OFFICE OF SPECIAL MASTERS

No. 00-170V

Filed: June 3, 2003

MARGARET ALTHEN,		
Petitioner,		
v.		**To Be Published**
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,		
Respondent.		

Ronald C. Homer, Boston, Massachusetts, for petitioner.

Gregory W. Fortsch, United States Department of Justice, Washington, D.C., for respondent.

ENTITLEMENT DECISION

GOLKIEWICZ, Chief Special Master.

I. PROCEDURAL BACKGROUND

In this matter filed under the National Vaccine Injury Compensation Program, petitioner claims she suffered optic neuritis and acute-disseminated encephalomyelitis ("ADEM") as a direct result of a tetanus toxoid ("TT") vaccination she received on March 28, 1997.[1] Petition for Vaccine Compensation ("Pet.") at 1, filed March 31, 2000. Petitioner places the onset of her optic neuritis at 18 days after the administration of the vaccine, when on April 15, 1997, she partially lost sight in her right eye. Id.; Petitioner's Exhibit 20 at 1 ("Affidavit of Margaret Althen"), filed December 12, 2000. "Within four days, [petitioner's] right eye was totally blind" and she was diagnosed with optic neuritis. P. Ex. 20 at 2. Petitioner alleges that by July 1997, she also developed acute disseminated encephalomyelitis. Id.

[1]The National Vaccine Injury Compensation Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (1986) (codified as amended at 42 U.S.C.A. §§300aa-1 through -34 (West 1991 & Supp. 2002)) ("Vaccine Act" or "the Act"). References shall be to the relevant subsection of 42 U.S.C.A. §300aa.

Respondent disputes that petitioner suffered any compensable injury related to her tetanus toxoid vaccination, arguing that neither injury alleged is listed on the Table and, at the time of the filing of the petition, petitioner provided no expert report or opinions from her own treating physicians causally linking the vaccine to her alleged ADEM or optic neuritis. Respondent's Report at 7, 8-9, filed February 5, 2001. Petitioner subsequently submitted a qualified expert report.

The court conducted an evidentiary hearing on June 14, 2002, to address the medical and legal causation issues. Dr. Derek Smith testified for petitioner and Drs. Roland Martin and Arthur Safran testified on respondent's behalf. See Transcript ("Tr."), filed July 12, 2002. The parties submitted their post-hearing briefs and the case is now ripe for decision. After considering the totality of the evidence, the court finds petitioner has not demonstrated by a preponderance of the evidence that her tetanus toxoid vaccination caused her injuries.

II. FACTUAL BACKGROUND

The facts are relatively undisputed in this case.[2] Petitioner was born on October 11, 1947. P. Ex. 1 at 21. Prior to the events at issue, petitioner sustained a right calcaneus fracture in January 1996, due to a car accident, and was diagnosed with adult Duane's Syndrome in the left eye, but was otherwise relatively healthy. P. Ex. 2 at 7; P. Ex. 18 at 1.

On March 28, 1997, petitioner received a tetanus toxoid vaccination ("TT") and a hepatitis A vaccination. P. Ex. 1 at 1. Approximately two weeks later, on April 15, 1997, petitioner sought treatment for a 3 to 4 day history of "discomfort/pain to [her optic disc]" with eye movements and the onset that morning of blurred vision in her right eye. P. Ex. 2 at 3. Petitioner also described a "steady" "posterior headache," "discomfort along the right side of her nose," and queasiness. P. Ex. 1 at 107. Petitioner denied a prior history of blurred vision, injury, infection, paresthesia, and arm or leg weakness. P. Ex. 2 at 7. Petitioner was diagnosed with "[r]ight disc edema – probable right optic neuritis." Id. at 3, 10; P. Ex. 4 at 122. This diagnosis was consistent with her April 21, 1997 brain MRI result, which revealed no "evidence of multiple sclerosis or demyelinating disease." P. Ex. 1 at 111. Thereafter, petitioner's vision deteriorated and on April 27, 1997, she suffered a "sudden loss of vision" over the course of two days. P. Ex. 3 at 38. Petitioner was treated for this and her earlier onset of vision problems with a course of steroids. Id. at 36; P. Ex. 1 at 107. Over the next few weeks, petitioner's physicians ruled out vasculitis based on her sedation rates, ANA results, and other vasculitis screening findings. P. Ex. 2 at 14, 16.

Near the last week in May 1997, petitioner again complained of sight loss in the right eye, this time accompanied by "tingling in the right hand." P. Ex. 1 at 87, 107. On June 4, 1997, she was admitted to the hospital for a one to two week history of a "viral type syndrome," consisting of aches, pain, headache, fevers, chills, nausea, vomiting, "some loose stools," "left sided weakness," and "confusion." Id. at 87, 98; P. Ex. 4 at 78. On admission, she had "right disc pallor," a 102 degree

[2]The facts are taken from the medical records filed in this case; no factual witnesses were presented at the trial.

temperature, and was "somewhat thrashing in bed." P. Ex. 1 at 87, 98. Her attending neurologist described her as "[q]uite confused," "unable to give a logical h[istory]," and failing to "answer most [questions]" although she "follow[ed] simple commands intermittently." P. Ex. 4 at 78. A June 6th EEG "showed a focal component in the patient's right temporal region raising the possibility of an infectious process or inflammatory process at that site." P. Ex. 1 at 100. Petitioner's June 11th "MRI with contrast . . . showed a subtle area of increased signal in the right parietal region, possibly reflecting underlying encephalitis." Id. at 99, 104. Various testing, including CSF, blood, and urine cultures, a cranial CT scan, and a chest x-ray, returned negative or otherwise excluded a number of etiologies for petitioner's acute illness, such as bacterial, lyme, syphilitic, TB, viral (e.g. herpes simplex virus), fungal, and Rocky Mountain Spotted Fever. Id. at 87, 99; P. Ex. 4 at 78; P. Ex. 8 at 42, 47; P. Ex. 18 at 193; but see P. Ex. 18 at 192 (June 18, 1997 Epstein Barr Virus results suggestive of a recent or past EBV infection). Petitioner was initially presumed to have "meningitis/encephalitis," but ultimately her treating physicians discharged her on June 16, 1997, from the Rehabilitation Unit, with a diagnosis of "Encephalitis of unknown type." P. Ex. 1 at 99; see also P. Ex. 4 at 78 (noting a diagnosis of "[i]nfectious meningitis which may or may not [be] related to her [right] optic neuropathy"). Thereafter, petitioner received additional hospital care and was finally discharged home on June 21, 1997, with diagnoses of "[questionable] acute disseminated encephalomyelitis, right optic neuritis, congenital Duane's syndrome, [and] urinary tract infection."[3] P. Ex. 1 at 87.

On July 2, 1997, petitioner again fell ill, presenting to Hartford Hospital for admission with a one to two day complaint of left-eye blurred vision, nausea, and "increasing dizziness and gait instability." Id. at 90-91; see also P. Ex. 4 at 72 (a April 27, 1999 record giving the July 1997 history of readmission for "intractable vomiting" of unclear etiology). Treatment included Solu-Medrol. P. Ex. 1 at 91. Extensive testing revealed normal or negative C3/C4 levels, lyme, liver enzymes, serum electrolytes, BUN, creatinine, ANA, rheumatoid factor, anti-cardiolipin antibodies, and "RNP/SM and Sjogren syndrome antibodies A and B." Id. at 90-91; P. Ex. 18 at 357-87. Petitioner's July 2, 1997 MRI brain results showed "[m]ultiple abnormalities" with "nonspecific" findings, with "[t]he possibilities of encephalitis or ADEM or even an acute demyelinating process . . . in consideration." P. Ex. 4 at 24. Because of her June admission, petitioner's "presentation was not felt to be typical for multiple sclerosis" but her treating physicians did worry about another autoimmune demyelinating diastasis. P. Ex. 1 at 90-91. Her physician was not clear whether her condition was "due to acute disseminated encephalomyelitis or a form fruste of Behcet's disease." Id. Other differential diagnoses included ADEM, multiple sclerosis ("MS"), and vasculitis. P. Ex. 18 at 322. Petitioner was discharged on July 8, 1997. P. Ex. 1 at 90-91.

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[3]The records state that "within a short period of time [after her June admission, petitioner] developed tingling sensations in the feet in association with urinary retention." P. Ex. 1 at 90-91. A June 26, 1997 urological consult letter states that petitioner's voiding dysfunction "raise[d] the question of multiple sclerosis, however, this [did] not appear to be confirmed on [previous] MRI." Id. at 95.

Petitioner's health problems waxed and waned throughout 1997 and 1998. A September 2, 1997 brain MRI revealed "[i]mproving areas of white matter hyperintensity thought clinically to represent ADEM. This has significantly improved." P. Ex. 4 at 22. In early October 1997, petitioner was still followed for encephalomyelitis and complaints of "weakness [and] numbness in legs." P. Ex. 3 at 30. A December 5, 1997 brain MRI scan showed results "compatible with focal demyelination of the optic nerve." Id. at 66. In late January 1998, petitioner was "doing extremely well with no evidence of activity of her acute disseminated encephalomyelitis." P. Ex. 2 at 24. Petitioner then developed left optic neuritis in May 1998 (and again in January 1999). P. Ex. 4 at 72. In September 1998, neuro-ophthalmologist Dr. Lesser addressed petitioner's question of the hepatitis A's role in her illness, to which he replied that he did not "know, but it definitely could be a possibility since we do know that influenza vaccine can sometimes be a precipitating factor." P. Ex. 3 at 74.

