In the United States Court of Federal Claims

No. 00-170V
Filed September 30, 2003
TO BE PUBLISHED

MARGARET ALTHEN,	*	
Petitioner,	*	
v.	*	National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300-aa-1 to 300aa-34 (2000); *de novo* review; causation in fact.
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

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

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

MEMORANDUM OPINION

BRADEN, ***Judge***

On June 3, 2003, the Chief Special Master of the Office of Special Masters of the United States Court of Federal Claims ("Chief Special Master") issued an Entitlement Decision in this case, which he described as raising "difficult and involved medical and causation issues" under the National Childhood Vaccine Act of 1986, 42 U.S.C. § 300aa-1 to -34 (2000) ("Vaccine Act"). *See Althen* v. *Sec'y Dep't of Health and Human Servs.,* 2003 WL 21439669, at *9 (Fed. Cl. Spec. Mstr. June 3, 2003) ("*Althen*"). The Chief Special Master denied petitioner's claim for compensation and other relief. The court has issued this opinion on an expedited basis to facilitate any appellate review the respondent ("government") may wish to pursue, since the court has determined that the petitioner met the statutory burden to establish causation in fact by a preponderance of the evidence and therefore, as a matter of law, is entitled under the Vaccine Act to compensation, reasonable attorneys fees, and other costs.

RELEVANT FACTS AND PROCEDURAL BACKGROUND[1]

Petitioner is a college graduate and was a Public Health Administrator for the City of Hartford. (P. Ex.18 at 146). She is married; her daughter is now 22 years old. (P. Ex. at 147). On March 28, 1997, a tetanus toxoid[2] vaccination and a hepatitis A vaccination were administered to petitioner. *See Althen,* at *1 (P. Ex. 1 at 1). Prior to that time, petitioner enjoyed good health, although she had Duane's syndrome,[3] which affected her ability to look to her left without experiencing double vision. (P. Ex. 8 at 1). In addition, petitioner "had a history of hypothyroidism[4] probably on an autoimmune basis,"[5] for which she takes a prescription synthetic thyroid drug. (P. Ex. 21 at 1).

On April 15, 1997, petitioner sought medical treatment for blurred vision, which progressed in four days to a complete loss of sight in her right eye. *Id.* (P. Ex. 2 at 3; P. Ex. 20 at 23; P. Ex. 21 at 1). Petitioner also complained of a "steady" "posterior headache," "discomfort along the right side of her nose," "pain with eye movements," "sharp discomfort along her right temple" when bending over, and "queasiness." *Id.* (P. Ex. 1 at 107). Initially, petitioner was diagnosed by Dr.

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[1] The relevant facts recited herein are summarized from detailed factual findings found in *Althen,* at *1-*4. Citations to record evidence are noted within parentheses. (TR_) refers to the transcript of a June 14, 2002 hearing of the parties' experts. (P. Ex._) refers to petitioner's exhibits. (D. Ex._) refers to government's exhibits.

[2] Tetanus toxoid vaccine is a modified toxin of the bacteria *Clostridium tetani* and does not have viral components. *See* ADVERSE EVENTS ASSOCIATED WITH CHILDHOOD VACCINES: EVIDENCE BEARING ON CAUSALITY, Institute of Medicine 67-68 (1994) ("1994 IOM REPORT").

[3] Duane's syndrome "is a hereditary congenital syndrome in which the affected eye shows limitation or absence of abduction, restriction of abduction . . . narrowing the palebral fissure on adduction and widening on adduction, and deficient convergence. It is transmitted as an autosomal dominant trait. Called also *retraction syndrome*[.]" DORLAND'S MEDICAL DICTIONARY 1754 (29th Edition 2000) ("DORLAND'S").

[4] Hypothyroidism is the "[d]iminished production of thyroid hormone, leading to clinical manifestations of thyroid insufficiency, including low metabolic rate, tendency to weight gain, somnolence and sometimes myxedema [accumulation of excess watery fluid under the skin]." STEDMAN'S MEDICAL DICTIONARY 866 (27th Edition 2000) ("STEDMAN'S").

