OFFICE OF SPECIAL MASTERS
No. 99-594V
February 24, 2006
To be Published

* *
JANE STEVENS, *
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Petitioner, *
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v. *
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SECRETARY OF THE DEPARTMENT OF *
HEALTH AND HUMAN SERVICES, *
*
Respondent. *
* *

Ronald C. Homer, Sylvia Chin-Caplan, Boston, MA, for petitioner.
R. Lynn Harris, James A. Reistrup, III, Alexis B. Babcock, Washington, DC, for respondent.

MILLMAN, Special Master

DECISION[1]

On August 4, 1999, petitioner filed a petition on her own behalf for compensation under the National Childhood Vaccine Injury Act of 1986 (hereinafter the "Vaccine Act"), 42 U.S.C. §300aa-10 et seq., alleging that a hepatitis B vaccination she received on November 29, 1994 caused her transverse myelitis (hereinafter, "TM") and another hepatitis B vaccination she

[1] Vaccine Rule 18(b) states that all decisions of the special masters will be made available to the public unless they contain trade secrets or commercial or financial information that is privileged and confidential, or medical or similar information whose disclosure would clearly be an unwarranted invasion of privacy. When such a decision or designated substantive order is filed, petitioner has 14 days to identify and move to delete such information prior to the document's disclosure. If the special master, upon review, agrees that the identified material fits within the banned categories listed above, the special master shall delete such material from public access.

received on January 13, 1995 caused her to have worse symptoms of TM. In essence, this is a case of alleged challenge/rechallenge.

This case was assigned on the day it was filed to Chief Special Master Gary Golkiewicz and petitioner moved to suspend proceedings for a period of 120 days in order to provide documents and affidavits. Respondent filed a response on September 10, 1999 that petitioner file within 60 days a factual affidavit supporting her allegations. On October 6, 1999, the Chief Special Master granted petitioner's motion for a suspension for 60 days from the date of the Order. On February 3, 2000, petitioner filed a statement that the record was complete. On March 8, 2000, respondent filed a report in compliance with then-Vaccine Rule 4(b), contesting that hepatitis B vaccine can and did cause TM.

On July 13, 2000, petitioner moved for summary judgment which respondent opposed on August 31, 2000. Petitioner replied in opposition to respondent's opposition on October 10, 2000. On March 30, 2001, the Chief Special Master denied petitioner's motion for summary judgment, finding genuine issues of material fact, in a published Order. 2001 WL 387418. The Chief Special Master stated that petitioner must satisfy a five-prong test (henceforth known as "the Stevens test"): (1) medical plausibility; (2) confirmation of medical plausibility from the medical community and peer-reviewed medical literature; (3) proof of an injury that medical plausibility evidence and literature recognize; (4) a medically acceptable temporal relationship between vaccination and injury; and (5) elimination of other causes.[2]

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[2] The other special masters did not use or follow the Stevens five-prong test. For example, Special Master John Edwards refused to use the Stevens test in Malloy v. Secretary of HHHS, No. 99-0193V, 2003 WL 22424968, *16, n.9 (Fed. Cl. Spec. Mstr. Aug. 6, 2003), and discussed Stevens in the context of how other special masters may cope with the absence of epidemiologic evidence in Moberly v. Secretary of HHS, No. 98-01910V, 2005 WL 1793416,

The Federal Circuit in another case (Althen), affirming the U.S. Court of Federal Claims' reversal of the Chief Special Master's dismissal, subsequently held that prongs two and three of his Stevens test, requiring petitioner to provide objective confirmation in the form of peer-reviewed literature in support of a medically plausible theory linking the vaccination to petitioner's injury (prong two) and literature in support of the medical plausibility of petitioner's injury (prong three) were not in accordance with law. Althen v. Secretary of HHS, 418 F.3d 1274, 1279-80, 1281 (Fed. Cir. 2005). The Federal Circuit stated that the chief special master's other three prongs were a recitation of the Federal Circuit's well-established precedent. Althen, supra, at 1281.

In Althen, the Federal Circuit cited its 1994 opinion in Knudsen v. Secretary of HHS, 35 F.3d 543, 549 (Fed. Cir. 1994), stating that petitioners are not required to identify and prove specific biological mechanisms in order to prevail in a vaccine case. Althen, supra, at 1280. (In Knudsen, the Federal Circuit also stated that epidemiologic evidence, even if contrary to petitioner's allegations, did not determine if petitioner would prevail. In that case, petitioner

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*2, n.4 (Fed.Cl. Spec. Mstr. June 30, 2005), *remanded*, Moberly v. Secretary of HHS, No. 98-0910V, Order of the Judge (Fed. Cl., Dec. 27, 2005). In Doe v. Secretary of HHS, No. 99-670V, 2004 WL 3321302, *14, n.31 (Fed. Cl. Oct. 5, 2004), former Special Master Lavon French noted that although petitioner's counsel Clifford J. Shoemaker claimed he had fulfilled the Stevens test, the U.S. Court of Federal Claims per the Honorable Susan G. Braden had criticized the Stevens test in her decision in Althen. As the Honorable Emily C. Hewitt held in Guillory v. US, 59 Fed. Cl. 121, 124 (Fed. Cl. 2003), aff'd, 104 Fed. Appx. 712 (Fed. Cir. 2004)(mem.), "'Special masters are neither bound by their own decisions nor by cases from the Court of Federal Claims, except, of course, in the same case on remand.' *Hanlon v. Sec'y of Health & Human Servs.,* 40 Fed. Cl. 625, 630 (1998). Because ***Stevens*** was issued by Chief Special Master Golkiewicz the findings are not precedential and the special master was not bound by ***Stevens*** in deciding this case."

prevailed even though epidemiologic evidence was against petitioner's allegations. Knudsen, supra, at 550.)

Thus, the Federal Circuit has held in 1994 (Knudsen) and 2005 (Althen) that petitioners need not prove specific biological mechanisms, epidemiologic evidence, or objective confirmation from medical literature in order to prevail in this Program.

The Federal Circuit in Althen stated that Congress intended petitioners to be able to use circumstantial evidence in order to prove causation "in a field bereft of complete and direct proof of how vaccines affect the human body." Althen, supra, at 1280. The Federal Circuit reiterated what petitioners need to prove: (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 proximate temporal relationship between the vaccination and the injury. Althen, supra, at 1278, 1282. This is an iteration of the Federal Circuit's standard of proof in Grant v. Secretary, HHS, 956 F.2d 1144, 1148 (Fed. Cir. 1992), that petitioner must offer "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury. A reputable medical or scientific explanation must support this logical sequence of cause and effect."

On July 23, 2001, in the instant action, petitioner moved for an Omnibus Hearing on the issue of whether hepatitis B vaccination can cause various conditions. The Chief Special Master held a telephone conference on April 7, 2003 to discuss this Omnibus Hearing. The parties were working toward a November 2003 hearing date.

On May 7, 2003, the Chief Special Master reassigned the Hepatitis B - Neurological Demyelinating Omnibus Proceeding, of which this case was a paradigm case for TM (the other

three paradigm cases were for multiple sclerosis [MS], Guillain-Barre Syndrome [GBS], and chronic inflammatory demyelinating polyneuropathy [CIDP]), to former Special Master Margaret M. Sweeney.

On October 13, 14, and 15, 2004, former Special Master Sweeney held a hearing to determine whether hepatitis B vaccine can cause demyelinating diseases and, specifically, whether it caused the illnesses in four paradigm cases[3] in the Hepatitis B - Neurological Demyelinating Omnibus Proceeding.

On January 24, 2005, petitioners in Gilbert and Wederitsch moved for the production of documents (VAERS data). Respondent filed oppositions to petitioners' motions for production on February 25, 2005. On March 14, 2005, petitioners in Gilbert and Wederitsch filed responses to respondent's opposition. On May 3, 2005, former Special Master Sweeney issued an Order in Gilbert and Wederitsch directing the parties to explain their positions and the law more fully. Respondent filed his responses May 20, 2005. Petitioners filed their responses May 24, 2005. On June 6, 2005, former Special Master Sweeney issued Orders finding petitioners' responses to be insufficient. On November 10, 2005, former Special Master Sweeney issued a published, 20-page Order denying petitioners' motion for production. Gilbert v. Secretary of HHS, No. 04-455V, 2005 WL 3320085 (Fed. Cl. Spec. Mstr., Nov. 10, 2005), and Werderitsh, No. 99-319V, 2005 WL 3320041 (Fed. Cl. Spec. Mstr., Nov. 10, 2005).

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[3] This case (TM); Werderitsch v. Secretary of HHS, No. 99-638V (MS); Peugh v. Secretary of HHS, No. 99-319V (GBS); and Gilbert v. Secretary of HHS, No. 04-455V (CIDP). Initially, Cramer v. Secretary of HHS, No. 99-128V, was to be the CIDP case, but petitioner died. On July 19, 2004, petitioner's counsel informed former Special Master Sweeney that Gilbert would substitute as the paradigm case for CIDP.

On November 30, 2005, the parties filed their post-hearing briefs. The parties filed replies to their opponents' briefs on December 9, 2005. On December 14, 2005, former Special Master Sweeney was sworn in as a judge of the United States Court of Federal Claims.

On January 4, 2006, the Chief Special Master reassigned this case to the undersigned.

FACTS

Ms. Stevens was born on January 14, 1959. She received her first hepatitis B vaccination on November 19, 1994. Med. recs. at Ex. 2, p. 1. On December 10, 1994, Ms. Stevens saw Eric Klos, a chiropractor, for numbness, tingling, and difficulty writing. Med. recs. at Ex. 3, p. 1.

