2 at 4-5.

A week later, on May 22, 2003, Sarah saw Dr. Howo for a follow-up visit. P's Ex. 2 at 10-11. Sarah reported that she had experienced thigh stiffness in the morning, knee pain with swelling particularly in the left knee, ankle swelling, and a transient rash over her arms and elbows over the past nine months. Id. at 11. Dr. Howo noted that while Sarah's pain was extreme, Motrin provided effective relief. Id. An examination revealed that Sarah was not able to fully extend her arms. Id. Dr. Howo's impression was that Sarah had "arthritis consistent with juvenile rheumatoid arthritis" and he referred Sarah to the pediatric rheumatology department. Id. In addition, Dr. Howo ordered a lyme titer, which returned normal results. Id. He repeated the ESR test, which returned increasingly elevated results, and he ordered an ankle x-ray, which was unremarkable. Id.

Although contemporaneous medical records are lacking for the period of time from October 2001 through February 2003, Sarah's mother, Wendy Freeman, stated in her affidavit that she attributed Sarah's symptoms to the fact that "she was having a hard time with puberty." See Wendy Freeman's Affidavit (Affidavit). Mrs. Freeman's statements are supported by medical records that were created after February 2003 and prior to the filing of this suit. See P's Ex. 10 at 13 (indicating that Sarah's symptoms of pain and swelling worsened after the onset of her menstrual period).

D. Establishing a Diagnosis

On referral from Dr. Howo, Sarah consulted with Dr. Robert Sheets, a rheumatologist, on May 30, 2003. P's Ex. 3 at 4-5. Dr. Sheets noted that Sarah's joint symptoms, specifically her knee and thigh pain, had begun eight months earlier and that at the time of the consult, Sarah reported having difficulty going up stairs, swinging a golf club, bending down, and getting up from chairs. Id. at 4. Dr. Sheets' physical examination of Sarah revealed pain in her wrist, elbow, and knee, a rash over the knee and elbow, an urticarial rash on the thighs, and difficulty raising her arms overhead. Id. at 4. Dr. Sheets expressed the view that Sarah suffered from "some fluctuating arthritis with dermatitis." Id. He noted that the location of the dermatitis was atypical of a reaction to Motrin but the timing of onset would not preclude such a conclusion. Id. Dr. Sheets attributed Sarah's symptoms to either dermatomyositis, juvenile rheumatoid arthritis, lupus, or mixed connective tissue disease, all of which are autoimmune diseases. Id. Dr. Sheets ordered a comprehensive metabolic panel,[6] and directed Sarah to discontinue her

[6] The lab results from the ordered metabolic panel showed an elevated level of aldolase, a positive ANA with homogenous pattern, a positive anti-DNA antibody titer, normal creatine phosphokinase ("CPK"), and elevated C-reactive protein. Id. at 1.

use of Motrin and to see an ophthalmologist.[7] Id.

During a conference call between Dr. Sheets and Dr. Howo on June 4, 2003, Dr. Sheets recommended that Sarah start a course of Plaquenil[8] because she showed three symptoms consistent with lupus that could be indicative of "lupus in slow evolution."[9] P's Ex. 3 at 1. Dr. Sheets noted that Sarah's mother "felt that the diagnosis [of lupus in slow evolution] was much more likely than [a] reaction to a hepatitis B vaccine, and the herpes zoster infection that she had, both of which preceded the onset of these symptoms."[10] Id. Mrs. Freeman raised the possibility of Sarah's symptoms being caused by the hepatitis B vaccine, and Dr. Sheets noted that Mrs. Freeman had visited an online discussion board for parents who had noticed the onset of rheumatological symptoms in their children after receiving the hepatitis B vaccine. Id. As reflected in the medical records, Dr. Sheets expressed to both Dr. Howo and Sarah's mother that he was not persuaded that Sarah's symptoms were brought about by an adverse reaction to the hepatitis B vaccine. He explained:

> Given the fact that her hepatitis B vaccine was six months prior to the onset of any symptoms, this would seem to be not causative of any of her current symptoms. We do see patients who have incomplete criteria for lupus that have what we sometimes call lupus-like disease which is what I explained to Mrs. Freeman, and that over time most of the patients go on to develop full criteria for lupus, and we follow them on a monthly basis or sometimes

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[7] A June 3, 2003 ophthalmology exam showed no abnormalities. P's Ex. 4 at 1-2.