[5] An autoimmune disease is "any disorder in which loss of function or destruction of normal tissue arises from humoral or cellular immune responses to the body's own tissue constituents[.]" STEDMAN'S at 510.

Lesser, an opthamologist, as having "probable right optic neuritis."[6] *Id.* (P. Ex. 3 at 88; P. Ex. 4 at 122; TR. 13).

An April 21, 1997 brain MRI confirmed optic neuritis in petitioner's right eye, but revealed no "evidence of multiple sclerosis[7] or demyelinating disease."[8] *Id.* (P. Ex. 1 at 111). Nevertheless, Dr. Lesser advised petitioner that she had a 2 to 5 percent risk of developing MS within five years. (P. Ex. 3 at 88). On April 27, 1997, petitioner experienced "sudden loss of vision" over a two day period. *Id.* (P. Ex. 3 at 38). A few weeks later, petitioner complained of sight loss in her right eye, accompanied by "tingling along the ulnar side right hand" and numbness in that hand. *Id.* at *2. (P. Ex. 1 at 107). On May 23, 1997, petitioner was examined by Dr. Silvers, a neurologist, who reported "significant right optic neuritis." (P. Ex. 1 at 106). Dr. Silvers advised petitioner that in light of the most recent MRI, her risk of developing MS was "low . . . however, this risk is still real." (P. Ex. 1 at 106).

On June 4, 1997, petitioner was admitted to Hartford Hospital with fever, confusion, and neck stiffness. TR. 14 (P. Ex. 1 at 98; P. Ex. 21 at 1); *see also Althen,* at *2. On June 6, 1997, petitioner received an EEG that revealed a "focal component in the patient's right temporal region raising the possibility of an infectious process or inflammatory process at that site." *Id.* (P. Ex. 1 at 100). Petitioner's MRI also indicated "a subtle area of increased signal in the right parietal region, possibly reflecting underlying encephalitis." *Althen*, at *2 (TR 58-62). After an exhaustive battery of tests, petitioner was discharged to the hospital's acute rehabilitation unit on June 16, 1997, with a primary diagnosis of: "Encephalitis[9] of unknown type." *Id.* (P. Ex. 1 at 87, 99). MRI brain scans

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[6] Optic neuritis is an "inflammation of the optic nerve, . . . classified either as *intravascular*, affecting the part of the nerve within the eyeball . . . or *retrobulbar*, affecting the portion behind the eyeball." DORLAND'S at 1207; *see also* 1994 IOM REPORT at 83 ("Optic neuritis . . . [is a] focal demyelinating lesion [ ] that can occur in isolation or as components of diffuse demyelinating diseases such as ADEM and multiple sclerosis.").

[7] Multiple sclerosis is "a disease in which there are foci of demyelination of various sizes throughout the white matter of the central nervous system ("CNS"), sometimes extending into the gray matter. Typically, the symptoms of lesions of the white matter are weakness, incoordination, parethesias, speech disturbances, and visual complaints. The course of the disease is usually prolonged, so that the term *multiple* also refers to remissions and relapses that occur over a period of many years. The etiology [cause or origin] is unknown." DORLAND'S at 1611.

[8] Demyelinating disease is an "extensive idiopathic [of a cause unknown] loss of myelin sheaths [protein sheaths that cover nerve fibers] in the brain." STEDMAN'S at 588. Demyelinating disease "has long been known to follow viral and some bacterial infections and the administration of live attenuated and inactivated antiviral vaccines." 1994 IOM REPORT at 83.

[9]Encephalopathy is defined in the Vaccine Act "Qualifications and aids to interpretation" as "any significant acquired abnormality of, or injury to, or impairment of function of the brain. Among the frequent manifestations of encephalopathy are focal and diffuse neurological signs,

taken on June 5, 1997 and June 6, 1997 showed "A vague suggestion of some enlargement of the anterior temporal region on the left, and minimal loss of white matter/gray matter differentiation. However, this is not definitive and one cannot clearly evaluate the possibility of edema." (P. Ex. 18 at 109). On June 21, 1997, petitioner again was discharged, this time with a diagnosis of "questionable acute disseminated encephalomyelitis, right optic neuritis, congenital Duane's syndrome, [and] urinary tract infection." *Id.* (P. Ex. 1 at 87).