On December 13, 1994, Ms. Stevens saw Dr. Gerald Yorioka, complaining of tension in her neck for the past month and now tingling in her left arm and hand, and numbness in her right arm. For the past few days, this had been extending into her legs. She said she had received her first hepatitis B vaccination about two weeks before and wondered if the current symptoms were related to it. The most obvious symptom was her decreased ability to write. She was concerned because her symptoms were worsening. Med. recs. at Ex. 5, p. 1. She returned on December 16, 1994 with paresthesias in her arms and legs and a tightness across her abdomen. Med. recs. at Ex. 9, p. 76.

On December 19, 1994, Ms. Stevens returned to Dr. Yorioka in the same condition. Med. recs. at Ex. 5, p. 3. On January 4, 1995, she saw Dr. Yorioka with tingling sensations in her arms, left palm, and middle body. She thought her condition had improved in her legs and feet. She had some tightness in her neck. Med. recs. at Ex. 5, p. 4.

Ms. Stevens received her second hepatitis B vaccination on January 13, 1995. Med. recs. at Ex. 2, p. 1.

On January 25, 1995, she returned to Dr. Yorioka, stating her symptoms had increased in the prior three days and she was fatigued. He referred her to a neurologist. Med. recs. at Ex. 5, p. 4.

On February 8, 1995, Ms. Stevens saw Dr. Crispin S. Wilhelm, a neurologist. She stated that on December 8, 1994, nine days after the first hepatitis B vaccination on November 29, 1994, she had tingling in both arms and legs, and tightness and pain in her neck. She could not write and was clumsy. By the first of January 1995, she was considerably better with some residual palmar tingling. She received her second hepatitis B vaccination on January 13, 1995 but, on January 21, 1995, eight days later, she had a return of the same symptoms but they were worse: numbness and tingling in her legs, clumsiness in her right hand, trouble running, warm spots on her arms, painful jerking of her right arm, and a low energy level. She had no symptoms above the neck. Med. recs. at Ex. 2, p. 7.

On physical examination, Ms. Stevens had hypoactive reflects and a positive ANA of 1:40. Dr. Wilhelm's diagnosis was cervical myelopathy temporally related to the hepatitis B vaccine which occurred twice and which was hard to ignore. The level of the spinal lesion was C-6 or C-7. It was demyelinating (i.e., TM). He advised Ms. Stevens to avoid future hepatitis B vaccinations. Med. recs. at Ex. 2, p. 8.

Ms. Stevens returned to Dr. Wilhelm on February 16, 1995. Med. recs. at Ex. 4, p. 4. Her muscle spasms had nearly resolved but she still had significant pain in her left neck more than in her right. She did not have shooting pain in her right arm or any significant numbness. She still had tingling across her chest on down. She could write a little now, better than before, but could not hold a glass without dropping it. Her energy level was slightly better, but she got

markedly fatigued at times. She had mild impairment of fine movements in her right hand with 4+ distal strength. An MRI revealed semiconfluent areas of increased signal in her cervical spinal cord from C-3 to C-6, increased on T2 and enhanced with gadolinium. Dr. Wilhelm's diagnosis was probable TM. *Id.*

Ms. Stevens returned to Dr. Wilhelm on March 8, 1995. Med. recs. at Ex. 4, p. 5. She started to improve the prior week and could write and turn on her car ignition with her right hand and pull her seatbelt strap. She still had tingling in her arm, both sides of her trunk, and legs. Fine movements were more normal. Her spinal tap results showed normal protein and glucose although her IgG index was elevated. Dr. Wilhelm's impression was TM with evidence of demyelinating disease in the cerebrospinal fluid (CSF). Oligoclonal bands were present. *Id.*

Ms. Stevens saw Dr. Wilhelm on April 24, 1995. Med. recs. at Ex. 4, p. 6. She was gradually improving, walking better and better, with better use of her right hand, but with difficulty typing (she typed with two fingers) and writing. She had less tingling over her trunk with a tight feeling. She worked although she tired. Dr. Wilhelm's impression was improving TM following hepatitis B vaccine. There was no definite evidence of multiple sclerosis (MS) at this time although they did not image Ms. Stevens' brain. *Id.*

Ms. Stevens saw Dr. Wilhelm on December 18, 1995. Med. recs. at Ex. 4, p. 7. She had improving symptoms of TM but was still bothered by paresthesias, gait disturbance, fatigue, and right hand clumsiness. *Id.*

Ms. Stevens saw Dr. Wilhelm on February 15, 1996. Med. recs. at Ex. 4, p. 8. She had improving symptoms of myelopathy with some limitations of activity and walking and some residual paresthesias and fatigue. *Id.*

On May 24, 1996, Dr. Wilhelm wrote an Independent Medical Evaluation. Med. recs. at Ex. 4, pp. 9-10. He concluded that Ms. Stevens had stable symptoms of TM caused by two hepatitis B vaccinations administered on November 29, 1994 and January 13, 1995. Her condition was fixed and stable, i.e., she was neither improving nor deteriorating. She had residual symptoms of paresthesias from the mid-thoracic region on down and chronic fatigue and gait disturbance. *Id.* at 10.

On July 10, 1996, Dr. Reynold Karr, an allergist/immunologist, wrote a report in Ms. Stevens' workmen's compensation claim. Med. recs. at Ex. 9, pp. 19-23. Ms. Stevens' difficulty began exactly 10 days after receiving her first hepatitis B vaccination on November 29, 1994, beginning with tingling in her arms which became progressively more severe, extending to her legs and back over the next three days. *Id.* at 20. By early January 1995, her symptoms resolved except for persistent tingling in the palms of her hands. *Id.* On January 13, 1995, Ms. Stevens received her second hepatitis B vaccination. Exactly 10 days later, she had a return of the tingling, but her symptoms progressed rapidly. *Id.* Dr. Karr diagnosed post-hepatitis B vaccination reaction consisting of TM. *Id.* at 22.

On July 24, 1996, Dr. Eugene Wong, a neurologist, wrote his opinion in Ms. Stevens' workmen's compensation claim after examining her. Med. recs. at Ex. 9, pp. 9-17. Her main complaint was tingling. *Id.* at 9. Ms. Stevens had symptoms approximately 10 days after receiving hepatitis B vaccine on November 29, 1994, consisting of weakness of the right arm and right leg, as well as tingling below the level of her mid-chest and distal portions of her upper extremities. These symptoms improved and, by January 1995, she had resumed aerobics. She had residual tingling in her palms when she received her second hepatitis B vaccination on

January 13, 1995. Eight days later, she had a recurrence of similar symptoms but worse. She was much weaker and had difficulty walking, especially on stairs. She had spasms involving her right upper limb. *Id.* at 11.

Dr. Wong stated that Dr. Wilhelm had filled out an industrial injury form, indicating that his literature search had revealed previous cases of reports of myelitis following hepatitis B vaccinations with similar temporal profiles. *Id.* at 12. Dr. Wong concluded that Ms. Stevenson had two hepatitis B vaccinations probably "complicated" by TM. *Id.* at 15. He concurred "with Dr. Wilhelm's opinion that there has been a very distinct temporal relationship between the onset of Ms. Stevens' symptoms and the two hepatitis B vaccine injections." *Id.* He continued, "The differential diagnosis is multiple sclerosis, although her clinical picture does not have the temporal and anatomic dispersion which is characteristic for early manifestation of multiple sclerosis." *Id.* Ms. Stevens had reached maximum medical improvement. *Id.*

On October 10, 1996, Dr. Wilhelm wrote another Independent Medical Evaluation. Med. recs. at Ex. 4, pp. 12-13. He disagreed with a Category I rating of disability and opined that Ms. Stevens fit into a Category II rating of disability (permanent impairment). *Id.* at 13.

On December 19, 1996, The State of Washington, Department of Labor and Industries, awarded Ms. Stevens a workmen's compensation award of $6,107.64 for Category 2 disability (permanent dorso-lumbar and/or lumbosacral impairments). Med. recs. at Ex. 9, p. 2.

On February 18, 2004, Ms. Stevens saw Dr. Andrew Sohn, a rheumatologist, because of left knee inflammatory arthritis that began in early January 2004, although she has had occasional discomfort of the knees occasionally over the past few years. P. Ex. 32, p. 1

Dr. Sohn notes that Ms. Stevens has a history of TM and had seen Dr. Crispin Wilhelm, neurologist, previously, but the TM had been stable for a number of years. She has a numbing, tingling type of sensation in her hands which she attributed to the TM. *Id.* She also has chronic low back pains. *Id.* She teaches fourth and fifth grades special education. P. Ex. 32, p. 2. Dr. Sohn diagnosed inflammatory monoarthritis involving the left knee. *Id.*

Written Submissions

On November 8, 2001, petitioner filed the expert report of Dr. Derek R. Smith, a neurologist with a special interest in MS. Ex. 14. His curriculum vitae is Ex. 15. Attached to Ex. 14 are Tabs A through U consisting of medical articles to which Dr. Smith alludes in his report. He is a clinical instructor at Harvard Medical School, and an associate neurologist at Brigham and Women's Hospital in Boston. After reciting Ms. Stevens' history of neurologic symptoms following both hepatitis B vaccinations, Dr. Smith recounts a large number of case reports connecting hepatitis B vaccine with acute immune-mediated injuries of both the peripheral and central nervous systems, including TM. Controlled epidemiologic studies have been inadequate in accepting or rejecting an association of hepatitis B vaccine with neurologic illness. The medical community finds the association of hepatitis B vaccine and acute immune-mediated injuries of the central nervous system plausible, if not firmly established. Ex. 14, p. 2.