Between July 1997 and February 1999, petitioner's condition was characterized as autoimmune optic neuropathy with encephalopathy, acute demyelinating encephalomyelitis[4], "recurrent" acute demyelinating encephalomyelitis, and "[m]ultiphasic" acute demyelinating encephalomyelitis. Id. at 32, 34; P. Ex. 1 at 41-42, 50, 85. Lupus, Susac's Syndrome, Behcet's, and multiple sclerosis remained in the differential.[5] P. Ex. 1 at 85; P. Ex. 3 at 34; P. Ex. 4 at 74. By April 27, 1999, diagnoses of "neurosarcoid or isolated angiitis of the CNS" entered the picture. Neurologist Dr. Vollmer assessed either as "the most likely diagnoses" given petitioner's "2 year[] [history] without evidence of systemic involvement," although he retained MS as a possibility. P. Ex. 4 at 74. A MRI performed May 15, 1999, "reveal[ed] some small abnormalities scattered throughout the white matter, suggestive of vasculitis or sarcoid or parinfectious disease." Id. at 23. Dr. Vollmer believed this "pattern [was] not typical of multiple sclerosis" and opined that "[g]iven the lack of confirmatory evidence for multiple sclerosis, and lack of evidence of recent progression, I am unable to make a definitive diagnosis at this time. Nevertheless, I do not see evidence of multiple sclerosis, but remain concerned that there may be some other inflammatory disease." Id. On June 10, 1999, Dr. Silvers' neurologic follow-up notes state that "[w]hile primary CNS vasculitis is a thought, I would think that the absence of significant headache, the initial episode of a febrile encephalomyelitis and the MRI's would support a demyelinating illness." P. Ex. 1 at 37-38. At the

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[4]Dr. Lesser's June 4, 1998 letter to neurologist Dr. Silvers states that he thinks she has ADEM although the findings are "unusual and atypical." P. Ex. 3 at 78.

[5]See also P. Ex. 1 at 50 (Dr. Silvers stating that "[s]everal points against MS are her initial encephalomyelopathic presentation, along with her completely normal MRI and CSF"); see id. at 85 (Dr. Silvers stating that petitioner's "acute febrile encephalomyelitic illness . . . would be unusual for Multiple Sclerosis"); P. Ex. 3 at 85 (Dr. Lesser considering Susac's Syndrome unlikely given petitioner's negative history for hearing loss); P. Ex. 4 at 74 (neurologist Dr. Vollmer reporting in April 1999 that "Behcet's seems unlikely, given lack of meningitic symptoms or recurrent headaches plus the patient has no history of mouth or vaginal ulcers. . . . Multiple sclerosis is not suggested by the MRI and would be somewhat inconsistent with the episode of encephalopathy. Nevertheless, it remains in the differential diagnosis").

end of 1999, the diagnosis of "Probable multiphasic ADEM" remained present in the records. Id. at 11, 18; see also P. Ex. 1 at 21 (VAERS report completed December 22, 1999, listing as the adverse reaction "Acute Disseminated Encephalomyelitis").

On August 6, 2000, petitioner suffered a brain seizure. P. Ex. 25 at 58. Following a subsequent brain biopsy, petitioner was diagnosed with "vasculitis with secondary tissue destruction and demyelination consistent with primary angiitis," although the pathology report stated that "[c]linically and pathologically, this is an unusual presentation and evolution of cerebral vasculitis, and no agreement was reached on the nature of the disease" and "[m]orphologically, the features are those of a primary vasculitis of the brain." Id. at 46. A radiological record dated three months later, December 2, 2000, reported the existence of "[e]vidence of very minimal progression of Multiple Sclerosis changes in the left parietal lobe." Id. at 137. A record dated December 11, 2000, evinces petitioner's treaters' ongoing lack of confidence in the proper diagnosis for her condition:

> [The] biopsy suggested CNS vasculitis, but also shows some demyelination and macrophasias, suggesting possibly an acute demyelinating lesion. Unfortunately, the patient's history and MRI is not specific and does not eliminate the possibility that she has CNS vasculitis despite this. Therefore, I am unable to distinguish clearly between these two possibilities and do not believe that further lumbar punctures or other diagnostic tests will help clarify this issue.

P. Ex. 23 at 2. See also P. Ex. 25 at 25 (record dated March 3, 2001, stating that the biopsy "findings are rather nonspecific and the diagnostic possibilities in light of the biopsy would still be vasculitis and remotely a demyelinating disease. The distribution of the abnormal signal is rather nonspecific for demyelinating disease"). Petitioner continues to receive treatment for her ongoing illness.

III. EXPERT TESTIMONY

Petitioner's Expert: Derek R. Smith, M.D.[6]

Dr. Smith is "highly confident that, in the right individuals, a tetanus toxoid vaccination can cause central nervous system demyelination." Tr. at 35. He further opines that the tetanus toxoid vaccine more probably than not substantially contributed to Mrs. Althen's optic neuritis and subsequent demyelinating disorder. Id. at 12-13, 35, 39, 45; P. Ex. 21 at 2 (Medical Expert Report of Dr. Smith), filed July 6, 2001.

Dr. Smith's opinion of general causation is rooted in the theory of "degeneracy." Tr. at 30. This theory, which is based on the evolution of the molecular mimicry concept, raises the "possibility" that in addition to responding to the specific antigen or peptide, in this case the tetanus antigen, T cells can *also* mistakenly respond to non-specific or non-native antigens such as central nervous system ("CNS") myelin antigens. Id. at 28, 30. Per Dr. Smith, this mistake occurs because "the T cells can't . . . distinguish between the [vaccine's] peptide and the normal body protein [or self-antigen]." Id. at 30. Dr. Smith believes this evolution of the molecular mimicry theory makes "plausible" the causal relationship between tetanus and demyelinating illnesses.[7] Id. at 31.

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[6]Dr. Smith is a board-certified neurologist, with a sub-speciality in multiple sclerosis and neuroimmunology, currently serving as a Clinical Instructor at Harvard Medical School and as an Associate Professor of Neurology at Brigham and Women's Hospital in Boston, Massachusetts. His research interests include immune mechanisms in multiple sclerosis, clinical trials in multiple sclerosis, and immune deviation via therapeutic modalities. Dr. Smith has published on multiple sclerosis and neurologic injuries. He treats exclusively MS patients, about 100-150 per month. His practice consists of rendering first and second opinions, following multiple sclerosis patients long-term, and conducting clinical trials for future treatments of MS. He has researched the pathophysiology of MS by "looking at the T cell function in patients with MS" and assessing the normality of their functioning within the immune system. See Tr. at 4-7; P. Ex. D at 1-3 (*Curriculum Vitae*), filed July 16, 2001. The court found Dr. Smith knowledgeable about his area of expertise and the facts of this case; he testified cogently and credibly.

[7]Dr. Smith touched on several other theories, but none were well-developed through the testimony or he otherwise failed to persuasively attach these theories to the tetanus toxoid vaccine. For instance, he analogized peripheral and central nervous system disorders, based on the IOM's 1994 findings of a probable causal relation between tetanus toxoid and two injuries, brachial neuritis and acute inflammatory demyelinating polyradiculoneuropathy, also known as Guillain-Barré Syndrome ("GBS"). P. Ex. 21 at 2; Tr. at 18. Dr. Smith explained "that there is antigenic sharing between the central and peripheral nervous system, and that MS patients may have have [sic] involvement of the peripheral nervous system in their disease." P. Ex. 21 at 2; see also Tr. at 18-19. Hence, T cells activated in the peripheral nervous system could enter the central nervous system through their normal traversing of the protective blood brain barrier, presumably allowing then for the T cells' attack on central nervous system antigens which are shared with the peripheral system.

Dr. Smith also believes the tetanus vaccination is responsible for Mrs. Althen's *chronic* condition. Id. at 37. Dr. Smith explains that an acute immune response can become chronic, as in petitioner's case, through "epitope spreading" which is the "spreading or the increase in the variety of the peptides or antigens to which . . . the T cells are responding and [the] increase in the variety of the T cells as well."[8] Id. at 33, 34. As these new T cells are created, the inflammation caused by the initial T cell receptor immune response is either prolonged by this event, or the T cells can become auto-reactive at a later date to a self-antigen, explaining the chronicity of the acute demyelinating event. Tr. at 33-34. Dr. Smith opines that epitope spreading "is probably an important part of . . . why many autoimmune diseases become chronic." Id. at 34. In petitioner's case, he testified, "the initial inflammatory events probably initiated some epitope spreading . . . some creation of a variety of memory cells, and it's because of that, that she then went on to develop a relapsing form of illness." Id. at 37.

In support of his opinions, Dr. Smith states that degeneracy of T cell responses is a widely recognized principle in medicine, accepted in the field of neuroimmunology and supported by the literature. Id. at 30-31, 32, 38. He acknowledges the Institute of Medicine's ("IOM") findings that the evidence is inadequate to accept or reject a causal relation between diphtheria-tetanus or tetanus toxoid and CNS demyelination (including ADEM, transverse myelitis, and optic neuritis), but he believes the degeneracy theory has developed *since* the IOM report, evolving through laboratory work rather than confined to "epidemiologic literature" as was the IOM's review. Id. at 38-49. He asserts further that studies by Dr. Martin and Kai W. Wucherpfennig "demonstrate[] that wider variety of antigenic epitopes than previously imagined may be involved in the T cell responses which underly the immunopathogenesis of CNS inflammatory disorders such as MS." P. Ex. 21 at 2; see also P. Ex. B (Kai W. Wucherpfennig & Jack L. Strominger, Molecular Mimicry in T Cell-Mediated Autoimmunity: Viral Peptides Activate Human T Cell Clones Specific for Myelin Basic Protein, 80 Cell 695 (1995)). For Dr. Smith, "[t]his work suggests that specific segments of the tetanus toxoid protein may potentially trigger the activation of T cells which in some individuals can then lead to immune mediated injury of the peripheral or central nervous system." P. Ex. 21 at 2. He believes the degeneracy theory goes to the biologic plausibility argument. Tr. at 48-49.