On July 2, 1997, petitioner once again was admitted to Hartford Hospital, this time because of "increasing dizziness" and "gait instability." *Id.* (P. Ex. 1 at 90-91; P. Ex. 4 at 72; P. Ex. 21 at 1). In addition, an examination revealed petitioner was almost completely blind in her right eye. (P. Ex. 27 at 59). On this occasion, a MRI brain scan showed "multiple areas of white matter abnormality," noting the possibility of "encephalitis or ADEM[10] or even an acute demyelinating process." *Id.* (P. Ex. 4 at 24; P. Ex. 21 at 1). Based on petitioner's symptoms a month earlier, the resident physician concluded that: "The possibilities of encephalitis or ADEM or even an acute demyelinating process are in consideration." (P. Ex.27 at 35). Another of petitioner's hospital physicians concurred that her "presentation was not felt to be typical for multiple sclerosis [but he was concerned about] another autoimmune demyelinating diastasis." *Id.* (P. Ex. 1 at 91). He also was uncertain whether petitioner's condition was "due to acute disseminated encephalomyelitis or a form fruste of Behcet's disease."[11] *Id.* (P. Ex. 1 at 90-91). Another Hartford Hospital doctor

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increased intracranial pressure or changes lasting at least six hours in level of consciousness, with or without convulsions. The neurological signs and symptoms of encephalopathy may be temporary with complete recovery, or may result in various degrees of permanent impairment." 42 U.S.C. § 300aa-14(b)(3)(A). Encephalitis refers to an "encepholopathy caused by an inflammatory response in the brain. This is usually manifested with systemic constitutional symptoms, particularly fever and pleocytosis of the cerebrospinal fluid. However, the terms *encepholopathy* and *encephalitis* have been used imprecisely and even interchangeably in the literature." 1994 IOM REPORT at 337.

[10]ADEM is an abbreviation for "acute disseminated encephalomyelitis," which like multiple sclerosis is a demyelinating disease affecting the nerve fibers in the nervous system, which is "characterized by perivascular lymphocyte and mononuclear clear cell infiltration and demyelination . . . It is believed to be a manifestation of an autoimmune attack on the myelin of the central nervous system. Clinical manifestations include fever, headache, vomiting, and drowsiness progressing to lethargy and coma; tremor, seizures, and paralysis may also occur." DORLAND'S at 589. ADEM also is "characterized by acute depression of consciousness and multifocal neurologic findings occurring within days to weeks (5 days to 6 weeks) following an inciting event. It is characterized pathologically by diffuse foci of perivenular inflammation and demyelination most prominent in the white matter of the brain and spinal cord." 1994 IOM REPORT at 83 (citation omitted).

[11]Behcet's disease is "characterized by simultaneously or successively occurring recurrent attacks of genital and oral ulcerations . . . often with arthritis; a phase of generalized disorder, occurring more in men than women, with variable manifestations, including dermatitis, erythema nodosum, thrombophlebitis, and cerebral involvement." STEDMAN'S at 1748.

reported a differential diagnoses[12] of ADEM, multiple sclerosis, or vasculitis.[13] *Id.* (P. Ex. 18 at 322). On July 8, 1997, petitioner again was discharged. *Id.* (P. Ex. 1 at 90-91).

From April 1997 to May 1998, petitioner had a total of seven MRI brain scans. (P. Ex. 4 at 72). "[B]y 7/97 [punctate lesions] had blossomed into a right temporal parietal lesion followed thereafter by development of lesions disseminated through the central nervous system[.]" (P. Ex. 4 at 72). On May 28, 1998, a lab test indicated that petitioner's myelin basic protein levels were "indicative of an accute demylinating episode, such as occurs with multiple sclerosis." (P. Ex. 18 at 560). By June 4, 1998, petitioner's attending physician concluded that she had developed ADEM, although "the findings are unusual and atypical." (P. Ex. 3 at 78). On July 27, 1998 and again on January 7, 1999, petitioner experienced optic neuritis in her left eye. *Id.* at *3 (P. Ex. 4 at 72; P. Ex. 21 at 2).