Dr. Smith was unaware of a mechanism of injury relating hepatitis B vaccine and central nervous system injury. Causation may have to do with viral proteins and peptides activating myelin reactive T cells. *Id.* Dr. Smith states that TM is the correct diagnosis for Ms. Stevens' illness. In his opinion, hepatitis B vaccine probably significantly contributed to her developing TM. His basis is that she had worsening neurologic symptoms together with elevated laboratory

immunologic measures on two separate discrete occasions each after the administration of hepatitis B vaccine. In the first episode, the worsening of symptoms occurred eight days post-vaccination. In the second episode, the worsening of symptoms occurred nine days post-vaccination. This shows a remarkable symmetry and is well within the time period one would expect for a post-vaccinal immune-mediated reaction. Both vaccinations would have activated a restricted population of T cells which then directed an immune response against Ms. Stevens' cervical cord, resulting in her neurological injuries. She had no other cause for her TM. Ex. 14, p. 3. Dr. Smith subsequently withdrew from this case.

In a status report respondent's counsel filed March 25, 2002 in response to charges from petitioner's counsel that respondent's experts intimidated Dr. Smith to withdraw from this case, respondent stated that, in February 2002, Dr. Roland Martin, one of respondent's experts (although unpaid), sent an e-mail to Drs. Howard Weiner and David Hafler who lead the research group in which Dr. Smith works. Dr. Martin's e-mail to them expressed concern at Dr. Smith's testimony in some vaccine cases in which Dr. Smith interpreted Dr. Martin's published scientific studies. Dr. Martin inquired of Drs. Weiner and Hafler whether Dr. Smith was authorized to use Harvard Medical School letterhead for his opinion. Respondent's expert Dr. Arthur Safran spoke with Dr. Weiner in February 2002 regarding the same subject.

On April 26, 2002, petitioner's counsel filed a status report and motion to compel, stating that, in March 2002, petitioner's counsel called Dr. Smith to arrange time to prepare for trial and learned that he had met with his supervisor, Dr. Howard Weiner, Chief of Neurology at Brigham and Women's Hospital, because the respondent's experts in this case had contacted Dr. Weiner to inform him that Dr. Smith was ruining his reputation by testifying in the Vaccine Program. As

a result, Dr. Smith told Dr. Weiner he would testify in only one additional case and would withdraw from other cases. In February 2002, Dr. Hafler, the chief for Dr. Smith's research program, approached Dr. Smith and told him that people he had known and trusted for many years told him that Dr. Smith was doing things of a questionable nature and hurting his scientific reputation. Dr. Smith assured Dr. Hafler that he was not engaged in activities that were damaging his reputation. Then Dr. Smith left for vacation. Upon his return, Dr. Weiner requested a meeting with him. Also present at this meeting was Dr. Khoury, who directs the MS Clinic at Brigham and Women's Hospital where Dr. Smith practices clinically. Dr. Weiner told Dr. Smith he had received three letters and e-mails from Dr. Roland Martin, Dr. Barry Arnason, and Dr. Safran (all doctors who are associated with respondent and two of whom are experts in this case) telling him that Dr. Smith was hurting his reputation and making false assertions about Dr. Martin's work on the T-cell receptor subunit as well as misrepresenting Dr. Martin's work. Dr. Smith persuaded Dr. Weiner about Dr. Smith's role and the proceedings in the Vaccine Program, but was not able to persuade Dr. Khoury. At the end of the meeting, Dr. Smith told Drs. Weiner and Khoury that he would curtail his work in the Vaccine Program by participating in only one more hearing and that Dr. Weiner would convey his decision to Drs. Martin, Arnason, and Safran. Petitioner moved to compel production of the e-mails from Dr. Martin, written correspondence from Dr. Arnason, and a synopsis from Dr. Safran of his phone conversation. Petitioner also moved to compel respondent's experts to disclose who initiated this effort and disclose the names and affiliations of others with whom they spoke about Dr. Smith.

On May 24, 2002, the Chief Special Master issued an Order denying petitioner's motion to compel because Dr. Smith did not want this matter pursued any further.

The undersigned assumes that respondent's counsel was unaware of the coercive efforts of respondent's experts to undermine petitioner's expert Dr. Smith. If that assumption were wrong, the undersigned would recommend to the Chief Judge of the U.S. Court of Federal Claims that disciplinary proceedings be undertaken pursuant to CFC Rule 83.2(d). The parties are aware that frequently the same experts appear in these vaccine cases. Some are good; some not so good. Therefore, when someone of the high caliber of Dr. Smith becomes part of the litigative process in this Program, his participation should be encouraged, not smothered. Hopefully, respondent's counsel has spoken to Drs. Safran, Martin, and Arnason to explain that bullying and besmirching of someone's reputation has no place in this Program when the sole basis for the bullying and besmirching is that the doctor is participating for the other side. Respondent's expert doctors should understand that hiding evidence is not consistent with congressional intent in enacting the Vaccine Act. Moreover, under the American Medical Association Code of Ethics, their behavior is unethical:

> 9.07 Medical Testimony:
> The medical witness must not become an advocate or a partisan in the legal proceeding.

AMA Council on Ethical and Judicial Affairs, "Code of Medical Ethics" (2002-2003 edition).

On February 11, 2002, respondent filed an expert report from Dr. Arthur Safran, a neurologist. Ex. C. Dr. Safran's curriculum vitae is Ex. D. Dr. Safran cites several studies showing no association between hepatitis B vaccine and MS or relapses of MS. Although no MRI was done of Ms. Stevens' brain, Dr. Safran suspects "there is a fairly substantial chance that lesions would be seen there." Ex. C, p. 2. If lesions were seen in Ms. Stevens' brain, then she would have MS (not TM). In any event, he considers waxing and waning of symptoms common

in TM and, therefore, Ms. Stevens' recurrence and worsening of symptoms after her second hepatitis B vaccine cannot be attributed to the vaccine. *Id.* He concludes there is no statistical association between TM and hepatitis B vaccine. *Id.*

On October 29, 2003, respondent filed a supplemental report from Dr. Safran. Ex. G. He states that the likely diagnosis for Ms. Stevens is MS because of the recurrence, fatigue, and abnormal immunoglobulin banding. The Institute of Medicine concluded that evidence favors rejection of hepatitis B vaccine causing MS. Hepatitis B vaccine is a surface antigen and does not contain living or active virus. Ex. G, p. 1. Evidence is insufficient to conclude that hepatitis B vaccine causes a central nervous system demyelinating disorder. *Id.* He concludes that Ms. Stevens may well have MS. Ex. G, p. 6.

On March 3, 2004, respondent filed another supplemental report from Dr. Safran. Ex. K. He notes Ms. Stevens' fatigue which is a feature of MS as well as depression, but there is still no imaging study of her brain. *Id.*

Petitioners submitted approximately 300 medical articles, case notes, letters in medical journals, etc. Respondent submitted approximately 23 medical articles, etc.

Attached to Dr. Smith's report of November 8, 2001 (P. Ex. 14), are articles (Tabs A through U). Tab D is a case report, "Myélite aiguë après vaccination contre l'hépatite B [Acute myelitis following hepatitis B vaccination]. Les complications neurologiques sont exceptionnelles avec le vaccine contre l'hépatite B. Leur sémiologic clinique peut être déroutante," by F. Mahassin, et al., 22 *Presse Méd* 1997-98 (1993), which describes a man who experienced myelitis 21 days after his third hepatitis B vaccination.

Tab G is a letter, "Myélite aiguë après immunisation contre l'hépatite B par un vaccine recombinant [Acute myelitis after immunization against hepatitis B through a recombinant vaccine]," by A. Senejouz, et al., 20 *Gastroenterol Clin Biol* 401-02 (1996), which describes a woman who experienced myelitis 6 days after her second injection of recombinant hepatitis B vaccine. The authors state that arguments in favor of diagnosing this woman's myelitis as post-vaccinal are the chronology of its occurrence after vaccination and the absence of other causes.

Tab I is a poster description after a neurology convention, "PO6.079. Central Nervous System Demyelination After Recombinant Hepatitis B Vaccination: Report of 25 Cases," by O. Gou, et al., 48 *Neur* 3: A424 (1997). The authors describe 25 females from ages 9-50 years who had onset of primary central nervous system demyelination within seven days and eight weeks after their first hepatitis B vaccination or three to six weeks after a subsequent injection.

Another of petitioners' submissions was "MR Imaging in a Case of Postvaccination Myelitis," by L.M. Tartaglino, et al., 16 *Amer J Neuroradiol* 3:581-82 (1995). Tab A of P. Ex. 27. (It is also P. Ex. 23, p. 83, and P. Ex. 20, Tab MMMM. Further references to Tartaglino will be to Tab A of P. Ex. 27.) The case note discusses a 40-year-old man whose symptoms of progressive lower-extremity numbness and difficulty walking (diagnosed as acute TM) began two weeks after he received his first hepatitis B vaccination. After he received his second hepatitis B vaccination, one month later, his sensory disturbances ascended to the nipple level and he had difficulty walking. Tab A, p. 581. MRI revealed a swollen edematous cord extending from C-3 to T-9 (from the cervical spine to the thoracic spine). There was diffuse hypointense signal relative to the spinal cord. Postgadolinium images showed extensive enhancement isolated to the posterior columns from C-6 to T-8. *Id.*

The authors state:

> Neurologic complications after vaccination are well known but rare. They include seizures, Guillain-Barré syndrome, peripheral neuropathy, cranial nerve palsies, transverse myelitis, and encephalopathy.... In this case of transverse myelitis, although pathologic proof is not possible, the striking temporal relationship between symptoms and the two doses of hepatitis B vaccine strongly suggests that the vaccine was the cause.