[8] Plaquenil is "used, usually with other medications, to treat certain auto-immune diseases (lupus, rheumatoid arthritis) when other medications have not worked or cannot be used. . . . It can reduce skin problems in lupus and prevent swelling/pain in arthritis, though it is not known exactly how the drug works." See http://www.webmd.com/drugs/drug-6986-Plaquenil+Oral.aspx?drugid=6986&drugname=Plaquenil+Oral.

[9] Dr. Sheets stated in his report of June 4, 2003, that for a diagnosis of lupus, a person must have symptoms representing four out of eleven documented symptoms. Sarah's slightly positive ANA and DNA antibodies, along with her arthritis, are considered three symptoms of lupus. Dr. Sheets notes that the presence of a clear-cut rash would be an additional criteria, to confirm a diagnosis of lupus. P's Ex. 3 at 1.

[10] Respondent's Rule 4 Report characterizes this medical records differently stating that Sarah's mother disagreed with Dr. Sheets' opinion because it was "her belief that Sarah's symptoms were a reaction to a previous hepatitis B vaccine and herpes zoster infection." Id.

> every six weeks. Much less commonly, the symptoms and laboratory findings do resolve and what appears to be evolution of a lupus-like disease disappears. We have clearly seen this in patients who have not had hepatitis B vaccine.

P's Ex. 3 at 1-2. Implied in Dr. Sheets' notes is his belief that Sarah's joint pain represented the onset of her lupus-like symptoms.

Dr. Sheets saw Sarah for a follow-up visit two weeks later, on June 17, 2003. P's Ex. 9 at 1. He noted that Sarah's pain had decreased, that she was able to play golf, and that she was no longer experiencing difficulty with stairs. P's Ex. 9 at 1. A physical exam revealed some weakness in her legs. Id. Dr. Sheets attributed that weakness to her arthritis pain. Id. at 2. The sustained urticarial rash on Sarah's thighs and forearms was believed to be residual from an allergic reaction to Motrin. This proposed diagnosis appeared to be corroborated by Mrs. Freeman, who recalled that Sarah had reacted similarly to Advil in the past. P's Ex. 9 at 2. Dr. Sheets recommended that Sarah see a dermatologist to biopsy her lesions to determine whether the lesions were consistent with urticarial lesions or evanescent urticarial vasculitic lesions.[11] P's Ex. 9 at 3. Dr. Sheets further observed that an ophthalmologist would screen Sarah for uvetis, an inflammatory eye condition that, if present, would be consistent with lupus.[12] Id. Dr. Sheets maintained his diagnosis of arthritis attributable either to evolving lupus, juvenile rheumatoid arthritis or some sort of immune complex vasculitic disease. He recommended additional testing and encouraged Sarah to continue taking Naprosyn.[13] Id.

Subsequently, Sarah visited Dr. Buell of the Air Force Pediatric Clinic on August 6, 2004, for cold symptoms. P's Ex. 11 at 6-7. Sarah's mother reported to Dr. Buell that Sarah had an autoimmune disease as a result of a hepatitis B vaccination that flares up

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[11] On December 7, 2006, petitioner's counsel filed Petitioner's Response to Respondent's Request for Additional Information (P's Response to R's Request) and indicated that Sarah received no additional treatment from a dermatologist and therefore no additional information is available with respect to the nature of her rash. P's Response to R's Request at 2.

[12] Ophthalmology appointments on June 30, 2003, and July 3, 2003, resulted in no findings consistent with lupus. P's Ex. 10 at 6-8; P's Ex. 11 at 20.

[13] Naprosyn is a nonsteroidal anti-inflammatory drug. Naprosyn works by reducing hormones that cause inflammation and pain in the body. See http://www.drugs.com/naprosyn.html. When Dr. Sheets examined Sarah at her May 30, 2003 visit, he discontinued Sarah's use of Motrin because of the timing of the appearance of her "urticarial-appearing rash" and started her on Naprosyn. See P's Ex. 9 at 3.

every six months. P's Ex. 11 at 6. Dr. Buell opined that Sarah may have immune thrombocytopenia purpura[14] ("ITP") secondary to a viral illness. P's Ex. 11 at 6. Lab work indicated that Sarah had mononucleosis and an Epstein-Barr virus ("EBV") infection. Id. at 10. Rest, fluids, Tylenol, and the continuation of Naprosyn were the recommended treatments, and Sarah was referred to a rheumatologist for further evaluations of her "lupus like syndrome."[15] P's Ex. 11 at 15.