At the request of Dr. Lesser and Dr. Silvers, Dr. Vollmer, Director of the Neuroimmunology Program at Yale University, examined petitioner on April 27, 1999. He concluded that neurosarcoid or isolated angiitis[14] was " the most likely diagnosis," although multiple sclerosis "remains in the differential diagnosis." *Id.* (P. Ex. 8 at 4). On May 15, 1999, another MRI brain scan "reveal[ed] some small abnormalities scattered throughout the white matter, suggestive of vasculitis or sarcoid or parainfectious disease." *Id.* (P. Ex. 4 at 23). Dr. Vollmer observed this "pattern [was] not typical of multiple sclerosis," but concluded that "[g]iven the lack of confirmatory evidence for multiple sclerosis, and the 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.* (P. Ex. 4 at 23; P. Ex. 8 at 6).

On June 10, 1999, Dr. Silvers noted in petitioner's medical record that, "[W]hile primary CNS vasculitis is a thought, I would think that the absence of a significant headache, the initial episode of a febrile encephalomyelitis and the MRI's [sic] would support a demyelinating illness." *Id.* (P. Ex. 1 at 37-38); *see also* P. Ex. 1 at 21 (Vaccine Adverse Event Reporting System, dated December 22, 1999, stating petitioner's reaction to the March 28, 1997 tetanus toxoid vaccine was adverse and that she was diagnosed as having "Acute Disseminated Encephalomyelitis").

On March 31, 2000, petitioner filed the information required to initiate an action under the Vaccine Act.

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[12] A differential diagnosis is "the determination of which of two or more diseases with similar symptoms is the one from which the patient is suffering, by a systematic comparison and contrasting of the clinical findings." STEDMAN'S at 492.

[13] Vasculitis is an "inflammation of the blood or lymph vessels of the central nervous system." DORLAND'S at 1934.

[14] Angiitis is "isolated vasculitis [inflammation of the blood or lymph vessels] of the central nervous system." DORLAND'S at 81.

Following a May 4, 2000 examination, Dr. Silvers concluded that petitioner had a primary diagnosis of "Probable multiphasic ADEM." (P. Ex. 1 at 11). On August 6, 2000, petitioner experienced a brain seizure and again was admitted to Hartford Hospital. *Id.* at *4 (P. Ex. 18 at 93). A brain *biopsy was performed that "showed clear* evidence of inflammation in the central nervous system." TR. 14. (emphasis added). Petitioner was diagnosed with "vasculitis with secondary tissue destruction and demyelination consistent with primary angiitis." *Id.* (P. Ex. 25 at 46). On August 17, 2000, a Hartford Hospital Department of Radiology Report noted that petitioner's symptoms were "consistent with an acute demylinating process which includes MS or a previously suspected diagnosis of encephalitis." (P. Ex 25 at 133).

And, a Radiology Report, dated December 2, 2000, reported "[C]linical Indication: Multiple Sclerosis," but also noted "very minimal progression of Multiple Sclerosis changes in the left parietal lobe." *Id.* (P. Ex. 26 at 137). On December 11, 2000, Dr. Vollmer summarized petitioner's condition as a:

> relapsing neurologic syndrome that began with an acute illness in 1997, associated with fever and altered mental status. However, she has continued to have relapses since that time with loss of vision which comes on very quickly and also a left hemiparesis that evolved over a matter of a few days. This was associated with a seizure like episode. A biopsy suggested CNS vasculitis, but also show 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.

(P. Ex. 23 at 2).

EXPERT PROCEEDINGS BEFORE THE CHIEF SPECIAL MASTER

On June 14, 2002, the Chief Special Master presided over a hearing of the parties' experts.

A. Petitioner's Expert-Dr. Derek R. Smith, M.D.

The Chief Special Master found that petitioner's expert, Dr. Derek R. Smith, M.D., was "knowledgeable about his area of expertise and the facts of this case; he testified cogently and credibly." *Althen*, at *4 n.6.