Id.

Describing the results of the MRI, the authors state that those findings in TM include cord expansion, increased signal, and an enhancement pattern that can be normal, diffuse, peripheral, or slightly nodular. Their patient had abnormal enhancement in the posterior columns, corresponding to his clinical difficulties. *Id.* The authors suspected that the rare complications of vaccine reaction are underreported because of the delay in symptom occurrence and the difficulty in disproving an idiopathic or postviral cause. Ex. A, p. 582.

Petitioner also filed "Immunopathogenesis of acute transverse myelitis" by D.A. Kerr and H. Ayetey, 15 *Curr Op in Neur* 339-47 (2002). P. Ex. 20, Tab PP. The authors discuss the history of acute transverse myelitis (ATM) as well as its causes. Under the heading "Post-vaccination acute transverse myelitis," the authors state:

> Several reports of ATM following vaccination have recently been published. Indeed, it is widely reported in neurology texts that ATM is a post-vaccination event. One publication reports a case of post 'flu vaccine myelitis in which a 42-year-old man with a history of bilateral optic neuritis developed ATM 2 days after an influenza vaccination.... A separate study ... reported a 36-year-old individual who developed a progressive and ultimately fatal, inflammatory myelopathy/polyradiculopathy 9 days after a booster hepatitis B vaccination. The patient had no fever or systemic illness and did not respond to extensive immunotherapy. ... The

> suggestion from such studies is that a vaccination may induce an autoimmune process resulting in ATM.

P. Ex. 20, Tab pp, pp. 340-41.

Petitioners filed "Brief Report. Two Episodes of Leukoencephalitis Associated with Recombinant Hepatitis B Vaccination in a Single Patient" by D. Konstantinou, et al., 33 *Clin Infect Dis* 1772-73 (2001). P. Ex. 20, Tab UU. The authors express concern about reports of hepatitis B vaccine causing central nervous system demyelinating diseases. P. Ex. 20, Tab UU, p. 1772. They report two separate instances of leukoencephalitis in a 39-year-old woman, the first occurring four weeks after her second hepatitis B vaccination, and the second occurring 11 days after her third hepatitis B vaccination. Brain biopsy and MRIs were performed. Histologic examination was consistent with demyelinating disease. Follow-up visits showed no abnormal neurologic findings other than residua.

The authors concluded that their case showed a strong suggestion of causation from hepatitis B vaccine because of the following factors: (1) absence of previous disseminated neurologic disease; (2) resolution of the lesions; (3) the absence of new neurologic deficits; (4) the occurrence of two similar but separate clinical and radiological neurolgic events soon after administration of the second and third doses of hepatitis B vaccine. P. Ex. 20, Tab UU, p. 1773.

Petitioner filed "Short report. Recurrent demyelinating transverse myelitis in a high titer HBs-antigen carrier," by M. Matsui, et al., 139 *J Neur Sci* 235-37 (1996). P. Ex. 20, Tab CCC. The authors describe a 46-year-old man (not a vaccinee) who was a carrier of an extremely high titer hepatitis B surface antigen (HBs antigen) and who had three attacks of acute TM. His cerebrospinal fluid had elevated levels of myelin basic protein. Corticosteroid therapy eliminated

circulating immune complexes composed of HBs antigen, indicating that immunity to hepatitis B virus was a factor in forming the demyelinating lesion in his spinal cord at the T8 and C2 to T7 levels. The authors opined that this man might illustrate autoimmunity triggered by molecular mimicry between myelin basic protein and hepatitis B virus antigens. P. Ex. 20, Tab CCC, p. 237.

There are no epidemiological studies in support of the allegation that hepatitis B vaccine causes TM.

TESTIMONY

Dr. Vera S. Byers, an immunologist, testified first for petitioner. Tr. at 10. She is not board-certified in immunology, never having taken the test. Tr. at 19. She is in the department of dermatology at the University of California in San Francisco and does grand rounds there. Tr. at 20. She has published over 100 articles on autoimmunity. Tr. at 14. When the body is exposed to an antigen, it can produce macrophages or T-cells to kill the antigen or produce an inflammatory response and then have B-cells produce antibodies. Tr. at 17. In an immune response resulting in autoimmune disease, the immune system turns the body against itself, which can cause demyelinating diseases such as MS. Tr. at 18. She has never published an article on or done research in hepatitis B vaccine. Tr. at 19. She does not treat patients, but goes out into the field and takes histories of people exposed to toxic chemicals and then writes reports on them. Tr. at 20.

Myelin surrounds the nerve fiber that extends from the axon. In demyelinating diseases, the CD-4 positive T-cell produces cytokines that cause inflammation which draws in macrophages that result in demyelination. Tr. at 22. In the central nervous system, this can

cause TM and MS. In the peripheral nervous system, this can cause Guillain-Barre Syndrome (GBS) and chronic inflammatory demyelinating polyneuropathy (CIDP). *Id.*

There is reactivity all along the myelin sheath. Tr. at 25. The activated CD4 cells and T-cells slip easily through the blood-brain barrier. Tr. at 27. Some of the theories for the demyelinating processes are molecular mimicry, degenerate specificity, bystander effect, and the liberation of sequestered antigens and superantigens. Tr. at 27-28. With molecular mimicry, when the foreign protein or a piece of it looks very much like a self-antigen, one can produce T-cells that react against the self body proteins. Tr. at 28.

A T-cell is not as specific as once thought and a wide variety of triggers can set them off. Tr. at 30. An inflammatory response or cytokine storm can activate autoreactive T-cells which produce an autoimmune disease. Tr. at 32. The inflammatory response produces macrophages which result in demyelination. Tr. 33. Holes in the myelin sheath expose proteins which are denatured that the body does not recognize. Tr. at 36. This produces more inflammation. *Id.* This explains a disease's becoming chronic. Tr. at 37.

Dr. Beyers testified that it would be difficult to predict accurately whether or not a particular antigen would cross-react with a T-cell. Tr. at 41. She stated that it is biologically plausible that a variety of things, including hepatitis B, can cause neurologic disorders and it is not essential that the inciting agent look like the native protein. Tr. at 47-48. The Institute of Medicine stated in 2002 that it was theoretically possible for hepatitis B vaccine to cause demyelinating disorders. Tr. at 48.

Demyelinating diseases can be those involving the central nervous system and those involving the peripheral nervous system. Tr. at 49. They can be monophasic or polyphasic. *Id.*

Generally, acute disseminated encephalomyelitis, TM, Guillain-Barre, and optic neuritis occur as one set of symptoms and then resolve, unlike MS. *Id.* However, the monophasic illnesses can rarely recur, for example, after a second hepatitis B vaccination. Tr. at 49-50. When they do recur, this is good evidence of rechallenge. Tr. at 50. Depending on the nature of its recurrence, TM could actually be MS. *Id.* For this to be so, the recurrence has to have a different neurologic manifestation. Tr. at 51. And for this to be so, the recurrence has to have a gap of at least six months. *Id.* If the recurring symptoms are exactly the same manifestation, that is a relapse. *Id.* Chronic inflammatory polyneuropathy is a peripheral disease. Tr. at 53. Dr. Byers is not familiar with people having both a peripheral nervous system lesion and a central nervous system lesion. Tr. at 54.

Hepatitis B vaccine is considered a foreign protein because it is recombinant. Tr. at 56. Dr. Byers thought the evidence in the literature for recurrence (rechallenge) of ADEM after recominent hepatitis B vaccine was quite good. Tr. at 57-58. Rechallenge means that after an agent that is suspected of causing the problem is cleared from the body, and the symptoms resolve, you get challenged again and the same thing happens. Tr. at 58-59. The Institute of Medicine accepted rechallenge of a demyelinating disease after three vaccinations of tetanus toxoid vaccine. Tr. at 59-60.

TM is a subclass of ADEM to many people. Tr. at 60. Forty percent of TM cases are associated with a recent infection or vaccination. *Id.* There are case reports of people developing TM after hepatitis B vaccination. Tr. at 61.

Rechallenge cases of MS are more difficult to interpret than rechallenge cases of monophasic disease because MS has a relapsing and remitting course. Tr. at 77. The Physicians

Desk Reference (PDR) lists GBS, MS, TM, and peripheral neuropathy occurring in greater than 1 percent after hepatitis B vaccination. Tr. at 83. That is a high number. Tr. at 84. The appropriate temporal relationship is within 30 days. Tr. at 97. Dr. Byers concluded it is biologically plausible that hepatitis B vaccine can cause demyelinating disorders. Tr. at 98.

On cross-examination, Dr. Byers admitted that she did not know of any studies that found that hepatitis B surface antigen acts as a superantigen. Tr. at 100. Degenerate specificity of T-cells is actually a very common occurrence in the human body. Tr. at 100-01. One would not expect demyelination within one day of vaccination unless there had been a fairly high concentration of antibodies because of prior repeated boosters. Tr. at 102-03. Otherwise, one day onset is difficult. People would be happier with a seven-day onset or maybe even four days. Tr. at 103. Upper respiratory infections can also cause demyelinating diseases. Tr. at 104. There is no replicating virus in hepatitis B vaccine. Tr. at 105.Viral infections are associated with the initial onset as well as exacerbations of MS. Tr. at 106.