Tr. at 19-21. Second, he proposed that the demyelination in this case could have resulted from "bystander activation," a theory he described as "well recognized in immunology" and founded in the literature, where the vaccine itself could have "incited and recruited, sort of in a bystander fashion, some T cells that may have been . . . circulating in Ms. Althen's system." Id. at 35, 39. This "could have been just enough to push those over and . . . become activated enough that they caused the demyelination." Id. at 35. Essentially, under the bystander theory, the "activation of the immune system" "can promote other parts of the immune system to become active." Id. at 37.

[8]Dr. Smith explains that "an immune response . . . is initially very restricted to a few different types of T cells"; it is when a few of the T cells become "more widespread" "because of continuing inflammation" that "involve[ment] [of] more different T cells, more different antigens" results, leading to the chronic demyelinating illness. Tr. at 33.

In turning to the specifics of petitioner's case, Dr. Smith recognizes that identifying Mrs. Althen's condition is difficult, but believes calling her illness relapsing ADEM or MS "is not a big issue[,] [t]hose are probably the same entity," "the underlying inflammatory process is undoubtedly the same in each instance," and her condition evidently developed following her March 28, 1997 vaccinations. Id. at 15; P. Ex. 21 at 2. He does, however, disagree with a diagnosis of vasculitis, believing that the pathological findings do not meet "the strictest standard for vasculitis" and "are consistent" instead with "acute multiple sclerosis." Tr. at 15, 16. But see P. Ex. 21 at 2 (describing petitioner's condition as "relapsing acute disseminated encephalomyelitis or fulminant multiple sclerosis or primary CNS vasculitis" and acknowledging that her "clinical history does not fit neatly into one specific diagnosis").

Regardless of her diagnosis, Dr. Smith finds the onset of injury temporally appropriate in this case, based on literature discussing viral illnesses and the onset or relapse of multiple sclerosis; that literature places the time frame at three weeks. Tr. at 38. In addition, he finds her medical history absent of alternative causes.[9] He notes the records show "no preceding viral infection" or "other explanation" for her "sudden onset of profound immune responses in the central nervous system" and she presented with optic neuritis, "a frequent presenting symptom for central nervous system demyelination."[10] Id. at 13-14. Dr. Smith also thinks it "highly unlikely" that her optic neuritis is a discrete acute event unrelated to the June events. Id. at 62. To that end, he rejects that a virus is responsible for petitioner's post-optic neuritis flu-like symptoms because while "[g]enerally, autoimmune processes follow viral infections[,] [i]n this case, it would appear that the . . . central nervous system was affected first." Id. at 55. That is, "there was no evidence of a viral infection before there was clear evidence of central nervous system demyelination." Id. at 57. He also explained that with "massive inflammation in the brain," one can also have "fever and evidence of systemic inflammation because the brain is, after all part of the body, and . . . even diarrhea because the gastrointestinal tract is, . . . to some degree under the control of the sympathetic nervous system, and, therefore, the central nervous system."[11] Id. at 55-56. Thus, "it's very difficult to know, with somebody with massive central nervous system inflammation, whether or not there may, *also*, be a systemic infection." Tr. at 56 (italics added). For Dr. Smith, the fact that Mrs. Althen suffered a CNS onset before her systemic symptoms tells him her post-optic neuritis condition was not viral-related. Id. He also points to her negative test results to refute a CNS infection. Id. Finally, Dr. Smith believes Mrs. Althen's second hepatitis A vaccine, administered the same day as her tetanus toxoid vaccine, while in theory perhaps a contributor to her illness, was not implicated by his

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[9]He believes that due to her "previous history of autoimmune thyroiditis," she "showed a previous predisposition to autoimmunity." Tr. at 13.

[10]Dr. Smith testified that alternative causes for optic neuritis include other non-CNS autoimmune diseases but not many infectious causes; there are, however, mitochondrial disorders which can appear with an optic neuritis-like event. Tr. at 61.

[11]Dr. Smith testified that white blood cell increases can also occur with massive CNS inflammation. Tr. at 57-58.

findings. Id. at 62-63. In addition, Mrs. Althen did not adversely react to her earlier hepatitis A vaccination. Id. at 62. Thus, he cannot "assign relative likelihoods [of the hepatitis A vaccine's contribution] otherwise." Id. at 63.

Respondent's Expert: Arthur P. Safran, M.D.[12]

Dr. Safran rejects a causal relationship between Mrs. Althen's tetanus toxoid vaccine and her illness. R. Ex. A at 2 (Medical Expert Report of Dr. Safran), filed November 20, 2001. He recognizes, as did Dr. Smith and Mrs. Althen's treating physicians, the difficulty in characterizing petitioner's unique illness but believes the "most likely" diagnosis is "vasculitis or angitis of the central nervous system."[13] Id. at 1-2; Tr. at 134-35, 138-39, 145, 160-63. He retains multiple sclerosis in the differential diagnosis, but as a less likely alternative given her early MRI results showing no lesions.[14] R. Ex. A at 1; Tr. at 134, 138-40, 162, 163. His reasons for focusing on vasculitis are several. First, he notes that "[t]hree blood relatives [of Mrs. Althen's] have aneurysmal abnormalities" and "[a]neurysms are identified as being associated with vasculitis." R. Ex. A at 1. Second, Mrs. Althen's "brain biopsy [in 2000] shows some evidence of demyelination, as well as vasculitis." Id. Third, petitioner's treating physicians did not treat her for MS, but for vasculitis. Tr. at 134, 135. Fourth, petitioner suffered initially the onset of optic neuritis, which a "vasculitic illness" "is known to cause." Id. at 160-62. Finally, her onset fell within a medically accepted time

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[12]Dr. Safran is board-certified in internal medicine and neurology and currently serves as an Associate Clinical Professor, Instructor, and Lecturer on neurology at Boston University School of Medicine, Tufts University School of Medicine, and Harvard Medical School respectively. His administrative appointments include Chief of Neurology at MetroWest Medical Center and the Medical Director of its Braintree Rehabilitation Unit, a multiple sclerosis clinic. He also serves as an Attending Neurologist and Associate Physician at Boston area hospitals. In his clinical practice, Dr. Safran treats patients with various neurologic disorders of the peripheral and central nervous systems, the largest percentage being multiple sclerosis patients. Dr. Safran has published journal and other reference material articles on multiple sclerosis. See Tr. at 131-32; R. Ex. B at 1-4 (*Curriculum Vitae*), filed November 20, 2001. The court is familiar with Dr. Safran from previous testimony before this court. While Dr. Safran's testimony was credible, it did not add significantly to the resolution of the issues before the court.

[13]Dr. Safran defines vasculitis as "an inflammation disorder of blood vessels" which "can be limited to the central nervous system" or can be "more generalized." Tr. at 135. He does not know the causes of vasculitis/angitis. Id. at 163.

[14]Dr. Safran rejects ADEM in this case, that condition being "a monophasic disease" rather than a "relapsing remitting illness," meaning "it comes, it lasts for a period of time, and then it stops leaving you with some or no residual." R. Ex. A at 2; Tr. at 134, 144. In his view, "recurrent ADEM is multiple sclerosis" and "[m]any patients initially thought to have acute demyelinating encephalomyelopathy ultimately are found to have multiple sclerosis." R. Ex. A at 2; Tr. at 144. See also Tr. at 152.

period for an immune mediated illness. Id. at 157, 159. Thus, he concludes that her entire course, from the April onset of optic neuritis to the subsequent symptoms, represents all one vasculitic illness. Id. at 160-62.

Regardless of the characterization of petitioner's illness, Dr. Safran finds no support in the literature to link the tetanus toxoid to a neurological condition manifesting two weeks post-vaccination as optic neuritis which progresses into vasculitis or MS. R. Ex. A at 2. Nor is he aware of case reports or epidemiology supporting a link between the tetanus toxoid and CNS disorders, despite the large number of individuals routinely receiving the vaccine. Tr. at 137, 138, 147, 151. In his view, the low incidence rates and "the unique nature of [petitioner's] occurrence . . . make[s] the [causal] connection exceedingly remote," although he concedes anything is possible. Id. at 159. Finally, Dr. Safran finds flawed Dr. Smith's reliance on the IOM's finding of a probable relationship between tetanus toxoid and GBS, a peripheral nervous system disorder, to explain the immune process between the vaccine and the CNS. He states: "The cells [involved in myelination in the two systems] are different, and the epidemiology is not shown." Id. at 136; see also Tr. at 137, 156.