Dr. Smith is a board-certified neurologist, with a sub-speciality in multiple sclerosis and neuroimmunology. *Id.* He is currently a Clinical Instructor at the Harvard Medical School and also an Associate Professor of Neurology at Brigham Women's Hospital in Boston. *Id.* Dr. Smith has published writings regarding multiple sclerosis and neurologic injuries. *Id.* Dr. Smith exclusively treats patients with multiple sclerosis (approximately 100-150 persons per month), providing first and second opinions and long-term treatment. *Id.* (TR 4-6). In addition, Dr. Smith is engaged in conducting clinical trials for future treatment of multiple sclerosis and has an interest in immune mechanisms in multiple sclerosis, clinical trials in multiple sclerosis, and immune deviation

concerning therapeutic modalities. *Id.* He also has been engaged in research "looking at T cell[15] function in patients with MS and trying to identify differences as compared to normal controls in terms of the way that . . . T cells are . . . either functioning or interacting with the rest of the immune system." *Id.* (TR 7).

Dr. Smith testified that he is "highly confident that, in the right individuals, a tetanus toxoid vaccination can cause central nervous system demyelination." *Althen*, at *4. (TR 35). Dr. Smith's July 10, 2001 written opinion noted that petitioner "had a history of hypothyroidism probably on an autoimmune basis." (P. Ex. 21 at 1). In addition, he testified that the tetanus toxoid vaccine administered to petitioner in March 1997 "probably" played a role in petitioner's illness. "There was no preceding viral infection. There was *no other explanation* for why she could have had a sudden onset of profound immune responses in the central nervous system." (TR 13, 37) (emphasis added). Dr. Smith also testified that the tetanus toxoid vaccine more probably than not substantially contributed to petitioner's optic neuritis and subsequent demyelinating disorder that progressed from March 28, 1997 to the present. (TR 12-14; P. Ex. 21 at 1-2).

The medical theory on which Dr. Smith based his expert opinion is known as the theory of "degeneracy," resulting from growing knowledge about "molecular mimicry."[16] *Id.* Dr. Smith explained to the Chief Special Master that "the reason one gives vaccinations is in order to create memory cells, T cells, B cells that will respond to the pathogen that is being vaccinated against in the future." *Id.* (TR. 11-13, 35, 39). The body's T cells, however, can "degenerate" and mistakenly respond to non-specific or non-native antigens, such as CNS myelin antigens, rather than the vaccine's antigen. *Id.* (TR 27-31). This mistake can then trigger an inflammatory response, which ultimately manifests itself as a demyelinating disease through "epitope spreading,"[17] resulting in a chronic condition, such as that developed by petitioner. *Id.* at *5 (TR 33-34, 37). Dr. Smith reported that the degeneracy of T cells is "a widely recognized principle in medicine, accepted in the field of neuroimmunology and supported by the [medical] literature." *Id.* (TR 30, 32). Dr. Smith

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[15] A "T cell" is one that "initiates immune responses against specific agents . . . The function of T cells . . . is to start both unspecific immune responses, activate cells that are not specific, but would provide an inflammatory environment that is conductive of eliminating [a] foreign agent, and also, stimulate the activation, maturation of so-call D lymphocytes, which make antibodies." (TR 82).

[16] Molecular mimicry is a "phenomenon wherein, two separate peptides or proteins are not identical, but because of the structure or their component of amino acids, in terms of . . . the way they may look to the immune system, they appear to be identical[.]" (TR 21).

[17] An "epitope" is the "simplest form of an antigenic determinant, on a complex antigenic molecule, which can combine with antibody or T cell receptor." STEDMAN'S at 610. "Epitope spreading" is a "process that was described in the experimental model for MS and has been repeated many times; whereby, an immune response that is initially very restricted to a few different types of T cells with a few different T cell receptors over time, because of continuing inflammation, can become more widespread and involve more different T cells, more different antigens." (TR 33).

acknowledged, however, that the 1994 IOM REPORT concluded that there was insufficient evidence at that time to accept or reject a causal relationship between tetanus toxoid vaccine and demyelinating disease, but he believed that developments in laboratory and clinical work since 1994 may supplant the epidemiologic literature, on which the 1994 IOM REPORT's conclusions were based. (TR 44).[18]