As reflected in Sarah's medical records from early 2005 and onward, her treating physicians consistently documented that she had a diagnosis of a lupus-type disorder. A sports participation physical dated February 2, 2005, from the Air Force Pediatric Care Center at Luke Air Force Base in Arizona, indicated that while Sarah had been asymptomatic for six months, she had a "lupus-like autoimmune syndrome" that "mom thinks related to immunization." P's Ex. 11 at 4.

Nearly one year later, on February 17, 2006, Sarah was again evaluated for a sports participation physical at the Air Force Pediatric Care Center by Ronald Gosnell, M.D. P's Ex. 11 at 2-3. Dr. Gosnell's report from that evaluation states that Sarah had suffered from lupus-like symptoms two to three years earlier and that her present examination was normal except for a persistent hypopigmented patch on her face and neck for which she was referred to dermatology. P's Ex. 11 at 2-3.

On May 3, 2007, Dr. Gosnell again evaluated petitioner. The notes from this visit reflect that Sarah was "diagnosed with Lupus-like syndrome due to Hep B and JRA a few years ago (medical records incomplete)." P's Ex. 14 at 2. Under the Assessment and Plans section of this visit, Dr. Gosnell wrote systemic lupus erythematosus and referred Sarah to John Tesser, a rheumatologist at Arizona Arthritis and Rheumatology. Id. at 4.

On May 15, 2007, Sarah was evaluated by Dr. Tesser, and his assessment was that her urticaria was more suggestive of lupus than rheumatoid arthritis. He suggested that she begin a course of Plaquenil because it is indicated for both lupus and rheumatoid arthritis. P's Ex. 14 at 6. After various tests were completed, Dr. Tesser diagnosed Sarah

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[14] Immune thrombocytopenic purpura (ITP) is a "blood disorder characterized by the destruction of blood platelets due to the presence of antiplatelet autoantibodies." See http://www.medterms.com/script/main/art.asp?articlekey=24151. ITP can be triggered by drugs, or associated with infection, pregnancy, or immune disorders such as systemic lupus erythematosus. See id.

[15] Sarah's mother declined to have her examined by a rheumatologist and therefore no records are available from this consult. See P's Response to R's Request at 2.

with probable SLE, vitiligo, and urticaria. See P's Ex 14 at 7. His patient report states that he had a lengthy discussion with Sarah and her mother regarding autoimmunity (specifically SLE) and that he addressed disease manifestations, treatment options that included Plaquenil, and his recommendations for surveillance of Sarah's condition. See id. at 8.

Dr. Tesser examined Sarah again for her SLE in June 2007 and May 2008. See P's Ex. 18 at 14-16. During his subsequent examination of Sarah on June 10, 2008, Dr. Tesser noted that she was taking over-the-counter Aleve but that she was considering a trial of Plaquenil. See P's Ex. 18 at 10. At the time of this evaluation, her disease course was described as moderate, and Sarah's presentation of symptoms included swollen hands, shortness of breath on exertion and arthralgia. See P's Ex. 18 at 10.

The pivotal issue in this case is whether petitioner's SLE was caused by or significantly aggravated by the hepatitis B vaccine series administered between February 22, 2001, and October 17, 2001.

II. Legal Standards

The Vaccine Injury Table lists certain injuries and conditions that if found to occur within a prescribed time period create a rebuttable presumption of causation between the administered vaccine and the injury or medical condition alleged by a petitioner. 42 U.S.C. § 300aa-14(a). Because rheumatological injuries in general, and SLE in particular, are not included among the injuries and conditions listed on the Vaccine Injury Table, this is not a Table Injury case, and no presumption of vaccine causation attaches to petitioner's claim. Rather, petitioner must prove causation in fact. See id.