Respondent's Expert: Roland Martin, M.D.[15]

Dr. Martin limited his hearing testimony to his own research and knowledge of the general causation issues in this case.[16] Tr. at 68. Dr. Martin is unaware of "published data, either in clinical

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[15]Dr. Martin's expert report can be found at R. Ex. C, filed Nov. 20, 2001. Dr. Martin is board-certified in neurology and electrophysiology and currently serves as the Acting Chief of the Cellular Immunology Section in the Neuroimmunology Branch at NIH where they "study T cell immunology and its relation to neuro-immunological disorders[,] particularly MS." He is also an Adjunct Professor of Neurology at the University of Maryland's Baltimore Medical School and an Adjunct Professor at Howard University in neurology, immunology, and genetics. At NIH, he directs a laboratory and "clinical service that focuses entirely on neuroimmunological questions" with 85% of cases relating to MS specifically. They "run clinical trials [and] . . . study basic immunology of MS, the mechanism of onset and perpetuation of the disease"; he also sees patients with MS, ADEM, and vasculitis. Dr. Martin has served on scientific advisory committees relating to multiple sclerosis and immune tolerance and acted as an *ad hoc* reviewer for numerous scientific journals, including those discussing neurology, multiple sclerosis, immunology, neuroimmunology, and virology. He has also published on viral meningoencephalitis, multiple sclerosis, autoimmune T cell reactions, Lyme disease, rubella panencephalitis, and demyelinating diseases. See Tr. at 65-67; R. Ex. D at 1-3, 5-23 (*Curriculum Vitae*), filed November 20, 2001. Dr. Martin demonstrated significant knowledge about his medical field and its application to the general causation issue in this case. He presented cogent, credible testimony.

[16]Dr. Martin did not review petitioner's medical records, but accepts that petitioner unquestionably suffers from a CNS disorder and suffered the onset of her optic neuritis within a medically appropriate time period for immune mediated responses. Tr. at 68, 69, 77, 119-20. With what facts Dr. Martin was made aware of, he believes Mrs. Althen's May and June 1997 symptoms

characteristic form or in basic immunology either in animal models or in vitro, suggesting that tetanus toxoid can trigger central nervous system specific T cells or start a demyelinating disease of the central nervous system." Id. at 69, 91; see also Tr. at 84-85, 126. He does, however, accept the evolution of the molecular mimicry concept[17] and that science "now believe[s] that T cells are able to recognize a wide variety of antigen." Tr. at 70-71; see also id. at 96. He thus concedes the biologic plausibility of Dr. Smith's theory of degeneracy, that some T cells will recognize model antigens and respond, but notes that there must exist some similarity in the interface between the peptides of the tetanus vaccine and the self-antigen for the foreign antigen, the tetanus, to cause or trigger a stronger immune response to the self-antigen.[18] Tr. at 96-98, 103-04. Dr. Martin explains this in the context of the tetanus vaccine: "[W]hat the immunological community, at the moment, thinks is necessary to trigger a strong immune response" is, "in the case of bacteria, signals on the surface that are strongly recognized by cells of the innate immune system that are not specific for antigen, but recognize these evolutionary very preserved signals of something dangerous." Id. at 72. Tetanus toxoid does not provide these signals as it is "an *attenuated* or *modified* toxin of the bacteria" and does not contain a virus. Id. at 73.

Dr. Martin testified further that the plausibility of Dr. Smith's causal theory could be demonstrated by showing "that T cells that can be relatively easily demonstrated cross-react with one component with the brain [or CSF] making this entire framework that we discussed plausible in that particular case, and that there is crossover activity with the component of the nervous system." Tr. at 120-21; see also id. at 118-19. Of course, he notes, the intended consequence of a vaccination *is* that the T cells react to the foreign antigen. Tr. at 120. Additionally, consistent with Dr. Smith's

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are "not compatible with MS or a demyelinating disease" but with a viral or bacterial meningitis. Id. at 76. Thus, in contrast to Dr. Safran's opinion, he opines that the link between her optic neuritis and later symptoms is speculative. Id.

[17]Dr. Martin defines molecular mimicry as "similarities between a foreign antigen such as tetanus toxoid and a self antigen, e.g., a myelin component" or the notion that "a self-antigen from various organs or tissues of the body can be, can have similarities with parts of an antigen or protein from a foreign agent; for example, a virus or bacteria." R. Ex. C at 1; Tr. at 70. However, he opines that molecular mimicry alone cannot "trigger an autoimmune disease" according to the available scientific evidence. R. Ex. C at 1, 2; see also Tr. at 72. The only instance in which Dr. Martin can conceive of the possibility of an autoimmune disease through molecular mimicry is "in individuals with a particularly susceptible genetic background, and in addition strong unspecific factors that stimulate the immune system such as a viral infection." R. Ex. C at 2; see also Tr. at 99, 109, 113, 118 (susceptibility of developing an autoimmune disease influenced by timing, other stimuli present, genetics or environmental factors).

[18]He also notes that T cells cannot be activated to become memory T cells (to be activated at a later time, for instance) by peptides alone; the T cell needs a co-stimulatory response and will not recognize whether the peptide is from an immunization or infection. Tr. at 101-03.

testimony, he would expect onset within the range of seven days to four weeks following vaccination. Id. at 119-20.

Dr. Martin does agree with Dr. Smith and the literature that it is scientifically "plausible" "that the chronic disease could be maintained by epitope spreading." Id. at 107-08. He notes the literature has shown in animal models that during a persistent virus the animal "may, also, develop cells responding to nervous system antigens," resulting in an ongoing nervous system injury. Id. at 106. However, Dr. Martin believes that in the models, it is the initial "T reactive cells" which "remain[] the most important"; thus, for him, "to what extent [epitope spreading] contributes to the disease is not clear [at] the moment." Id. at 107, 108.

Finally, Dr. Martin considers it likely or possible, although he sees no evidence supporting this, that the tetanus toxoid's ability to cause a peripheral nervous system autoimmune disease, such as GBS, means it could similarly cause a CNS disorder. Tr. at 78, 81.

IV. THE VACCINE ACT AND RELEVANT JURISPRUDENCE

Entitlement to compensation under the Vaccine Act rests on petitioner's ability to establish causation either through the statutorily prescribed presumption of causation (for on-Table injuries) or by proving causation-in-fact (for off-Table injuries). See §11(c)(1); 42 C.F.R. §100.3 (1997). Claimants must prove their case by a preponderance of the evidence. §13(a)(1)(A). This requires that the trier of fact "believe that the existence of a fact is more probable than its nonexistence before [the special master] may find in favor of the party who has the burden to persuade the [special master] of the fact's existence." Hodges v. Secretary of HHS, 9 F.3d 958, 963 (Fed. Cir. 1993) (Newman, J., dissenting) (citing Concrete Pipe and Products of California, Inc. v. Construction Laborers Pension Trust for Southern California, 508 U.S. 602 (1993), quoting In re Winship, 397 U.S. 358, 371-72 (1970) (Harlan, J., concurring)).

This case involves off-Table injuries. Thus, the evidence must preponderate in favor of a finding that the vaccination in question more likely than not actually caused the injury alleged before petitioner may receive an award. See, e.g., Bunting v. Secretary of HHS, 931 F.2d 867, 872 (Fed. Cir. 1991); Hines v. Secretary of HHS, 940 F.2d 1518, 1525 (Fed. Cir. 1991); Grant v. Secretary of HHS, 956 F.2d 1144, 1146, 1148 (Fed. Cir. 1992). See also §§11(c)(1)(C)(ii)(I) and (II). To meet this preponderance of the evidence standard, "[a petitioner must] show a medical theory causally connecting the vaccination and the injury." Grant, 956 F.2d at 1148 (citations omitted); Shyface v. Secretary of HHS, 165 F.3d 1344, 1353 (Fed. Cir. 1999). A persuasive medical theory is shown by "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury." Hines, 940 F.2d at 1525; Grant, 956 F.2d at 1148; Jay v. Secretary of HHS, 998 F.2d 979, 984 (Fed. Cir. 1993); Hodges, 9 F.3d at 961; Knudsen v. Secretary of HHS, 35 F.3d 543, 548 (Fed. Cir. 1994). Furthermore, the logical sequence of cause and effect must be supported by "[a] reputable medical or scientific explanation" which is "evidence in the form of scientific studies or

expert medical testimony." Grant, 956 F.2d at 1148; Jay, 998 F.2d at 984; Hodges, 9 F.3d at 960.[19] See also H.R. Rep. No. 99-908, Pt. 1, at 15 (1986), reprinted in 1986 U.S.C.C.A.N 6344. While petitioner need not show that the vaccine was the sole or even predominant cause of the injury, petitioner bears the burden of establishing "that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Shyface, 165 F.3d at 1352-53. Petitioners do not meet their affirmative obligation to show actual causation by simply demonstrating an injury which bears similarity to a Table injury or to the Table time periods. Grant, 956 F.2d at 1148. See also H.R. Rep. No. 99-908, Pt. 1, at 15 (1986), reprinted in 1986 U.S.C.C.A.N 6344. Nor do petitioners satisfy this burden by merely showing a proximate temporal association between the vaccination and the injury. Grant, 956 F.2d at 1148 (quoting Hasler v. United States, 718 F.2d 202, 205 (6th Cir. 1983), cert. denied, 469 U.S. 817 (1984) (stating "inoculation is not the cause of every event that occurs within the ten day period [following it]. . . . Without more, this proximate temporal relationship will not support a finding of causation")); Hodges, 9 F.3d at 960. Finally, a petitioner does not demonstrate actual causation by solely eliminating other potential causes of the injury. Grant, 956 F.2d at 1149-50; Hodges, 9 F.3d at 960.