Dr. Smith also testified that the onset of petitioner's initial inflammatory condition, optic neuritis, occurred within a medically accepted time period. *Id.* at *6 (TR 38). In addition, in his judgment, whether petitioners's condition is diagnosed as relapsing ADEM, MS, or CNS vasculitis "is not a big issue" as "the underlying inflammatory process is undoubtedly the same in each instance." *Id.* (TR 15; P. Ex. 21 at 2). Finally, Dr. Smith testified that he could ascertain no alternative causes to the tetanus toxoid vaccine in petitioner's medical history that would explain the onset of her demyelinating illness or its chronic nature. *Id.* (TR 13-14, 38, 55-57, 62).

B. The Government's Experts

1. Dr. Arthur P. Safran, M.D.

The Chief Special Master found the testimony of one of the government's experts, Dr. Arthur P. Safran, M..D., "credible, [although] it did not add significantly to the resolution of the issues before the court." *Althen,* at *6 n.12. Dr. Safran is board-certified in both internal medicine and neurology. *Id.* Currently, he serves as an Associate Clinical Professor at Boston University School of Medicine, an Instructor at Tufts University School of Medicine, and a Lecturer at Harvard Medical School. *Id.* The topic of his academic instruction is neurology. *Id.* Dr. Safran also serves as an Attending Neurologist and Associate Physician at various Boston hospitals. *Id.* Dr. Safran's clinical practice includes patients with various neurological disorders of the peripheral and CNS, primarily multiple sclerosis patients. *Id.* (TR 132). In addition, Dr. Safran has published journals and other reference materials on multiple sclerosis. *Id.*

Dr. Safran rejected a causal relationship between petitioner's tetanus toxoid vaccine and her subsequent illness, which he concluded is "an undiagnosed disease of the nervous system, with manifestations suggesting differential diagnosis lies between multiple sclerosis and vasculitis of the central nervous system, favoring the later." (R. Ex. A at 1; TR 134-35, 138-39, 145, 160-63). Dr.

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[18] *See, e.g.*, S. Schwartz et al., "Acute disseminated encephalomyelitis; a follow-up study of 40 adult patients," *Neurology,* May 22, 2001, at 1 ("many patients initially diagnosed with ADEM develop clinically definite MS upon long-term follow up") (P. Ex. 40 at 1, 4); *see also* G. Schwartz et al., "Acute midbrain syndrome as an adverse reaction to tetanus immunization," 15 *Intensive Care Medicine* 53 (1988) ("The occurrence of nearly identical episodes was remarkable, as well as the relatively rapid return to normal consciousness and neurological status after deep coma."); G. K. Schlenska,"Unusual Neurological Complications Following Tetanus Toxoid Administration," 215 *J. Neurology* 299 (1977) ("Neurological complications [after tetanus shots] occurred extremely rarely . . . it is less well known that tetanus toxoid may contain traces of antibody producing protein, which is responsible for these complications.").

Safran concluded that petitioner's illness was more likely "vasculitis or angiitis of the central nervous system," based on: an April 1997 onset of optic neuritis, which he characterized as a "vasculitis illness;" a 2000 brain biopsy indicating "some evidence of demyelination, as well as vasculitis;" petitioner's past physician treatment history; a family history of aneurysms, which are "associated with vasculitis;" and the fact that the onset of petitioner's illness fell within a medically acceptable time period for immune mediated illness. *Id.* at *6. (TR at 134-35, 157-59, 160-62). Dr. Safran admitted, however, that when he rendered his expert opinion on petitioner's diagnosis, he overlooked P. Ex. 35, indicating that petitioner's physician had prescribed AVONEX™, a drug used to treat MS, in 2002. (TR 155).

He further testified that he was unaware of medical reports, medical literature, or epidemiology that linked tetanus toxoid either to CNS disorders or a neurological condition that manifested itself two weeks after vaccination as optic neuritis and then progressed into vasculitis or multiple sclerosis. *Id.* at *7 (R. Ex. A at 2; TR 137-38, 147, 151). Therefore, he concluded that a causal connection between petitioner receiving the tetanus toxoid vaccine and her illness was "remote." *Id.* (TR 159).