To establish entitlement to Program compensation in this case, petitioner must prove, by a preponderance of the evidence, that the hepatitis B vaccination series that she received either caused or significantly aggravated her SLE. See 42 U.S.C. § 300aa-13(a)(1)(A). To satisfy the burden of proving causation in this off-Table case, petitioner must show that "the vaccination brought about her 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 the vaccination and the injury." Althen v. Sec'y of Health and Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005). To satisfy the burden of proving significant aggravation in an off-Table case, a petitioner must satisfy the Althen requirements and must establish, consistent with 42 U.S.C. § 300aa-33(4) that the injury was "a change for the worse in a preexisting condition which result[ed] in markedly greater disability, pain, or illness accompanied by substantial deterioration of

health. See also Shalala v. Whitecotton, 514 U.S. 268, 272 (1995); Loving v. Sec'y of Health and Human Servs., 86 Fed. Cl. 135, 144 (2009) (setting forth six elements of proof for significant aggravation claims, three of which mirror the language of 42 U.S.C. § 300aa-33(4) and the other three of which reflect the Althen standard).

After issuing its decision in Althen, the Federal Circuit issued a decision in Capizzano v. Secretary of Health and Human Services, 440 F.3d 1317 (Fed. Cir. 2006), denouncing the requirement of "either epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect." Id. at 1325. The Federal Circuit found such approach to be "inconsistent with allowing 'the use of circumstantial evidence envisioned by the preponderance standard.'" Id. (citing Althen, 418 F.3d at 1280).

The Federal Circuit's decisions in Althen and Capizzano instruct that a petitioner need not produce particular types of evidence to satisfy her burden of proof. The decisions do not preclude, however, courts from considering medical literature when evaluating expert testimony. As informed by the Supreme Court in Daubert, whether a theory or technique has been subjected to peer review and publication is a "pertinent consideration." 509 U.S. at 593. Accordingly, to establish eligibility for compensation, petitioner must support her theory of causation with a "sound and reliable medical or scientific explanation." Knudsen, 35 F.3d at 548; see also Grant, 956 F.2d at 1148 ("A reputable medical or scientific explanation must support this logical sequence of cause and effect.").

Under the Act, petitioner's showing of entitlement is rebuttable. If petitioner's injury can be shown to be "due to factors unrelated to the administration of the vaccine described in the petition," see 42 U.S.C. § 300aa-13(a)(1)(B), petitioner's claim must fail.

At present, the jurisprudence suggests that the party bearing the burden of eliminating others possible causes for the sustained injury may turn on whether petitioner has presented sufficient evidence of causation to establish a prima facie case. In Pafford, the Federal Circuit observed that as a practical matter, a petitioner may be required to eliminate potential alternate causes where the petitioner's other evidence on causation is insufficient. See Pafford, 451 F.3d at 1359; see also Althen, 418 F.3d at 1281 (stating that a claimant under the Vaccine Program bears the burden of eliminating other causes for the suffered injury).

But the Federal Circuit assigned the burden differently in Walther v. Sec'y of Health and Human Servs., 485 F.3d 1146, 1150 (Fed. Cir. 2007). In Walther, the Federal

Circuit stated that the burden of proving alternative causation rests with respondent. Walther, 485 F.3d at 1150; see also Althen, 418 F.3d at 1278 (stating that the government bears the burden of establishing causation of the injury by factors unrelated to the vaccine); Knudsen v. Sec'y of Health and Human Servs., 35 F.3d 543, 547 (Fed. Cir. 1994) (citing Whitecotton v. Sec'y of Health and Human Servs., 17 F.3d 374, 376 (Fed. Cir. 1994), rev'd on other grounds sub nom., Shalala v. Whitecotton, 514 U.S. 268 (1995)). Respondent bears the burden of proving alternative causation by preponderant evidence, and respondent establishes alternative causation (a factor unrelated to the administration of the vaccination) by satisfying the Althen factors, specifically, a medical theory of causal connection, a logical sequence of cause and effect, and a proximate temporal relationship between the asserted injury and a factor unrelated to the received vaccination. See Walther, 485 F.3d at 1151; Althen, 418 F.3d at 1278; Knudsen, 35 F.3d at 547; Whitecotton, 17 F.3d at 376.

If petitioner fails to establish their prima facie case, however, the issue of alternate causation need not be reached.

III. Case Analysis

The parties have filed a joint stipulation of facts in this case, and the parties' medical experts agree that Sarah has a diagnosis of SLE. The parties' respective experts do not agree, however, on what caused Sarah to develop SLE.