Furthermore, as found by this court, in the absence of epidemiological evidence, petitioner must provide proof of (1) medical plausibility, (2) confirmation of medical plausibility from the medical community and literature, (3) an injury recognized by the medical plausibility evidence and literature, (4) a medically acceptable temporal relationship between the vaccination and the onset of the alleged injury, and (5) the elimination of other causes. See Stevens v. Secretary of HHS, No. 99-594V, 2001 WL 387418, at *23-*26 (Fed. Cl. Spec. Mstr. Mar. 30, 2001). See also White v. Secretary of HHS, No. 98-426V, 2002 WL 1488764, at *11-*17 (Fed. Cl. Spec. Mstr. May 10,

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[19]The general acceptance of a theory within the scientific community can have a bearing on the question of assessing reliability while a theory that has attracted only minimal support may be viewed with skepticism. Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579, 594 (1993). Although the Federal Rules of Evidence do not apply in Program proceedings, the United States Court of Federal Claims has held that "Daubert is useful in providing a framework for evaluating the reliability of scientific evidence." Terran v. Secretary of HHS, 41 Fed. Cl. 330, 336 (1998), aff'd, 195 F.3d 1302, 1316 (Fed. Cir. 1999). In Daubert, the Supreme Court noted that scientific knowledge "connotes more than subjective belief or unsupported speculation." Daubert, 509 U.S. at 590. Rather, some application of the scientific method must have been employed to validate the expert's opinion. Id. Factors relevant to that determination may include, but are not limited to:

> whether the theory or technique employed by the expert is generally accepted in the scientific community; whether it's been subjected to peer review and publication; whether it can be and has been tested; and whether the known potential rate of error is acceptable.

Daubert v. Merrell Dow Pharmaceuticals, Inc., 43 F.3d 1311, 1316 (9th Cir. 1995) (Kozinski, J.), on remand from 509 U.S. 579 (1993); see also Daubert, 509 U.S. at 592-94.

2002); Watson v. Secretary of HHS, No. 96-639V, 2001 WL 1682537, at *19 (Fed. Cl. Spec. Mstr. Dec. 18, 2001).

The court addresses petitioner's off-Table claim in light of these governing principles.

V. DISCUSSION

This case presents difficult and involved medical and legal causation issues. The parties presented credible testimony from three highly credentialed and experienced experts. The only issue the court must resolve is whether petitioner satisfied the standard established in Stevens.[20] As shown below, for purposes of the court's analysis and conclusion, it does not matter whether petitioner's injury is characterized as ADEM, multiple sclerosis, vasculitis, or some other demyelinating illness. The undersigned now turns to the Stevens prongs.

Prong One of Stevens

Prong One of the Stevens causation-in-fact standard, medical plausibility, is demonstrated by "proffering a theory of biologic mechanism by which a *component* of the vaccine can cause the type of injury suffered." Stevens, 2001 WL 387418, at *23 (italics in original). As explained in Stevens, "[t]his is not a rigorous burden."[21] Id. "Experts routinely rely on fundamental scientific or medical concepts rooted in the literature on immunology, neurology, toxicology, and other disciplines to show that a component of the vaccine is capable of causing the alleged injury." Id. However, "[w]hile demonstrating a biologic mechanism requires support from science or medicine for implicating a component of the vaccine, petitioners need not prove here that the literature associates *the vaccine itself* with the alleged injury (which is instead the inquiry in Prong Two)." Id. Nor is presentation of a "*detailed medical and scientific exposition* on the biological mechanisms" required. Knudsen v. Secretary of HHS, 35 F.3d 543, 549 (Fed. Cir. 1994) (italics added).

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[20]Respondent insists on incorrectly characterizing the Stevens analysis as an "*alternative* evidentiary standard." Respondent's Written Closing Argument at 9, filed February 19, 2003 (italics added). Stevens is appropriately characterized as this court's application of the controlling case law to the types of evidence routinely presented and testified to in vaccine cases.

[21]Respondent has latched on to this phrase as an indication that this court is improperly reducing petitioner's statutory burden of proof; some clarification is warranted. Petitioner's burden under Prong One is not "rigorous," in the undersigned's experience, because hundreds of cases have shown just that – the Institute of Medicine and the experts frequently support, as they did here, that identifiable components of the vaccine can cause the injuries alleged. The relative ease with which some petitioners have satisfied this prong is a *reflection of medical reality,* as seen in cases presented before this special master; it is **not** a reflection of any reduction of any burden imposed by the Act.

In this case, petitioner's expert's theory of degeneracy is based on the premise that T cells coming into contact with the tetanus antigen or peptide, a "component" of the vaccine, can *also* mistakenly respond to a variety of non-specific or non-native antigens such as central nervous system self-antigens. Tr. at 28-30, 31. This theory of degeneracy (as well as Dr. Smith's theory of epitope spreading) is deemed theoretically possible, even scientifically plausible, by Dr. Martin.[22] See, e.g., id. at 84, 88, 96, 98, 103, 104, 105-08, 111, 122-24. See also Tr. at 70 (Dr. Martin testifying it is theoretically possible that the tetanus toxoid vaccine can trigger CNS disorders); id. at 88 (Dr. Martin testifying that there is a possibility that immunizations can cause CNS disorders).[23]

Dr. Smith's theory of medical plausibility through degeneracy (and its predecessor molecular mimicry) also finds support in the field of immunology, although not in the context of the vaccine itself which is nevertheless not part of petitioner's burden under Prong One. In Petitioner's Exhibit B, authors Wucherpfennig and Strominger hypothesize in the context of molecular mimicry that "[s]tructural similarity between viral T cell epitopes and self-peptides could lead to the induction of an autoaggressive T cell response." P. Ex. B at 695.[24] The authors explain:

> The mechanism(s) leading to clonal expansion of MBP [myelin basic protein]-reactive T cells remains to be identified, but could involve recognition of viral peptides with sufficient structural similarity to the immunodominant MBP peptide. . . . The initiation of autoimmunity by such a mechanism could then lead to sensitization to other CNS self-antigens by determinant spreading.

Id. (citations omitted). Wucherpfennig and Strominger conclude then that "[m]olecular mimicry of this immunodominant self-peptide by viruses therefore presents a possible mechanism for the induction of autoimmunity in MS." Id. at 696. The medical community's acceptance of the *evolution* of the molecular mimicry concept is also evident from petitioner's literature. The authors of Petitioner's Exhibit C, which counts respondent's expert Dr. Martin among the writers, state that "[a] novel concept for the occurrence of autoimmunity may be proposed on the basis of the following assumptions: (1) the self-peptide pool/MHC is a stimulus for T-cell survival; (2) TCR recognition is *highly degenerate*; and (3) a wide range of ligands with different affinities exists for each TCR."

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[22]Dr. Safran deferred to the expertise of Drs. Smith and Martin in discussing the immunological theory proposed in this case. Tr. at 146, 151, 156.

[23]Dr. Martin made clear that he does not disagree with the scientific possibilities proffered by Dr. Smith or that it is possible that "cross-activity may be involved" in relating immunizations and CNS disorders, but he fervently disagrees with Dr. Smith's ultimate evidentiary leap, that because of degeneracy or epitope spreading, it is more probably than not the case that *tetanus toxoid* can cause the injuries suffered here. Tr. at 83-85, 88.

[24]Kai W. Wucherpfennig & Jack L. Strominger, Molecular Mimicry in T Cell-Mediated Autoimmunity: Viral Peptides Activate Human T Cell Clones Specific for Myelin Basic Protein, 80 Cell 695 (1995).

P. Ex. C at 167 (footnotes omitted) (italics added).[25] Dr. Martin and his colleagues concluded that "[t]he *high degeneracy* of T-cell antigen recognition, as a result of significant contribution of the MHC to TCR affinity, has important consequences for many aspects of T-cell immunology." Id. (italics added).

Respondent's medical literature is equally supportive of Dr. Smith's causal mechanisms. For instance, in regards to molecular mimicry, Maier et al. state:

> One hypothesis to explain the link between infection and autoimmunity predicts that sequence similarity between microbial and self antigens (molecular mimicry) can activate autoreactive lymphocytes, thus enabling such cross-reactive lymphocytes to cause autoimmune damage in the host. Numerous reports demonstrate cross-reactive T cells which recognize both a defined microbial peptide and a highly homologous self peptide.

R. Ex. E at 448 (endnote omitted).[26] See also id. at 455 (in explaining the study findings' relationship to molecular mimicry: "Our data together with other available evidence suggest that cross-reactivity leading to T cell activation is a very frequent event") (endnotes omitted); R. Ex. F at 658 ("Alternatively, a structural similarity between microbial and self-antigens ('molecular mimicry') could have a key role in activating autoreactive T cells.").

The authors also state, in line with Dr. Smith's degeneracy theory, that "there is increasing evidence that individual T cells can recognize a variety of peptides, which do not possess strong sequence homology. Structural analyses have further illustrated the *degenerate* recognition of peptide-MHC complexes by individual TCR." R. Ex. E at 448 (endnotes omitted) (italics added).[27]

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[25]Bernhard Hemmer et al., Probing degeneracy in T-cell recognition using peptide combinatorial libraries, 19 Immunol. Today 163 (1998).

[26]Bert Maier et al., Multiple cross-reactive self-ligands for *Borrelia burgdorferi*-specific HLA-DR4-restricted T cells, 30 Eur. J. Immunol. 448 (2000).