Dr. Safran also criticized Dr. Smith's reliance on the relationship between tetanus toxoid and Guillain-Barre Syndrome,[19] discussed in the 1994 IOM REPORT, to support a theory that a similar causal relationship could exist between the tetanus toxoid vaccine and CNS disorders. *Id.* (TR136-37; 156). Dr. Safran's reason for discounting this possibility was the "cells [involved in tetanus toxoid and CNS disorders] are different, and the epidemiology is not shown." *Id.*

2. Dr. Roland M. G. Martin, M.D.

The Chief Special Master found the testimony of the government's second expert witness, Dr. Roland M. G. Martin, M.D., to be "cogent" and "credible" and that he demonstrated "significant knowledge about his medical field and its application to the general causation issue in this case." *Id.* at *7 n.15.

Dr. Martin is board-certified in neurology and electrophysiology and currently is the Acting Chief of the Cellular Immunology Section of the Neuroimmunology Branch at the Department of Health and Human Service's National Institute of Health ("NIH"), which is involved in "T cell immunology and its relation to neuro-immunological disorders[,] particularly MS." *Id.* (TR at 65-67). In addition, Dr. Martin is currently 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. *Id.* Dr. Martin also sees private patients with MS, ADEM, and

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[19]Guillian-Barre Syndrome ("GBS") is "an acute, immune-mediated disorder of peripheral nerves, spinal roots, and cranial nerves, commonly presenting as a rapidly progressing, areflexive, relatively symmetric ascending weakness of the limb, truncal, respiratory, pharyngeal, and facial musculature, with variable sensory and autonomic dysfunction; typically reaches its nadir in 2–3 weeks, followed initially by a plateau period of similar duration, and then subsequently by a gradual but complete recovery in the majority of cases." STEDMAN'S at 1755.

vasculitis, has served on scientific advisory committees, and published and/or reviewed journal articles concerning multiple sclerosis and other neurological disorders. *Id.*

Dr. Martin testified that he is unaware of published data that suggests the tetanus toxoid vaccine can trigger CNS T cells or cause a demyelinating disease of the CNS. *Id.* at *7 (TR 69, 84-92, 126). "[Research] does not exclude the theoretical possibility [that tetanus toxoid can trigger CNS]. But it does not support [that possibility]." (TR 70). Dr. Martin was aware that the 1994 IOM REPORT acknowledged a link between tetanus toxoid and peripheral nervous system autoimmune disease, such as GBS, but he felt the level of occurrence was low. *Id.* at *8 (TR 78-81).

Dr. Martin, however, agreed with the theory of the evolution of molecular mimicry since it was now accepted that "T cells are able to recognize a wide variety of antigen." *Id.* at *7 (TR 71). Based on data from NIH and other laboratories, however, Dr. Martin believed that molecular mimicry "by itself is in all likelihood not sufficient to initiate an autoimmune disease. These may only occur in individuals with a particularly susceptible genetic background, and in addition strong unspecific factors that stimulate the immune system such as a viral infection." (D. Ex. C at 1-2). Dr. Martin, however, acknowledged that "The susceptibility for autoimmune disease is . . . relatively high. For example, the major HLA[20] idea that is associated with MS is found in about 25 percent of the population. If you take MS patients, about 50 to 60 percent have this one HLA. So, many, many people have the genetic background, but only one in a thousand develops MS. [T]hings need to . . . happen to overrun what naturally protects from these diseases." (TR 114). Since Dr. Martin did not review petitioner's medical records, however, he was unaware of petitioner's history of hypothyroidism, which Dr. Smith concluded was "probably on an autoimmune basis." (P. Ex. 21 at 1). Dr. Martin also agreed with Dr. Smith that a chronic inflammatory disease could be caused and maintained by "epitope spreading." *Id.* at *8 (TR 107-108).