In support of her causation claim, Sarah offered the opinion of Dr. Robert Sundel, a pediatric rheumatologist. Dr. Sundel graduated from Boston University, and then received training in pediatrics at the Columbia-Presbyterian Medical Center in New York. P's Ex. 17 at 2. Currently, Dr. Sundel is an associate professor of pediatrics at Harvard Medical School. Id.

Challenging the opinion offered by Dr. Sundel, respondent offered the opinion of Dr. Lawrence Kagen, a rheumatologist. Dr. Kagen obtained his undergraduate degree from New York University and then attended medical school at the New York University School of Medicine, and he is a professor of medicine at Cornell University Medical College in New York. See R's Ex. B at 1.

The qualifications of the parties' experts are undisputed.

1. Petitioner's Expert Opinion

Based on his review of petitioner's medical records, Dr. Sundel offered a medical

theory causally connecting the hepatitis B vaccination series that petitioner received to her claimed injury of SLE. In the view of Dr. Sundel, Sarah's condition "primarily manifested as polyarthritis, the symptoms of which first appeared several weeks after her third hepatitis vaccine." P's Ex. 16 at 2. Dr. Sundel stated that "the first manifestations of [Sarah's] condition were hives" that appeared after "each of the three hepatitis B vaccinations she received." He added that joint pains developed after the third dose of the hepatitis B vaccine. P's Ex. 16 at 2.

Dr. Sundel noted in his opinion that the "[d]evelopment of arthritis is well recognized following vaccination against hepatitis B." Id. In support of his opinion, Dr. Sundel observed that "[b]iologic plausibility, a tight temporal relationship, suggestive statistical and epidemiologic analyses, and plentiful case reports, have supported [the finding of] a causal link between the hepatitis vaccine and subsequent development of arthritis." Id.

Asserting that "Sarah clearly developed arthritis following her third hepatitis B vaccine," Dr. Sundel opined that, in the absence of another explanation for the development of her arthritis, Sarah's case at first glance "appears to have been another example of arthritis due to hepatitis B." Id. Dr. Sundel pointed out that although Sarah's initial symptoms did not meet the diagnostic criteria for SLE, "her arthritis had features of this systemic autoimmune condition from the time of her initial immunologic evaluation (including the characteristic ANA and anti-dsDNA autoantibodies)." Id. In retrospect, Dr. Sundel commented that there can be no doubt that Sarah's arthritis was but one manifestation of her SLE. See id.

Dr. Sundel identified as the determinative issue in this case the question of "whether Sarah's SLE was caused by the hepatitis vaccine." Id. He contended that "[e]ither the vaccine triggered an autoimmune reaction [that] initially manifested as arthritis, and then evolved into lupus, or Sarah's current case of SLE is actually independent of, and unrelated to, her early hepatitis B-associated arthritis." Id. at 3. While acknowledging that the propensity for the "hepatitis B vaccine to cause systemic lupus erythematosus has been less clearly demonstrated than has its ability to cause arthritis," he argued that the former interpretation of events–specifically that Sarah had an autoimmune reaction that resulted in the development of her lupus-like condition–is "far more reasonable than the argument that Sarah developed two unrelated autoimmune diseases before her [nineteenth] birthday, one caused by the hepatitis vaccine ([her] arthritis) and one not ([her] SLE)." Id.

Dr. Sundel noted that "[i]nfection with wild-type hepatitis B is more likely to cause autoimmune diseases, including vasculitis and arthritis[] than is virtually any other

type of infection." P's Ex. 16 at 3 (citing Steven-Huy Han, Extrahepatic Manifestations of Chronic Hepatitis B, 8 Clin. Liver Dis. 403-418 (2004) filed as P's Ex. 16, Tab A). Dr. Sundel conceded that the biological mechanism by which hepatitis B virus triggers pathologic autoimmunity is not medically clear, but he identified the various theories that have been advanced, which include "molecular mimicry, stimulation of genetically susceptible hosts, or unusual characteristics of the antibody-antigen interactions incited by [the hepatitis B] virus." P's Ex. 16 at 3.