Dr. Byers testified that the Institute of Medicine needs to be 99 percent certain before stating a vaccine causes demyelinating disease because of the public policy concerns. Tr. at 120. But she is 51 percent sure that, in rare cases, hepatitis B vaccine can trigger a demyelinating disease based on the case reports and her understanding of immunologic mechanisms. Tr. at 121.

The second witness for petitioner was Bonnie S. Dunbar, who has a doctorate in zoology and is a professor in molecular and cellular biology, but is not a medical doctor and is not qualified to make medical diagnoses. Tr. at 134-35, 165. At the time of her testimony, she was a Fullbright scholar living in Kenya where she was lecturing in biochemistry and in veterinary physiology and wildlife physiology. Tr. at 135. Her articles are either in reproductive biology or

in immunological technics utilizing protein chemistry. Tr. at 136. She received the Margaret Pittman award for her work in contraceptive vaccines. *Id.*

Before she went to Kenya, Prof. Dunbar was at Baylor University as a full professor in cell molecular biology and an adjunct professor in the department of obstetrics and gynecology. Tr. at 137. She had been working in infertility due to autoimmune causes. Tr. at 137. The only real model for autoimmunity is the baboon model because the baboon has a similar reproductive cycle to humans. Tr. at 138. In addition, she is doing work in HIV/AIDS in the baboon model, which led her to do research in primates in Kenya because so much of heterosexual transmission of HIV/AIDS depends on the mucosal immunity in the female reproductive tract. *Id.* She is also using vaccination of elephants for contraceptive purposes and sterilization because there are too many elephants to find enough to eat. Tr. at 140-41. Another area of Prof. Dunbar's work is HIV/AIDS in children and babies as it relates to hepatitis B disease, particularly in Kenyan orphanages. Tr. at 141.

What Prof. Dunbar has been doing for the last 25 years is taking an animal and inducing a specific autoimmune reaction, wether it be against sperm or eggs, to try to develop a contraceptive vaccine. *Id.* She has immunized over 80 different zoo species, including primates and elephants. Tr. at 143. She discovered that if she took proteins from one species and injected them into another species (such as pig proteins into rabbits), the proteins not only elicit a dramatic immune response but the vaccinated animal also makes antibodies to the self-proteins. Tr. at 143-44. She has broken autoimmune tolerance and generated autoimmune infertility. Tr. at 144. But she did not just develop antibodies in the vaccinated animal that inhibited sperm from binding, she also developed in the vaccinated animal an immune reaction that completely

destroyed its ovaries. *Id.* It took anywhere from three to six months for this autoimmune dysgenesis to occur. *Id.* Prof. Dunbar has concluded that many women become infertile because they have antibodies against the male sperm. Tr. at 145.

Prof. Dunbar because interested in hepatitis B vaccine when her brother, who worked in her laboratory at Baylor, received hepatitis B vaccine and had flu-like symptoms shortly thereafter.[4] Tr. at 146. After the second hepatitis B vaccination, within a few weeks, he was in bed mostly. Tr. at 146-47. Another of her workers also became ill after receiving hepatitis B vaccine. Tr. at 146.

Prof. Dunbar telephoned VAERS and spoke to someone at the FDA who told her that hepatitis B vaccine was a big problem. Tr. at 147. She looked at the VAERS data which showed reports of optic neuritis, lupus, arthritis, GBS, neurological disorders, and dermatologic disorders, and started looking at the literature. Tr. at 147-48. She was able to chart out these illnesses in association with hepatitis B disease, the plasma-derived hepatitis B vaccine, and the recombinant hepatitis B vaccine. Tr. at 149.

Prof. Dunbar showed by doing samples in three or four vaccinees that they had antibodies that reacted with myelin-associated proteins. Tr. at 151. But all of her research was destroyed in a flood at Baylor. *Id.* Due to some testing of people's genomes, she and her associates preliminarily concluded that there might be a subset of vaccinees, presumably Caucasian, who have a genetic susceptibility to a neurologic reaction to hepatitis B vaccine. Tr. at 152-54. She would like to know if peptides were similar to hepatitis B surface antigen. Tr. at 154-55. Some of these proteins are similar enough to be involved in cross-reactivity, perhaps T-cell or antibody

[4] Bohn D. Dunbar v. Secretary of HHS, No. 98-627V.

reactivity. Tr. at 156. One needs only 40 to 60 percent of similarity or identity for T-cell activation. Tr. at 157. With current research, one does not even need to have that similarity. *Id.*

MS patients have antibodies that recognize those peptides. Tr. at 158. At the time, she had some evidence of similarity and a basis for molecular mimicry that could account for some of these reactions. Tr. at 159. Her medical student assistant who reacted two weeks after receiving her second hepatitis B vaccine had optic neuritis, from which she mostly recovered. Tr. at 160. Ten days after the third hepatitis B vaccination, the student was hospitalized and had permanent visual damage. *Id.* This was a classic challenge response. *Id.*

The FDA said that you want rechallenges with both a similar response and a more severe response after the rechallenge. Tr. at 161. We are seeing just basic immune reactions generating serious autoimmune degenerative problems. Tr. at 162. It is the molecule itself that is causing these reactions. *Id.*

With the natural hepatitis B virus, there are dramatic genetic variations in how people react to the disease. Some ethnic groups just carry the virus. Looking at the vaccine, we see subsets of people that are nonresponders. They do not make antibodies to hepatitis B. Tr. at 163. Looking at gene pools, however, does not seem to be politically well-accepted. Tr. at 164.

Prof. Dunbar testified that there is biologic plausibility, temporal correlation with the hepatitis B vaccination, and rechallenge which should prompt scientists to look at the mechanisms. Tr. at 164-65.

Prof. Dunbar admitted that she does not have extensive hepatitis B vaccine experience. Tr. at 169. But she knows how to manipulate proteins, has written textbooks on immunological techniques, and knows how the immune system deals with peptides and proteins. *Id.* One of the

problems in researching vaccine reactions is that people simply look at antibodies and do not look at the cytotoxic or cellular immunity. Tr. at 181.

Dr. Roland Martin testified first for respondent. Tr. at 189. He is a board-certified neurologist. *Id.* He heads that cellular immunology section at the National Institutes of Health whose main interest is MS[5] and the molecular mechanisms leading to it, with a subsidiary interest in Lyme's disease. Tr. at 190. A third of his staff works on molecular mimicry and T-cell clones that are from MS patients. *Id.*

Cross-reactivity happens all the time to protect us from environmental agents. Tr. at 193. We have only a very limited number (25 million) T-cells in our body to orchestrate immune responses. Tr. at 194. We would never be able to protect ourselves with this small number of T-cells if there were not a tremendous amount of cross-reactivity. *Id.* Experimentally, a T-cell recognizes thousands and thousands of peptides. *Id.* Sequence homology or similarity is not acceptable any more. Tr. at 195. There is little evidence to show molecular mimicry in almost all autoimmune diseases. Tr. at 197. Something else is required to cause pathologic autoimmunity. Tr. at 198. In experiments with mice raised in the same environment, once the animals have four lupus genes, they all get the disease lupus. Tr. at 199-200. In MS, there are probably several hundred genes involved. Tr. at 200. Environmental factors may be a smaller modifier of disease expression than we currently think. Tr. at 201.

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[5] Respondent filed an expert report from Dr. Martin, dated February 8, 2002, in which Dr. Martin states that Ms. Stevens appears to have had TM and that the time window of its occurrence after hepatitis B vaccination "is compatible with the times between infection and neurological illness that is described for postinfectious demyelinating episodes such as transverse myelitis." R. Ex. A, p. 1. However, Dr. Roland did not find grounds for supporting a conclusion of causation based on case reports or experimental findings, and deemed Ms. Stevens' TM could be coincidental after her vaccination. He does not discuss challenge/rechallenge in his letter.

When he studied a T-cell line from someone who developed MS after receiving hepatitis B vaccine, he found cross-reactivity, but it was weak. Tr. at 203. One needs to confirm these reactivities in multiple repetitive essays in order to confirm cross-reactivity, which did not happen in this case. Tr. at 204. Cross-reactivity is much much broader than we originally thought. Tr. at 207. There are antigens that are completely dissimilar and can still be cross-reactive. *Id.*

MS is a very complex genetic trait of many weakly associated genes that contribute to susceptibility for MS. Tr. at 208. There is potentially an environmental trigger that may be needed around puberty or earlier or later. *Id.* It is unclear what that trigger is. *Id.* It could be upper respiratory infections and probably many different agents. *Id.* What is absolutely critical is the genetic predisposition which is a very complex one and not understood. Tr. at 208-09.

His staff had one patient whose MS was worse four weeks after a vaccination, but he could not make any conclusions about causation. Tr. at 214-15. The possibility that vaccines cause demyelinating diseases cannot be excluded. Tr. at 217. If an individual had had reactions twice to vaccination, and the temporal relationship is appropriate, he would not recommend a third vaccination. *Id.* You can expect that an acute reaction will take a few days to a maximum of three to four weeks. Tr. at 219. Anything occurring earlier than a day must be due to a superantigen stimulation. Tr. at 219-20. Dr. Martin would expect that the time frame could be anywhere from five to six days to four weeks to assume a temporal relationship in an acute event. Tr. at 220. Dr. Martin would want to see the expansion or stimulation of T-cells by either the vaccine or the infectious agent and the cross-reacting protein from the cerebrospinal fluid or from the brain or the nerve root. Tr. at 222.