[27]The court is aware of contrary evidence in the record that questions the sufficiency of the postulated mechanisms for autoimmunity. See, e.g., R. Ex. F at 658 ("However, in vivo evidence that molecular mimicry precipitates autoimmune disease *is lacking*. Actually, a single T-cell receptor can recognize many peptides, not all of which show strong sequence homology. The idea that cross-reactivity between a microbial peptide and a self-peptide causes autoimmunity *may therefore be simplistic*.") (footnotes omitted) (italics added) (Thomas Kamradt & N. Avrion Mitchison, Tolerance and Autoimmunity, 344 New Eng. J. Med. 655 (2001)); R. Ex. G at 185 ("However, to what extent the widespread peptide–cross-reactivities observed *in vitro* with some T cell clones can be extrapolated to actually inducing autoimmune disease *in vivo* is *still largely unresolved*.") (end italics added) (Matthias Regner & Paul-Henri Lambert, Autoimmunity through infection or immunization?, 2 Nature Immunol. 185 (2001)). See also Tr. at 84 (Dr. Martin

Respondent's Exhibit G is similarly supportive: "For many years molecular mimicry has provided a fertile framework for the field of autoimmune disease. *Attention to this scenario has even increased, with accumulating evidence that antigen recognition by the T cell receptor (TCR) is highly degenerate*." R. Ex. G at 185 (italics added).

In the article written by Drs. Kamradt and Mitchison, it is further noted that "[o]ptic neuritis is a common initial manifestation of multiple sclerosis and one from which patients often recover. Yet both patients with a single episode of optic neuritis and those in whom multiple sclerosis is eventually diagnosed *have T cells that recognize central nervous system antigens*." R. Ex. F at 658 (footnotes omitted) (italics added).

Moreover, the Institute of Medicine recognizes that molecular mimicry might be the mechanism supporting a biologically plausible relation between vaccines and demyelinating diseases of the central nervous system, thus lending credibility to the plausibility of Dr. Smith's theory of causation in this case. The IOM stated, in its 1994 report entitled, Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality:

> [I]t is biologically plausible that injection of an inactivated virus, bacterium, or live attenuated virus might induce in the susceptible host an autoimmune response by deregulation of the immune response, by nonspecific activation of the T cells directed against myelin proteins, *or by autoimmunity triggered by sequence similarities of proteins in the vaccine to host proteins such as those of myelin. The latter mechanism might evoke a response to a self-antigen, so-called molecular mimicry* (Fujinami and Oldstone, 1989).

Kathleen R. Stratton et al., Institute of Medicine, Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality 48, 84 (1994) (hereinafter "IOM 1994 Report") (italics added).[28] While the IOM uses "biologic plausibility" in assessing causality in a manner different than applied here, "what is important is that petitioner demonstrate 'a possible causal association [which] fits existing biologic or medical knowledge.'" Stevens, 2001 WL 387418, at *23, n.68 (citing Christopher P. Howson et al., Institute of Medicine, Adverse Effects of Pertussis and Rubella

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testifying that "[t]here is no good experimental or causalistic or medical evidence that it [i.e., degeneracy] leads to immune disease based on that mechanism by itself. That is why I disagree [with Dr. Smith's opinion]"); id. at 108, 122. However, on balance, the evidence preponderates in petitioner's favor under Prong One.

[28]The special masters frequently rely on the IOM's conclusions as a sound source for answering difficult issues of medical plausibility and causation. Due to the IOM's statutory charge, the scope of its review, and the cross-section of experts making up the committee reviewing the adverse events associated with vaccines, the court considers their determinations authoritative and subject to great deference. See, e.g., Watson v. Secretary of HHS, No. 96-639V, 2001 WL 1682537, at *5, n.11 (Fed. Cl. Spec. Mstr. Dec. 18, 2001); Stevens, 2001 WL 387418, at *2, n.5, *23, n.68.

Vaccines 54 (1991)). See also IOM 1994 Report at 22. Petitioner's expert has clearly done just that. The court is convinced that petitioner has satisfied Prong One of Stevens by offering a plausible medical explanation for how a component of the vaccine could cause the demyelinating injury alleged. The court now turns to an evaluation of petitioner's evidence under Prong Two of Stevens.

Prong Two of Stevens

Prong Two takes the theoretical plausibility in Prong One and advances it to a pragmatic level: it requires that petitioner provide confirmation from the relevant medical community that it is seeing, reporting (in peer-reviewed literature), and discussing a "suspected or potential association" between *the vaccine received* and the alleged injury. Stevens, 2001 WL 387418, at *24. As stated in Stevens, "[t]he court is concerned with the *fact* that a relationship is reported, rather than how that relationship is defined or by what criteria." Id. (italics in original). This concept is nicely expressed through Dr. Safran's testimony that "acceptability" within the medical community of a causal relation can be supported by "[s]omething short of published epidemiological data." Tr. at 166-67. Prong Two "is also not a demanding burden"; there is a variety of objective resources from which petitioners may gather their support.[29] Stevens, 2001 WL 387418, at *24. These resources include epidemiological studies, animal studies, case series, case reports, anecdotal reports, journal articles, manufacturing disclosures, Physician Desk Reference citations, and institutional findings, like those reported by the Institute of Medicine. Id. The experts play a critical and helpful role in explaining to the court how the pieces of information submitted confirm or negate the association of the injury alleged with the vaccine received. Without some objective confirmation that the vaccine administered is potentially associated with the injury alleged, petitioner's causal claims are mere speculation and thus insufficient. See Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579, 590 (1993) (stating that scientific knowledge "connotes more than subjective belief or unsupported speculation"). Petitioner need not demonstrate to a scientific certainty that the vaccine can cause the injury alleged. Rogers v. Secretary of HHS, No. 94-89V, 2000 WL 1337185, at *14 (Fed. Cl. Spec. Mstr. June 6, 2000).

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[29] In Stevens, the undersigned concluded Prong Two was "not a demanding burden." Stevens, 2001 WL 387418, at *24. Without a doubt, clarifying the Stevens standard is an evolving process, requiring that the court "fine tune" the prongs as further experience dictates. See, e.g., id. at *37 ("Finally, in proposing this five-prong analysis as a means of meeting the preponderance of evidence standard, the court stresses its flexibility and pragmatism. . . . The court fully expects that future cases will result in refinements to the criteria, clarifying intentions and defining acceptable proofs."). The court makes clear that to meet Prong Two, petitioners must produce objective, supportive medical literature recognizing a potential causative role of the vaccine. Relating the evidence to the vaccine received ensures that petitioner's plausibility argument under Prong One advances to what Daubert requires – objective confirmation within the relevant medical community. While Prong Two is not necessarily a difficult burden in the sense that petitioner may meet the prong with any number of different medical and scientific resources, Prong Two can prove a high hurdle for petitioner if the medical community is not confirming or recognizing the vaccine's role as advanced by petitioner. In fact, petitioner failed Prong Two in this case.

In this case, petitioner received the tetanus toxoid vaccine. When asked to provide literature in support of the link between tetanus toxoid vaccine and CNS disorders, Dr. Smith testified that it "is far from proven" and "in the case of tetanus, there have not been adequate epidemiologic studies to conclusively say whether or not it may provoke central nervous system demyelination." Tr. at 18, 50. Dr. Safran was unaware of literature either "thinking about" or statistically linking the tetanus toxoid vaccine and CNS disease, although he concedes that "acceptability" within the medical community of a causal relation can be supported by "[s]omething short of published epidemiological data." Id. at 147, 151, 166-67. Dr. Martin testified that despite his "agree[ment] with the theoretical possibility" of Dr. Smith's opinions, he "currently do[es] not have the evidence supporting it." Id. at 122; see also Tr. at 123, 124. It is for this reason that he is "concluding differently than Dr. Smith." Tr. at 122.[30]

Turning to the literature, the IOM concluded that "[t]here is biologic plausibility for a causal relation between vaccines and demyelinating disorders." IOM 1994 Report at 85. In fact, the IOM references case reports describing ADEM, optic neuritis, and other demyelinating diseases following the administration of the tetanus toxoid vaccine, but the Institute also concluded "there has not been a pathologically proven case of ADEM following administration of tetanus toxoid, DT, DPT, or Td." Id. at 83-85. Oddly, this portion of the report was not submitted by either party and the court did not find literature further describing these case reports in the record; the section of the 1994 report submitted by petitioner relates to GBS instead, which is not an illness alleged here (see P. Ex. A). Ultimately, despite the existence of these case reports, the IOM concluded that "[t]he evidence is inadequate to accept or reject a causal relation between tetanus toxoid, DT, or Td and demyelinating diseases of the CNS (ADEM, transverse myelitis, and optic neuritis)."[31] P. Ex. A at 86. And

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[30]Despite respondent's repeated recognition that for causation-in-fact to be legally established, epidemiologic studies are not required, their evidentiary presentations are to the contrary. Respondent's experts clearly entered the hearing predisposed to an opinion that causality can only be proven by epidemiology, despite medical literature, case law and respondent's own position to the contrary. See, e.g., IOM 1994 Report at 88-89; Stevens, 2001 WL 387418; Watson v. Secretary of HHS, No. 96-639V, 2001 WL 1682537, at *8 (Fed. Cl. Spec. Mstr. Dec. 18, 2001). Dr. Safran opined that causation is implausible if many individuals receive the vaccine but the occurrence of a vaccine-related condition is statistically low. Tr. at 163-67. He also testified that "were there some epidemiologic connection, we would have known it long ago." Id. at 138. In addition, Dr. Martin testified that he disagrees with the IOM's acceptance of a causal relation between GBS and tetanus toxoid because of its inability to establish relative risk estimates. Id. at 81. He would require sufficient proof in a "susceptible animal system" before he would accept a tetanus toxoid-CNS disease causal link. Id. See also Tr. at 112, 119.