Dr. Sundel identified here Sarah's hives as the "first manifestations of [her] condition." Sarah's hives appeared after each administration of the vaccine. See id. The hives "were initially sporadic, becoming more persistent following the third injection." Id. Her receipt of the third hepatitis B vaccination was followed "within weeks, by the onset of joint complaints." Id. Dr. Sundel explained that

> the timing of the vaccination prior to Sarah Freeman's development of arthritis, the acknowledged causal link between hepatitis B vaccine and chronic arthritis, and the absence of alternative explanations for the development of the disease, all support the contention that the hepatitis B vaccine was the likely cause of Sarah Freeman's severe, debilitating arthritis. Accepting this, it strains credulity to propose that Sarah Freeman's arthritis was unrelated to her SLE. Rather, acknowledging the compelling evidence that Sarah's arthritis was caused by her hepatitis B vaccines leads inescapably to the conclusion that her current condition, SLE, was indeed the result of her hepatitis B vaccinations in 2001.

P's Ex. 16 at 4.

Dr. Sundel asserted that placing Sarah's development of SLE into proper statistical context makes the proposed sequence of vaccine-related events more likely than not. P's Ex. 16 at 3. Informed that childhood systemic lupus occurs in approximately 6 in 100,000 cases, with the majority of cases occurring in older adolescents, Dr. Sundel stated that the likelihood of Sarah spontaneously developing SLE at the age of 12 would be more on the order of 8 in 1,000,000, an even more rare and unlikely occurrence. P's Ex. 16 at 3.

For consideration in addition to the factors that Dr. Sundel recited in support of his opinion, the undersigned inquired about the significance of the appearance of a rash after each of petitioner's vaccinations. The parties stipulated to the appearance of the rashes and the undersigned questioned whether the reappearing rashes constituted evidence of a possible rechallenge reaction to the vaccinations by petitioner. The undersigned put the parties on notice prior to the scheduled hearing that she intended to consider the issue of

possible rechallenge in her evaluation of the evidence. See July 22, 2009 Order of the undersigned (identifying petitioner's rash after each of her received hepatitis B vaccinations as suggestive evidence of a positive rechallenge as factor that militated in petitioner's favor).

Following the issuance of the July 22, 2009 Order, respondent moved to cancel the hearing and requested a ruling on the record.

2. Respondent's Expert's Opinion

In opposition to petitioner's expert report, respondent filed the expert opinion of Lawrence J. Kagen, M.D, a rheumatologist, on January 25, 2008. See R's Ex. A. Dr. Kagen concurred with Sarah's diagnosis of systemic lupus erythematosus. But he asserted that the relationship of hepatitis B vaccines to her diagnosed condition was uncertain. R's Ex. A.

Dr. Kagen challenged petitioner's theory of causation on four grounds. First, petitioner's symptoms of joint pain began a considerable time after the completion of her immunization series. R's Ex. A at 4. Second, no scientifically controlled studies have been conducted linking SLE with hepatitis B vaccine administration. R's Ex. A at 4. Third, petitioner's knee pain may have predated her immunization series. Id. (referring to a note in the Sarah's medical records from February 22, 2001, which documents knee pain of one year's duration, which at the time was thought to be patellar tendonitis). Fourth, most cases of SLE occur without relation to immunization. Id.

In support of his position that Sarah's symptoms "began a considerable time after the immunization period was completed," R's Ex. A at 4, Dr. Kagen referred to a note from Dr. Sheets, one of Sarah's treating physicians, dated June 4, 2003. In that note, Dr. Sheets stated that "[g]iven the fact that [Sarah's] hepatitis B vaccine was six months prior to the onset of any symptoms [of joint pain], this would seem to not be causative of any of her current symptoms." Id. Dr. Kagen stated that "[j]oint pain, arthralgia is a typical feature of patients with SLE which may have a variable course, worsening or remitting in the absence of antigenic challenge." R's Ex. C at 7. Apparently informing the views both of Dr. Kagen and Dr. Sheets about whether Sarah's condition may have been vaccine-related was the delayed onset of Sarah's joint pain. Both Dr. Kagen and Dr. Sheets focused on Sarah's joint pain rather than her rashes as the symptom signaling the onset of her condition (or the possible worsening of a preexisting condition).