If someone emigrates from a country with a low rate of MS, like Japan, before puberty to a country with a high rate of MS, like the US, she will keep the low risk of MS. But if she emigrates after puberty, she takes the high risk of MS and we do not know why. Tr. at 228-29. He would not expect a vaccination to cause an autoimmune reaction unless it included a live virus. Tr. at 239. Although Dr. Martin agrees that you need host susceptibility, some kind of environmental antigen at the proper time, local inflammation, release of self antigens, and a sufficient number of autoreactive T-cells to have an autoimmune reaction, he would not say a vaccine causes this without epidemiologic support. Tr. at 243-44.

Dr. Martin stated it is accepted that costimulation is needed to activate T-cells and this system may be disturbed in MS patients. Tr. at 246. Dr. Martin would accept 30 days as an appropriate time frame for GBS to be caused by an infectious agent or vaccination. Tr. at 257. Data is good that antibodies are more important than T-cells to cause the disease process in damaging myelin, but they are one factor among many. Tr. at 259-60. Antibodies are important in one of four subgroups of MS. Tr. at 260. Antibody or immune complexes do not play a role. *Id.* He is aware that hepatitis B vaccine has led to vasculitis in the kidney and other organs, but he is not aware of a central or peripheral nervous system manifestation. Tr. at 260-61.

There are many potential causes of autoimmune neurological conditions. Tr. at 263. Giving a series of vaccinations can prime the vaccinee. Tr. at 272. For Dr. Martin to be convinced of vaccine causation, he would want to see if the antigen in question could induce an experimental disease that looks similar to the human disease. Tr. at 275. His next requirement would be that a certain component of the immune system has the ability to cross-react, i.e., an

antibody or T-cell which can transfer that disease to a healthy animal to see if these cells are able to cross-react with a component of the tissue that has been previously damaged. Tr. at 276-77.

On the second day of testimony, Dr. Lawrence H. Moulton testified first for respondent. Tr. at 353. He is a biostatistician and professor of international health and biostatistics at John Hopkins University. Tr. at 354. He spends a lot of time calculating data and detecting sources of bias in studies. Tr. at 355. He is co-director of the Institute for Vaccine Safety. Tr. at 357. Johns Hopkins has the largest School of Public Health in the world and has one of the few centers for vaccine research in the country. Tr. at 359. He developed statistical methods for evaluating vaccines and has been involved in phases one through four of vaccine safety evaluations. *Id.* He spends half his time on designing, conducting, and helping investigators evaluate randomized control trials. Tr. at 360-61.

He prefers epidemiologic studies that are cohort studies or population-based studies. Next in preference come case control studies. But they are still observational and do not have the strengths of the randomized control trial which eliminates confounding due to variables. Tr. at 361. He places very little value on case reports because they do not look at the denominator population. Tr. at 362.

The VAERS system was set up to be an early warning system. Tr. at 364. It is a passive reporting system. Tr. at 363. The quality of the reports is very low. Tr. at 364. When there is a rare outcome, the relative risk and the odds ratio are virtually the same. Tr. at 367. Dr. Moulton discussed a study which did not show any increased risk of adolescent MS following hepatitis B vaccination (and even that the vaccine could be protective), but explained that the lack of a link could be due to multiple variables: changes in climate, habits, time periods. Tr. at 371-73. As

Dr. Moulton stated, "I mean, who knows?" Tr. at 372. None of the other articles Dr. Moulton discussed had statistical significance and they had wide confidence intervals. Tr. at 374-82. There was a statistically significant risk of getting headache after hepatitis B vaccine. Tr. at 384.

To look at all age groups and all different periods before or after vaccination is a shotgun-type approach. Tr. at 384. There is not a lot of material reported. Tr. rat 385. In a cross-over study, where vaccinees and a group getting placebos changed places, there was again no statistical significance in the conclusion of no causation or even a protective effect, but the confidence intervals were tight. Tr. at 388.

In a study using the Vaccine Safety Data Link, which compiles records on immunizations and diseases from HMOs, there was no increased risk of either MS or optic neuritis. Tr. at 391-93. Dr. Moulton criticized one study for characterizing itself as prospective when it was retrospective, and relying upon the date of reporting of symptoms rather than of diagnosis. Tr. at 396-97. There also seemed to be a suspiciously small number of people excluded who had high risk of getting hepatitis B disease. Tr. at 398-401. Confounding variables can increase the odds ratio that a vaccine caused a disease. Tr. at 402-05.

Dr. Moulton concluded that there is very little data indicating a relationship between hepatitis B vaccine and any of the demyelinating diseases at issue in the Omnibus hearing. Tr. at 409. For MS, it looks as if the evidence is against both initiating MS and causing a relapse. Tr. at 410. Dr. Moulton is not a medical doctor. Tr. at 412. He has not seen anything to make him think there is any strong relationship between hepatitis B vaccine and demyelinating disorders. Tr. at 490. He has not seen a confidence interval above the 2.0 odds ratio level. Tr. at 491. He accepts there are rare complications from vaccinations. Tr. at 494.

Dr. Carlo Tornatore, a neurologist, testified next for petitioners. Tr. at 496. He is the director of the MS Clinic at Georgetown. Tr. at 497. He follows about 1,100 patients in his MS center, including patients with TM. Tr. at 498. He also follows patients with TM, CIDP, and a few GBS. Tr. at 498-99.

Dr. Tornatore reviewed the records in the instant action (the Stevens case). Tr. at 500. Twelve or 13 days after her first hepatitis B vaccination, she noted soreness across her shoulders and numbness starting on the right side of her body. She felt less coordinated. Tr. at 501. Of importance is her sensation of having a band around her which was tightening. This indicates spinal cord inflammation. *Id.* Six weeks after vaccination, she improved but still had some neck tightness and her sedimentation rate, which is a broad marker of inflammation, was 50. Tr. at 502.

Ms. Stevens received her second hepatitis B vaccination and, a week later, developed the same symptoms she had after the first vaccination but they were worse. *Id.* She saw a neurologist who diagnosed her as having TM. An MRI showed multiple areas of increased signal between C3 and C6 in the cervical spine. Tr. at 503. A spinal tap indicated inflammation and showed oligoclonal bands. *Id.*

Dr. Tornatore testified that there have been case reports of TM among hepatitis B vaccinees in a time frame appropriate for causation. Tr. at 503-04. Dr. Tornatore referred to the Institute of Medicine (IOM) report in 2002 (Ex. C, p. 39) stating that causality is shown in a challenge/rechallenge case where the diagnosis is correct and alternative causes are excluded. Tr. at 504-05. The Stevens case is one of challenge/rechallenge. Tr. at 505. Ms. Stevens had the same response to hepatitis B vaccine two separate times. The timing was appropriate for

causation. There is biologic plausibility because case reports have described TM after hepatitis B vaccine. *Id.* TM following vaccination is cogent to Dr. Tornatore. *Id.* TM is an autoimmune process. Tr. at 505-06.

This is going to be a very rare event and a challenge/rechallenge case is the only way to find this at a clinical level. Tr. at 508. Ms. Stevens' doctors ruled out other causes of her TM. Tr. at 510. Regarding whether Ms. Stevens had MS and not TM, Dr. Tornatore stated TM is inflammation of the spinal cord. Twenty to 25 percent of MS patients have TM as their first episode. Tr. at 511. They may then go on to have a second episode of inflammation involving a different neurologic area, such as the brain, optic nerves, brainstem. He agreed that TM can be the hallmark of someone who develops MS. *Id.* However, Ms. Stevens did not develop MS in the 10 years since her TM began. *Id.* She has not had any new problems. Tr. at 511-12.

The appropriate time frame for a reaction to a vaccination is 30 days. Tr. at 512. Ms. Stevens' symptoms began within the first week. Tr. at 513. This is a positive rechallenge case. *Id.* His opinion is that hepatitis B vaccinations caused her TM twice. *Id.* He sees no reason why Ms. Stevens would have had MS without hepatitis B vaccine. Tr. at 514.

Ms. Stevens did not have an MRI done on her spine after her first hepatitis B vaccination and never had an MRI done of her brain at all. Tr. at 517, 519. Dr. Tornatore did not think the chiropractor whom Ms. Stevens saw after the first vaccination worsened her condition. Tr. at 519. Her symptoms got worse after the second vaccination. Tr. at 520.

Dr. Thomas P. Leist, a neurologist, testified next for respondent. He is an assistant professor at Thomas Jefferson University and the director of the comprehensive MS center at the same university. Tr. at 552. He has a clinical practice in neuroimmunology. *Id.* Dr. Leist stated

that Ms. Steven's cervical lesion on MRI was less characteristic for TM because it was relatively long (Dr. Leist is basing his opinion on the report). Tr. at 557. It also showed enhancing areas and non-enhancing areas. *Id.* Lesions in the spinal cord indicate abnormality, without indicating the underlying pathology. Ms. Stevens' MRI indicated multiple lesions in the cervical spine. *Id.* By injecting gadolinium, one can find a focal blood-brain barrier compromise and an acute lesion. Tr. at 558. In Ms. Stevens' MRI, there were both acute and subacute or non-enhancing lesions. *Id.* That means there is a dissemination of the lesion activity over time. *Id.* The other explanation is that someone did not wait long enough with the gadolinium and, if he had, all the lesions would have been gadolinium-enhancing. Tr. at 559.