[31]The IOM acknowledges that a determination that a vaccine can cause an injury is occasionally gleaned from individual case reports, and in compelling cases, from even one case report as was the case with TT and GBS. IOM 1994 Report at 22, 88-89. For this reason, the IOM concluded that "the *absence* of convincing case reports cannot be relied upon to answer *Can It?* in

although the IOM found that "[a] number of case reports in the medical literature have described *GBS* following receipt of tetanus toxoid," and "the evidence favors a causal relation between tetanus toxoid and GBS," petitioner's expert failed to present persuasive medical or scientific evidence supporting that a causal association between the *vaccine* and a *peripheral* nerve system condition (e.g., GBS) correlates to the *central* nervous system injuries (i.e., ADEM or MS) suffered by petitioner.[32] Id. at 86-89. Furthermore, while Wucherpfennig and Strominger offer a possible explanation, they do so only in the context of viral peptides and the tetanus toxoid vaccine does not contain a virus:

> Since only activated T cells can cross the blood-brain barrier, activation of T cells specific for CNS-specific antigens occurs in the peripheral immune system in the absence of the self-antigen. Viral peptides with sufficient structural similarity to the immunodominant MBP peptide activate these autoreactive T cells allowing them to undergo clonal expansion and CNS infiltration. Recognition of the MBP peptide in the CNS initiates the autoimmune destruction of myelin in the white matter.

P. Ex. B at 701. The court is simply unable to determine from the expert testimony or the literature whether a *tetanus* peptide or antigen from the vaccine would also have the "sufficient structural similarity to the immunodominant MBP peptide" to "activate . . . autoreactive T cells," leading to CNS infiltration. See also Tr. at 78 (Dr. Martin testifying that "MS patients do not have manifestations in their peripheral nerve" and while Dr. Smith's analogous theory may be "possible," "there is no evidence in the moment supporting that"); id. at 136 (Dr. Safran testifying that "[t]he cells [involved in myelination in the two systems] are different, and the epidemiology is not shown").

Moreover, the court is hard-pressed to extend the literature's discussion or association of viruses or natural infections and autoimmune diseases to the tetanus toxoid vaccine which is an attenuated or modified form of bacteria toxin. Clearly, the literature supports that the medical

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the negative." Id. at 22 (italics in original). In other words, "that which has not been reported might indeed have occurred." Id. In the case *sub judice*, the experts did not explain whether individual case reports of vaccinees receiving tetanus toxoid might be meaningful to petitioner's theory of causation, and if so, in what manner or context. In fact, the court does not recall either expert presenting valuable testimony about case reports for the vaccine received. Absent persuasive support from credible experts or the medical literature that one or several case reports satisfy the requirements of Prong Two and the reasons therefor, the court cannot on its own attach medical and legal weight to the case reports referenced in the IOM's 1994 report. The court cannot conclude, without more, that these case reports demonstrate a "suspected or potential" causal relation.

[32]The undersigned rejected a similar argument in Trojanowicz v. Secretary of HHS, No. 95-215V, 1998 WL 774338 (Fed. Cl. Spec. Mstr. July 1, 1998) (reissued for publication Oct. 16, 1998), aff'd, 43 Fed. Cl. 469 (1999), wherein petitioners relied on the causal relationship between tetanus and GBS to posit a theory that the vaccine caused their child's CIDP, a central nervous system disorder.

community is discussing and reporting on autoimmune illnesses in the context of viruses and infections (both viral and bacterial), with the viral or infectious agent preceding either temporally the onset of the autoimmune disease or, alternatively, acting as a trigger or the cause of a number of diseases, including the demyelinating illnesses of GBS, ADEM, and MS. See, e.g., P. Ex. B at 695, 696, 699, 702-03; P. Ex. 38 at 17[33]; P. Ex. 39 at 408[34]; P. Ex. 40 at 1-3[35]; R. Ex. G at 185-87; R. Ex. H at 1, 3[36]; R. Ex. I at 291, 299[37]; R. Ex. J at 1101[38]; R. Ex. M at 1337-38[39]. See also Tr. at 93 (Dr. Martin testifying that neither infections or the tetanus immunization are proven to cause autoimmune responses, but that with infections, some cases are so convincing in their facts, "that [he] consider[s] it proven")[40]; id. at 89-90 (Dr. Martin citing epidemiology associating viral infections with MS exacerbations); id. at 166 (Dr. Safran testifying that while he is not an immunologist, he hears about the link between infections and autoimmune illnesses enough to believe "it more plausibly than . . . other things"). However, nowhere does this literature satisfy the proof required by Prong Two of Stevens, that there is a "suspected or potential association" between *the tetanus toxoid vaccine* and ADEM, MS, or any other possible diagnosis in this case.[41] In fact, some in the medical community

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[33]Trevor Owens, Fundamentals in Autoimmunity, in Clinical Neuroimmunology 13, 17 (1998).

[34]Brief Dictionary of Immunologic Terms, in Clinical Neuroimmunology 405, 408 (1998).

[35]S. Schwarz et al., Acute disseminated encephalomyelitis: A follow-up study of 40 adult patients, 56 Neurology 1313 (2001).

[36]Richard W. Orrell, et al., Grand Rounds – Hammersmith Hospitals: Distinguishing acute disseminated encephalomyelitis from multiple sclerosis, 313 Brit. Med. J. 802 (1996).

[37]J. Kesselring et al., Acute Disseminated Encephalomyelitis: MRI Findings and the Distinction from Multiple Sclerosis, 113 Brain 291 (1990).

[38]Surendra Singh, Pictorial Essay: Acute Disseminated Encephalomyelitis: MR Imaging Features, 173 Am. J. Radiology 1101 (1999).

[39]Neurology in Clinical Practice: The Neurological Disorders (Walter G. Bradley et al. eds., 2nd ed. 1996).

[40]Dr. Martin accepts that a study by Dr. Fujinami (referenced in the literature) can be interpreted to support that a viral infection may cause a subclinical disease and create memory T cells which may then be reactivated or triggered at a later time by a nonspecific stimuli, like tetanus, resulting in the onset of a different disease. Tr. at 109-11; but see id. at 127-29 (explaining that in the instance of a silent autoimmune condition, the response exists *initially* without symptoms, "but the process [goes] on and at some point it [becomes] apparent").

[41]Nor is there literature in the record supporting the analogy that the medical process responsible for the development of GBS following the TT is the same as that which might occur

believe that "as of today, the link between currently used immunizations and autoimmune disease is weak at best." R. Ex. G at 187. And to the extent vaccines are possibly implicated in demyelinating disorders in the literature submitted, it is done so in the context of rabies, smallpox, live virus vaccinations, or otherwise unidentified vaccines and petitioner has provided no persuasive reason for treating the tetanus toxoid the same as any of the vaccines mentioned.[42] See, e.g., P. Ex. B at 703; P. Ex. 40 at 2, 3; R. Ex. G at 187, 188; R. Ex. H at 3; R. Ex. I at 299; R. Ex. J at 1101, 1102; R. Ex. K at 1313-15; R. Ex. M at 1337-38.[43] Unfortunately for petitioner's case, the court simply cannot make the unsubstantiated evidentiary leap, that according to the medical community or peer-reviewed literature, there is a "suspected or potential association" between *the tetanus toxoid vaccine* and the alleged injuries.[44] This conclusion is further reinforced by Dr. Smith's own equivocal opinions, which frequently included words such as "possibility," "might very well," "could

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between TT and ADEM, MS, vasculitis, or any other injury alleged here.

[42]In Petitioner's Exhibit 40, the authors describe the follow-up study of 40 adult patients diagnosed initially with ADEM. In that study, only one patient had a preceding immunization and the vaccine was against diphtheria and tetanus; this patient's illness progressed to MS. P. Ex. 40 at 4. The authors noted that a "preceding . . . immunization was not a prerequisite for the diagnosis of ADEM." Id. at 9. The study does not conclude that the patient's ADEM or subsequent MS was causally related to the diphtheria and tetanus vaccination received.

[43]In the Principles of Neurology text, it is written that "[i]n the past, a similar illness [to encephalomyelitis] was observed *to follow* vaccination against rabies and smallpox and, reportedly, after *administration of tetanus antitoxin (rare)*, as discussed further on," but the portion of the text provided does not thereafter discuss the tetanus antitoxin or find affirmatively for any causal relationship between it and the illnesses suffered here. R. Ex. L at 976 (italics added) (Maurice Victor & Allan H. Ropper, Principles of Neurology 975-978 (7th ed. 2001)).

[44]Incidentally, it is not lost on this court that, given all the literature and expert testimony tentatively associating viruses with demyelinating diseases, petitioner's receipt of a second hepatitis A vaccination at the same time as her tetanus toxoid vaccine may have contributed to her illness. According to Dr. Martin, hepatitis A is an attenuated virus vaccine and attenuated viruses, unlike tetanus which is just a protein, retain the ability to infect cells. Tr. at 73. Dr. Smith agrees in theory that the hepatitis A vaccine could have acted as a foreign agent, triggering a T cell response which went on to attack the body although he opines that there is "much less [literature] out there on Hepatitis A" so he cannot "assign relative likelihoods otherwise." Id. at 62-63. Petitioner's neuro-ophthalmologist, Dr. Lesser, also did not know the role of the hepatitis A vaccine, but concluded "it definitely could be a possibility since we do know that influenza vaccine can sometimes be a precipitating factor." P. Ex. 3 at 74. Further, Dr. Smith testified that the processes initiated by infections or vaccines "are virtually identical," leading this court to ponder the actual effect of Mrs. Althen's hepatitis A vaccine on her health. Tr. at 10; see also id. at 11. Whether the hepatitis A vaccine played a role in Mrs. Althen's onset of a demyelinating disorder remains an open question which the court need not address given petitioner's failure to satisfy Prong Two of Stevens.

happen," "could have," and "my best guess." Tr. at 13, 19, 20, 28, 35, 39. In sum, Dr. Smith's testimony fails to satisfy Daubert or provide a "reputable medical or scientific explanation."[45] See Grant, 956 F.2d at 1148.