Supplementing Dr. Kagen's initial opinion with respect to the onset of Sarah's symptoms was an addendum from Dr. Kagen filed as Respondent's Exhibit C (R's Ex. C)

on May 8, 2008. In his filed Addendum, Dr. Kagen specifically addressed "the occurrence of [Sarah's] rash, hives, and joint pain, arthralgia." See R's Ex. C at 5. He noted that hives (also known as urticaria) can occur in patients with SLE "in the absence of known allergens, or antigenic challenge. This is thought to be due to immune dysregulation, which is a feature of this disorder." R's Ex. C at 5. Dr. Kagen stated that the frequency of hives in patients with SLE is reported in most studies to be between 4 and 7 percent.

Dr. Kagen identified a second form of hives known as urticarial vasculitis that can be distinguished by skin biopsy from the first type of hives that he described and that also occurs in patients with SLE. R's Ex. C at 5. Dr. Kagen reasoned that because Sarah's hives persisted during the course of her illness and recurred years after her immunizations, and because hives are noted in patients with SLE, in the absence of immunization or known exposure to allergens or antigenic challenge, he could not conclude either that Sarah's hives were related to her vaccinations, or that the appearance of the hives was attributable to Sarah's antigenic challenge with hepatitis B vaccine. Id. at 6.

Subsequently, in response to the undersigned's July 22, 2009 Order, inquiring whether additional testimony about the rashes that petitioner developed after each of her three hepatitis B immunizations would be necessary during the hearing to further inform Dr. Kagen's opinion, respondent's counsel filed a status report (R's SR) addressing the undersigned's "question concerning the nature and character of petitioner's rashes." R's SR at 1. Respondent stated that Dr. Kagen offered the following observations: "[t]he rashes reported in the medical record[s] of petitioner Freeman were described as recurrent transient hives and shingles. Both these skin manifestations occur in patients with systemic lupus erythematosus." Id. at 1.

The undersigned interprets Dr. Kagen's reply acknowledging that the recurring hives and shingles are characteristic symptoms that appear in lupus patients as a concession from respondent regarding the nature of the rash that petitioner developed after each of the hepatitis B vaccinations she received. And while Dr. Kagen has correctly observed that medical certainty does not obtain in this case, the Federal Circuit has made clear that proof of medical certainty is not required in Vaccine Proceedings. See Bunting v. Sec'y of Health and Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991).

IV. Evaluating the Claim

Petitioner's expert has offered an opinion of causation based on the filed medical

records, and on the stipulation of facts by the parties. The opinion of vaccine-related causation (or possibly even the significant aggravation of a preexisting condition)[16] is premised on the theory that an autoimmune process was set in motion by one of a variety of plausible biological mechanisms, that the autoimmune condition initially manifested as arthritis and evolved into a lupus-like condition (a proposed sequence of cause and effect that is logical), and that the appearance of Sarah's rashes occurred within a medically appropriate time frame for an autoimmune process.

The opinion of Dr. Sundel is bolstered by evidence suggesting that petitioner experienced the same positive rechallenge reaction after each of the received vaccinations. The IOM has determined on more than one occasion that rechallenge is strongly probative of a causal relationship. See Christopher P. Howson, et al., Institute of Medicine, Adverse Effects of Pertussis and Rubella Vaccines, 48 (1991) (hereinafter IOM 1991 Report) ("increasing severity of the event with increasing dose number would tend to support a causal interpretation"); Kathleen R. Stratton et al., Institute of Medicine, Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality, 21 ("causality is strengthened by evidence that the risk of occurrence of an outcome increases with higher doses or frequencies of exposure"). This guidance merits consideration by the undersigned here.

The parties stipulated early in these proceedings that Sarah experienced hives or a rash after each of the three administered hepatitis B vaccinations. Respondent's expert does not dispute the nature of petitioner's rashes. Thus, consistent with the guidance from the Institute of Medicine and with the circumstantial evidence present in this case, the undersigned is persuaded that the stipulated facts together with the record of this case support a finding of rechallenge, and that petitioner has satisfied her burden of proving entitlement to Program compensation.

As represented in Respondent's Status Report filed on November 30, 2009, the undersigned anticipates that respondent shall file a proffer **on or before Tuesday, December 22, 2009.**

IT IS SO ORDERED.

s/Patricia E. Campbell-Smith
Patricia E. Campbell-Smith
Special Master

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[16] If the noted rash and knee pain that preceded the receipt of petitioner's vaccination series were, in fact, symptoms of a developing condition, the record supports a finding that the symptoms became more severe and frequent after petitioner received the hepatitis B vaccination series.