Dr. Leist stated that Ms. Stevens' cerebrospinal fluid had oligoclonal bands and an increased IgG. *Id.* The lumbar puncture was done in February, two and one-half months after the initiall vaccination. Tr. at 560. Oligoclonal bands are important because they are almost a substitute for dissemination in time. *Id.* Oligoclonal bands are essentially antibodies, produced by B cells. *Id.* Dr. Leist stated it was difficult for him to state how long it takes for oligoclonal bands to arise, but probably the inflammatory process would have been going on for months. Tr. at 561. This leads Dr. Leist to doubt that the onset of Ms. Stevens' condition was after her first vaccination. *Id.*

In order to diagnose MS, Dr. Leist needs to see dissemination in time of lesions. Tr. at 562. At her first spinal tap, he has an indication that the process has been ongoing. *Id.* Because animals injected with live virus have cytotoxic T-cell responses in six or seven days, Dr. Leist doubts that Ms. Stevens' symptoms occurring seven days after vaccination are related to the vaccine because it is too short a time. Tr. at 563. He assumes that, since Ms. Stevens did not

fully recover from the symptoms after the first hepatitis B vaccine, it is not unreasonable to assume that if the second vaccination had worsened her condition, she should have reacted 24 hours later, not seven days later. Tr. at 564-65. It should have been much shorter if the vaccination were related to the symptoms. Tr. at 565. Thus, Dr. Leist concludes that these are two independent, unrelated events, that Ms. Stevens had TM that essentially progressed through the months over time and that her worsening of symptoms in late January was independent of the second vaccination. *Id.*

Ms. Stevens had another recurrence in late 1997 when she developed lower extremity dysesthesias or funny feelings in her lower legs, a tingling sensation, indicating she may have acquired a new lesion. Tr. at 566. (On cross-examination, Dr. Leist would not opine whether the problem with Ms. Stevens' lower legs was due to her resuming work in a school and lifting numerous students was sciatica. He preferred to call it low back pain. Tr. at 588.) This low back pain raised the issue for Dr. Leist that she has now developed MS. Tr. at 566. Typically, TM is one single lesion at a single level. Ms. Stevens has positive multiple areas of signal abnormality. Tr. at 567, 568. Dr. Leist would diagnose her as possible MS with a clear suspicion. Tr. at 568.

Dr. Leist testified that Ms. Stevens did not have two distinct episodes, one after each vaccination, but a continuum of an intermediate plateau and then a subsequent worsening. Tr. at 569. He believes that Ms. Stevens already had a demyelinating illness (a prodromal phase) when she had no clinical symptoms at the time she took her first vaccination. Tr. at 569-70.

Dr. Leist considers that Ms. Stevens had a cord intrinsic process, which can entail TM, MS, a cord tumor, and a number of other processes, after her first hepatitis B vaccination. Tr. at

572. The MRI she had in February shows that Ms. Stevens had spinal cord lesions. Tr. at 573. The natural disease hepatitis B can cause demyelinating disease infrequently. Tr. at 581. There is a potential for hepatitis B vaccine to cause demyelinating disorders. Tr. at 584-85.

Ms. Stevens had low back pain noted in Dr. Wilhelm's records of January 2, 1998 which started around November 20, 1997 after Ms. Stevens had returned to work and had to lift several children on subsequent days. Tr. at 587-88. One explanation is sciatica. Tr. at 590. Dr. Leist reiterated that Ms. Stevens has possible MS. Tr. at 591. It is probably months until oligoclonal bands appear. Tr. at 592. He does not think oligoclonal banding would have developed over the two months since Ms. Stevens' initial symptoms because there was not enough time. Tr. at 595. He did not think Ms. Stevens had any significant resolution of her symptoms between the first and second vaccinations. Tr. at 597. He considers it a monophasic illness with a plateau. *Id.* He also stated that a probable diagnosis of TM is appropriate. Tr. at 598. But it may be in the context of something else. *Id.* An onset of seven or eight days after vaccination is very close to the border of the plausible time for an immune response to occur. Tr. at 599.

On the third day of the hearing, Dr. Tornatore testified on rebuttal. Tr. at 811. He stated that, after reviewing all the medical records, Ms. Stevens does not have MS. *Id.* The presence of oligoclonal bands detected two months after the first vaccination could have been incited by the vaccination. Tr. at 813.

DISCUSSION

Petitioner is proceeding on a theory of causation in fact. To satisfy her burden of proving causation in fact, petitioner must offer "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury. A reputable medical or scientific explanation

must support this logical sequence of cause and effect." Grant, supra, at 1148. Althen, supra, at 1278; Agarwsal v. Secretary, HHS, 33 Fed. Cl. 482, 487 (1995); see also Knudsen, supra, at 548; Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579 (1993).

Without more, "evidence showing an absence of other causes does not meet petitioners' affirmative duty to show actual or legal causation." Grant, supra, at 1149.

Petitioner must not only show that but for the hepatitis B vaccine, she would not have had TM, but also that the vaccine was a substantial factor in bringing about her condition. Shyface v. Secretary, HHS, 165 F.3d 1344 (Fed. Cir. 1999).

In essence, the special master is looking for a reputable medical explanation of a logical sequence of cause and effect (Althen, supra, at 1278; Grant, supra, at 1148), and medical probability rather than certainty (Knudsen, supra, at 548-49). To the undersigned, medical probability means biologic credibility or plausibility rather than an exact biologic mechanism. As the Federal Circuit stated in Knudsen, supra, at 549.

> Furthermore, to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program. The Vaccine Act does not contemplate full blown tort litigation in the Court of Federal Claims. The Vaccine Act established a federal "compensation program" under which awards are to be "made to vaccine-injured persons quickly, easily, and with certainty and generosity." House Report 99-908, [99th Cong., 2d Sess. 18, *reprinted* in 1986 U.S.C.C.A.N. 6344], at 3, 1986 U.S.C.C.A.N. at 6344.
>
> The Court of Federal Claims is therefore not to be seen as a vehicle for ascertaining precisely how and why DTP and other vaccines sometimes destroy the health and lives of certain children while safely immunizing most others.

In the Office of Special Masters, the Federal Rules of Evidence are not followed.[6] Invariably, consistent with the legislative intent in creating the Vaccine Program, the special masters admit most evidence. But see, Domeny v. Secretary, HHS, No. 94-1086V, 1999 WL 199059 (Fed. Cl. Spec. Mstr. March 15, 1999), aff'd, (Fed. Cl. May 25, 1999) (unpublished), aff'd, No. 99-5130 (Fed. Cir. Apr. 11, 2000) (rejecting proffer of dentist's testimony for diagnosis of a neuropathy).

As the Federal Circuit stated in Knudsen, supra, at 548, "Causation in fact under the Vaccine Act is thus based on the circumstances of the particular case, having no hard and fast *per se* scientific or medical rules." The task before the undersigned is to determine medical probability based on the evidence before the undersigned in this particular case. Althen, supra, at 1281 ("judging the merits of individual claims on a case-by-case basis").

The first day's testimony of Dr. Byers, Prof. Dunbar, and Dr. Martin makes clear that the specific biologic mechanism that causes vaccine reactions is still unknown. They provided theories of immune-mediated reactions which convey biologic plausibility for the allegation that antigenic insults may in rare cases lead to neurologic injury. In order to prevail in this Program, the Federal Circuit in 2005 in Althen, supra, reiterated what it had held in 1994 in Knudsen: petitioner does not have the burden of proving a specific biologic mechanism in order to prevail. The testimony of Dr. Martin strongly indicates that the field of vaccine research has moved beyond where it was when the articles (even his own) were written. There would not be much

[6] CFC Rules, Vaccine Rule 8(b) Evidence. "In receiving evidence, the special master will not be bound by common law or statutory rules of evidence. The special master will consider all relevant, reliable evidence, governed by principles of fundamental fairness to both parties."

purpose in perusing articles whose value is considerably lessened by the advance of scientific research by the time the cases are tried.

The undersigned finds further clarity about biologic plausibility in the report of petitioner's expert Dr. Smith. He states that both of Ms. Stevens' hepatitis B vaccinations would have activated a restricted population of T cells which then directed an immune response against Ms. Stevens' cervical cord, resulting in her neurological injuries. Her responses after each of her two vaccinations occurred with remarkable symmetry, in Dr. Smith's words, and were well within the time period within which one would expect a post-vaccinal immune-mediated reaction.

Respondent's expert Dr. Martin wrote similarly that the time window of the occurrence of Ms. Stevens' TM was compatible with the times between infection and neurological illness that are described for postinfectious demyelinating episodes such as TM.

Whether the mechanism is T-cell activation, the older and apparently discredited theory of molecular mimicry, cytokine storm, or some other mechanism, the reputable medical or scientific understanding of immune reactions to antigenic stimuli such as vaccines is that these reactions occur and that there are reasons for them. Petitioner has proved by a preponderance of the evidence that there is biologic plausibility that hepatitis B vaccine can cause TM.

Respondent's experts Dr. Martin and Dr. Moulton refused to accept causation of TM from hepatitis B vaccine because of the lack of reputable supportive epidemiologic evidence. However, the Federal Circuit stated in Knudsen in 1994 that petitioner need not have substantiating epidemiologic support in order to prevail in this Program. Knudsen at 550. In Knudsen, even though epidemiological evidence supported the opposite conclusion, i.e., that

viruses were more likely to cause encephalopathy than vaccinations, the Federal Circuit held that that fact alone was not an impediment to petitioners prevailing. In Knudsen, the Federal Circuit stated, at 550:

> The bare statistical fact that there are more reported cases of viral encephalopathies than there are reported cases of DTP encephalopathies is not evidence that in a particular case an encephalopathy following a DTP vaccination was in fact caused by a viral infection present in the child and not caused by the DTP vaccine.

Legally, petitioner's evidence of causation that hepatitis B vaccine can cause TM is not undercut by the lack of reputable supportive epidemiologic evidence.