The Stevens Causation-in-Fact Standard: Additional Thoughts

Before closing, the court observes that this case illustrates the classic battle over the legal causation standard that frequently faces the special masters. Without articulated standards providing guidance, the experts bring their own beliefs and biases into the courtroom; respondent's experts routinely requiring greater evidence than petitioners' experts to meet the preponderance standard. Stevens attempts to guide the experts by defining "preponderance," addressing specifically the types of evidence presented in vaccine cases, and determining how much of this evidence is enough to warrant a finding of legal causation under the Vaccine Act. Despite respondent's protests about the legal correctness or sufficiency of the Stevens prongs, interestingly the government's own experts, in the case *sub judice*, rely in part on the same criteria utilized in Stevens to proffer *from their scientific standpoints* a causal relationship between viruses or viral infections and demyelinating diseases.[46] See, e.g., Tr. at 93 (Dr. Martin testifying that neither infections or the tetanus immunization are proven to cause autoimmune responses, but that with infections, some cases are so convincing in their facts, "that [he] consider[s] it proven"); id. at 166 (Dr. Safran testifying that while he is not an immunologist, he hears about the link between infections and autoimmune illnesses enough to believe "it more plausibly than . . . other things"). See also Tr. at 166-67 (Dr. Safran conceding that "acceptability" within the medical community of a causal relation can be supported by "[s]omething short of published epidemiological data"). Unfortunately for Mrs. Althen's case, this "acceptance" does not extend to the tetanus toxoid vaccine. As Dr. Safran testified, in responding to whether there is, in the literature, "even *thought* about [a] relationship between tetanus toxoid and the production of central nervous system disease," there is not. Tr. at

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[45]This was a complex case medically and factually speaking. However, because the court's decision rests on petitioner's failure to prove Prong Two, in that the literature submitted or testimony presented did not specifically relate to the tetanus toxoid vaccine, and therefore the medical community is not providing the necessary objective support for Dr. Smith's theory, the court need not resolve the outstanding factual issue in this case which is what is the true diagnosis of petitioner's illness. Nor must it address Prongs Three through Five, although all experts agree that optic neuritis can often be the first sign of a demyelinating injury and that the optic neuritis occurred within a medically appropriate time period for an immune mediated illness. See, e.g., Tr. at 13-14, 38, 74, 119-20, 157, 159, 161. Further, as evident from her medical records, Mrs. Althen's treating physicians employed extensive and exhaustive testing to eliminate alternative causes for her illness; none were found.

[46]As the undersigned stated in Stevens, the five prongs were derived based on testimony repeatedly offered since the beginning of the Program, *from both petitioners' and respondent's experts*, as to what evidence they rely on to formulate their causation opinions. Stevens, 2001 WL 387418, at *26, *37.

151. The medical community is not even "thinking about" (i.e., recognizing) the tetanus toxoid vaccine's connection to ADEM or MS, as Stevens demands. This fact leaves petitioner with a case supported merely by one possibility heaped upon another. This is not enough according to Stevens. While theoretical possibilities are indeed relevant to determining whether a vaccine can cause a particular injury, Stevens makes clear that this "can cause" analysis has two levels, requiring first that petitioner demonstrate causality in a theoretical sense (i.e., plausibility, which Mrs. Althen's expert successfully did here) and requiring second that petitioner also show a recognition or a suspected association (the "thinking about it" concept expressed by Dr. Safran), through the medical community or literature, of a causal relation between the vaccine and injury. It is the satisfaction of this second prong which moves petitioner's case beyond the theoretical causative connection towards the realm of probable or preponderance.[47] Without proof that the theoretical has risen to the extent of recognition or confirmation within the medical community or literature, petitioner's case is, at best, speculative. In the instant case, petitioner failed to prove that Dr. Smith's "theoretical possibilities" arose to the level of recognition by the medical community in the context of the tetanus toxoid vaccine. Thus, his theory remained speculative and legally deficient under the Daubert standards. See Daubert, 509 U.S. at 590.

To be sure, the quality or quantity of evidence sufficient to satisfy the preponderance of evidence standard in causation-in-fact cases under the Act is an unresolved legal issue. The Federal Circuit has awarded compensation for seemingly less than the proof required by Stevens. See, e.g., Golub v. Secretary of HHS, 243 F.3d 561, 2000 WL 1471643, at *3-*5 (Fed. Cir. 2000) (unpublished opinion) (holding that in the presence of "a *strong* temporal relationship," *"a less stringent standard*" applies and petitioner need only offer "the additional showing of a reasonable medical theory causally connecting the vaccination and the injury . . . to establish a causal link") (italics added). See also DeGrandchamp v. Secretary of HHS, No. 01-413V, 2003 WL __, slip op. at 15 (Fed. Cl. Spec. Mstr. May 15, 2003) (to be published) (awarding compensation following a determination of a medically plausible mechanism, temporal relationship, and the absence of other causes).[48] **Hence, arguably, contrary to the government's views, Stevens may in fact require too much from petitioner.**

Respondent does a disservice to petitioners and the Program by perpetuating the myth that Stevens is judicial legislating or relaxing of the burden of proof. Nothing can be further from the truth. This court has in no way altered the statutory playing field: petitioners bear the burden of proof, the preponderance of the evidence standard applies, and petitioners must support their case with a medical expert opinion or the medical records. See §13(a)(1). Stevens instructs the parties on how the evidence routinely submitted in vaccine cases comports with those statutory requirements. It is an effort to communicate the undersigned's accumulated experience after

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[47]When coupled with the remaining three prongs of Stevens, petitioner successfully meets the preponderance burden imposed by the Vaccine Act.

[48]Measured against either of the evidentiary standards applied in these two cases, petitioner likely would have prevailed in this matter.

evaluating hundreds of similar cases and deciding what type and how much evidence is sufficient to preponderate in petitioner's favor. That is not legislating, that is communicating accumulated knowledge from repeated decision-making.

Congress legislated the Office of Special Masters with the goal of creating "experts" in resolving these disputes. These experts are an integral part of the Program's objective of "consistent and certain" justice. To meet that objective, the special masters must move beyond case-by-case decision-making towards instruction – what types of evidence are persuasive, how much evidence is necessary, what causal relationships are pure speculation, which relationships are proven – to ensure that similarly-situated petitioners are treated alike and thus fairly.

Respondent could greatly enhance this process by breaking its silence and communicating its views on what evidence is necessary to prove causation-in-fact. Despite the Secretary's role in shaping causation under the presumptions afforded by the Table (see 42 U.S.C.A. §300aa-14(c) and (e)) and recognizing causation-in-fact claims for non-Table injuries (see, e.g., 60 Fed. Reg. 56289, 56292-56293 (November 8, 1995) (the Secretary stating that removals or exclusions of a condition from the Table or revisions to the Table definitions do not preclude entitlement because "[p]etitioners may still prevail by providing proof of causation in fact"); id. (the Secretary declining to add GBS to the Table for the tetanus toxoid vaccine and stating that "[w]hile there may be a causal relationship in extremely rare cases, the Secretary is unable to identify the circumstances in which the vaccine causes the condition," and any claims "should be addressed instead under the causation in fact standard")), the government has never explained, in this or any other vaccine case or public forum of which the undersigned is aware, what it considers sufficient evidence to prove legal causation in *causation-in-fact* cases. Respondent has stated consistently that epidemiological evidence is not required to prove causation-in-fact. See, e.g., White v. Secretary of HHS, No. 98-426V, 2002 WL 1488764, at *5, n.12 (Fed. Cl. Spec. Mstr. May 10, 2002). We also know that respondent recognizes some lesser proof of causation-in-fact because they concede causation-in-fact cases without the benefit of epidemiological studies. However, what we do not know is what pieces of medical evidence respondent relied upon to determine causation in such cases. Stevens is this court's best effort to evaluate the causation evidence. Instead of merely stating that Stevens is incorrect, respondent would greatly assist the Program by articulating the pieces of evidence that complete the causation puzzle.

Until the Federal Circuit provides firm guidance as to the correct legal standard, and in the absence of articulated, compelling reasons otherwise from respondent or petitioners under the Program, the undersigned intends to follow the five prongs established in Stevens in subsequent cases. The Stevens prongs offer the guidance and fairness demanded by the Act's purposes and, as was discussed fully in Stevens, are supported by the legislative history, vaccine jurisprudence, the medical and scientific fields, and traditional tort litigation.

VI. CONCLUSION

Congress designed the Program to compensate only those individuals who can demonstrate a causal or temporal link between their injuries and a listed vaccine by a preponderance of the evidence. In petitioner's case, the evidence simply does not move petitioner past Prong Two of the Stevens causation-in-fact standard. Based on the foregoing, the court finds after considering the entire record in this case that petitioner is not entitled to compensation under the Vaccine Act. In the absence of a motion for review filed pursuant to RCFC Appendix B, the Clerk of the Court is directed to enter judgment in accordance herewith.

IT IS SO ORDERED.

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Gary J. Golkiewicz
Chief Special Master