Dr. Moulton refused to agree to causation because the medical literature supporting petitioner's allegation of causation consisted of case reports (which are not peer-reviewed). He said he placed little value on them. But, the Federal Circuit in Althen stated that petitioner need not have substantiating objective, i.e., peer-reviewed, medical literature in order to prevail in this Program. Althen at 1279-80, 1281. Some of the challenge/rechallenge case reports, particularly Tartaglino, are strikingly similar to what Ms. Stevens experienced. One might call Tartaglino a case report on all fours for Ms. Stevens' case.

It is perhaps less than candid that none of respondent's experts thought these case reports intriguing enough to moderate their opinions. It is also noteworthy that none of respondent's experts gave credence to the opinions of Ms. Stevens' treating neurologist Dr. Wilhelm, and the two workmen's compensation doctors (Dr. Karr, an immunologist, and Dr. Wong, a neurologist), that Ms. Stevens had TM (not MS) and that hepatitis B vaccinations caused her TM. It would be hard for a petitioner to have a stronger case for causation than here, and the well-considered

confirmation of her treating neurologist and two others in the areas of immunology and neurology who evaluated her case should certainly have been in the thought processes of respondent's experts. But they were not.

Ms. Stevens experienced TM on two occasions, both in strong temporal relationship to her first and second hepatitis B vaccinations. She was recovering from her adverse reaction to the first hepatitis B vaccination when she had the second vaccination, and became worse in practically the same time period subsequent to the second vaccination as after the first vaccination. Although one may speculate as to the specific biologic mechanism that would cause recombinant hepatitis B vaccine (which is not a live virus vaccine) to cause TM, the ineluctable conclusion one reaches from this positive rechallenge case is that the vaccine did so. And since it did so in this case, the undersigned logically assumes that it can do so in other TM cases. The undersigned will leave the consideration of MS, GBS, and CIDP to the other cases involved in this Omnibus proceeding.

Respondent's expert Dr. Leist's opinion that Ms. Stevens had, as he phrased it, "possible MS with a clear suspicion," is not persuasive and does not satisfy the evidentiary standard of more likely than not (i.e., probable, not possible). Ms. Stevens' treating neurologist and the neurologist and immunologist who evaluated her for workmen's compensation considered whether she had MS and concluded that she did not. In fact, Dr. Wong, a neurologist, stated that, if she had MS, her symptoms after the second vaccination would have occurred in other sites and not in the same site as after her first vaccination. Moreover, Dr. Smith, another MS expert, agreed that she had TM and not MS. Dr. Martin, respondent's expert, opined in his written report that Ms. Stevens had TM. Lastly, Dr. Tornatore, who testified at the hearing and is also an

MS expert, stated she had TM, not MS. Dr. Safran opined in writing for respondent that Ms. Stevens had MS with the understanding that if she had had a brain MRI, there would have been a "fairly substantial chance" it would have shown lesions. This is pure speculation.

Dr. Leist was also speculative when he said that if Ms. Stevens had had a brain MRI and another spinal MRI, doctors might have seen other lesions. His reasoning that, if she were actually reacting to the hepatitis B vaccine, she would have reacted within a day after the second vaccination instead of in the same time period as after the first vaccination is exactly opposite to the reasoning of Dr. Tornatore, Dr. Wilhelm (her treating neurologist), Dr. Karr (workmen's compensation immunologist), and Dr. Wong (workmen's compensation neurologist) that the fact that the same interval of time occurred before the onset of the same symptoms (but worse the second time) after each vaccination confirms that Ms. Stevens was reacting to the vaccine.

Dr. Leist also opined that Ms. Stevens had an ongoing demyelinating disease without clinical symptoms at the time she received her first vaccination based on his interpretation of her sole spinal MRI that her lesions looked months old. The sole spinal MRI was done after her second vaccination, i.e., months after the onset of her initial symptoms. One might ask, if the lesions and the first vaccination occurred months before the MRI was done, how the MRI could indicate a pre-vaccination TM. There is no reason for the undersigned to assume that Ms. Stevens' TM began before her first vaccination since the age of the lesions matches the time of onset after the first vaccination. The undersigned regards Dr. Leist's testimony as speculative and result-oriented (i.e., since the vaccination cannot have caused the disease, lesions that were months old when the MRI months later [after the second vaccination] detected them means that they occurred before the first vaccination).

Dr. Leist also refused to agree that the Tartaglino case report was a "potential mimic" of Ms. Stevens' case. In the Tartaglino case report, a 40-year-old man experienced TM, with numerous spinal levels affected, most of which (but not all) were gadolinium-enhanced, two weeks after his first hepatitis B vaccination. After his second hepatitis B vaccination, without a specification of time of onset, he experienced the same symptoms in the same spinal levels. The authors concluded this case of positive rechallenge necessitated a conclusion of causation. Dr. Leist was unconvinced. He criticized the authors as neuroradiologists who did not have direct patient contact other than their contact with the MRIs. Tr. at 578. He concluded there was insufficient information in this case report to draw any conclusion other than that it shows interesting MRI behavior. *Id.*

The fact that the Tartaglino case report directly rebuts the basis for Dr. Leist's conclusion that Ms. Stevens has MS (the man's spine in the case report had involvement of numerous spinal levels, some of which were not gadolinium-enhanced) and his conclusion that hepatitis B vaccine had nothing to do with her illness made little or no impression on Dr. Leist. He testified that someone with TM would have but a single lesion. The case report shows the man had more levels involved than Ms. Stevens: from his cervical level to his thoracic level. Dr. Leist testified that the failure of all of Ms. Stevens' lesions to be enhanced by gadolinium meant these were lesions occurring over time (diagnostic of MS) unless the doctors did not give the gadolinium enough time to enhance all the spinal areas. But the man in the case report had both enhanced and non-enhanced levels with gadolinium.

Rare events, such as TM in Herkert,[7] Tufo,[8] and Lodge,[9] have not appeared in epidemiological studies pertaining to vaccination so far, and have not been explained with the knowledge of the specific biologic mechanism, yet petitioners have prevailed in those cases. The Federal Circuit in Knudsen, supra, did not find lack of epidemiological support or a specific biological mechanism an impediment to petitioners' prevailing.

As Dr. Martin, respondent's expert, recognized, there is strong evidence in a case of challenge/rechallenge that in itself indicates causation in fact. See, e.g., Larive v. Secretary of HHS, No. 99-429V, 2004 WL 1212142 (Fed. Cl. Spec. Mstr. May 12, 2004) (hepatitis B vaccinations followed by steadily worsening symptoms of focal segmental glomerulosclerosis; petitioner proved causation in fact of significant aggravation; both sides' doctors agreed that the timing of petitioner's symptoms after vaccinations was consistent with their understanding of an appropriate time interval when a triggering factor provokes symptoms. 2004 WL at *11).

The timing here is appropriate for immune-mediated responses. Case reports, especially the Tartaglino and Konstantinou[10] ones, support the medical understanding that a positive rechallenge case strongly indicates causation in fact. Ms. Stevens experienced the same neurologic symptoms after the same antigenic insults within practically the same period of time.

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[7] Herkert v. Secretary of HHS, No. 97-518V, 2000 WL 141263 (Fed. Cl. Spec. Mstr., Jan. 19, 2000).

[8] Tufo v. Secretary of HHS, No. 98-108V, 2001 WL 286911 (Fed. Cl. Spec. Mstr., Mar. 2, 2001).

[9] Harris v. Secretary of HHS, No. 93-333V, 2001 WL 530644 (Fed. Cl. Spec. Mstr., May 2, 2001).

[10] The Konstantinou case report discussed positive rechallenge of leukoencephalitis from recombinant hepatitis B vaccinations.

She had TM within a week to a week and one-half after two hepatitis B vaccinations. She had no pre-vaccination neurologic disease. Her subsequent history is consistent with her initial diagnosis of TM. As in the Konstantinou case, Ms. Stevens improved over time with minor residua and no new neurologic deficits. Ms. Stevens' subsequent medical records show no new neurological deficits but lower back strain after lifting special education students and monoarthritis in her knee.

All the undersigned must do, under the Federal Circuit decisions in Grant, Knudsen, and Althen, is hold that a reputable medical or scientific theory causally connects hepatitis B vaccine and TM, a logical sequence of cause and effect shows that hepatitis B vaccine caused Ms. Stevens' TM, and a proximate temporal relationship exists between petitioner's hepatitis B vaccinations and her TM in order for petitioner to prevail.

Petitioner has satisfied her burden of showing a logical sequence of cause and effect between hepatitis B vaccine and her TM based on: (1) the medical records, including the opinions of her treating and workmen's compensation doctors; (2) the testimony of Dr. Tornatore and the report of Dr. Smith; and (3) the case reports which confirm that hepatitis B vaccine can cause TM.

Petitioner's evidence is supported by reputable medical and scientific theories of how, in rare cases, the neurological system reacts to antigenic insults (the current understanding of immune-mediated diseases). She has shown a proximate temporal relationship in the time intervals between vaccinations and immune-mediated responses.

Moreover, the repetition of the same symptoms in nearly the same time sequence after each of her hepatitis B vaccinations constitutes positive rechallenge, a hallmark for causation.

Petitioner has prevailed in proving that hepatitis B vaccinations caused her TM.

CONCLUSION

Petitioner is entitled to reasonable compensation. The undersigned hopes that the parties may reach an amicable settlement, and will convene a telephonic status conference soon to discuss the filing of life care plans, unless the parties agree on a joint life care plan. The parties should be aware that alternate dispute resolution is available to them as well, and if they choose ADR, they should contact the undersigned. Should the parties not be able to settle this case, the undersigned will hold a damages hearing.

IT IS SO ORDERED.

_____ _____

DATE

Laura D. Millman
Special Master