Dr. Martin did not dispute that petitioner has a CNS disorder and that the optic neuritis occurred within a medically appropriate time for immune mediated responses. *Id.* at *7 n.16. (TR 68, 69, 77, 119-20). Unlike Dr. Smith, however, he saw no link between petitioner's optic neuritis and her later symptoms. *Id.* Dr. Martin concluded that petitioner's symptoms were "not compatible with MS or a demyelinating disease," but with either a viral or bacterial meningitis. *Id.*

THE *STEVENS* "ANALYTICAL FRAMEWORK"

The Chief Special Master was the author of a 2001 decision, *Stevens* v. *Sec'y Dep't of Health and Human Servs.,* 2001 WL 387418 (Fed. Cl. Spec. Mstr. Mar. 30, 2001) ("*Stevens*"), wherein he fashioned and applied what he characterized as "*the* appropriate analytical framework for evaluating off-Table, so called causation in fact claims." *Stevens,* at *6 (emphasis added). According to the Chief Special Master, this "framework" addresses the "difficulties special masters encounter when weighing evidence against the general principles of causation." *Stevens*, at *23.

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[20] HLA is an "Abbreviation for human leukocyte antigens[.]" STEDMAN'S at 825.

The *Stevens* "analytical framework" has five elements:

1) "Proof of medical *plausibility*," which is established by "proffering a *theory* of biologic mechanism by which a *component* of the vaccine can cause the type of injury suffered." *Stevens,* at *23 (emphasis added);

2) "Proof of conformation of medical *plausibility* from the medical community *and* literature." *Id.* at *23-24 (emphasis added);

3) "Proof of an injury recognized by the medical *plausibility* evidence and literature." *Id.* at *25. (emphasis added);

4) "Proof of a medically acceptable temporal relationship between the vaccination and the onset of the alleged injury." *Id.*; and

5) "Proof of the elimination of other causes." *Id.* at * 26.

See also April 19, 2001 Chief Special Master Order (advising the other special masters that the *Stevens* analysis will be followed by the Chief Special Master in a number of "subsequent cases," including *Althen*).

THE CHIEF SPECIAL MASTER'S APPLICATION OF THE *STEVENS* "ANALYTICAL FRAMEWORK" IN THIS CASE

The Chief Special Master in this case found that the "proof of medical plausibility" element of the *Stevens "analytical framework"* was satisfied by petitioner's expert opinion that T cells that come into contact with the tetanus antigen or peptide can "mistakenly respond to a variety of non-specific or non-native antigens such as central nervous system self-antigens . . . trigger[ing] CNS disorders[.]" *Althen,* at *9. (TR 28-31). The Chief Special Master also was persuaded that petitioner satisfied this element because the 1994 IOM REPORT stated that: ("[I]t *is biologically plausible* that . . . sequence similarities of proteins in the vaccine to host proteins, such as those of myelin . . . *might evoke a response to a self-antigen, so-called molecular mimicry.*"). *Althen,* at *11 (quoting 1994 IOM REPORT at 48, 84) (emphasis added).

The Chief Special Master, however, found that petitioner did not satisfy *Stevens'* second element, medical *plausibility* evidence and literature, *i.e.*, "confirmation from the relevant medical community that it is seeing, reporting (in peer-reviewed literature), and discussing a "'suspected or potential' association between *the tetanus toxoid* vaccine and [the alleged injuries.]" *Althen,* at *14. Without such "objective confirmation that the vaccine administered is potentially associated with the injury alleged, petitioner's causal claims are mere speculation and thus insufficient." *Id.* at *12.

On July 2, 2003, petitioner filed a timely motion for review of the Entitlement Decision. Petitioner seeks review on two bases. First, petitioner asserts that "the use of the *Stevens'* 'Prongs' is an abuse of discretion and not in accordance with the law." *See* Pet. Mem. In Support of Motion For Review at 10. Alternatively, assuming that the *Stevens*' "analytical framework" is lawful,

petitioner argues that all five of the *Stevens*' "Prongs" were satisfied in fact. Therefore, petitioner argues that the decision of the Chief Special Master, holding only the first of the "Prongs" was satisfied, was arbitrary and capricious. *Id.* at 17-18.

On August 4, 2003, the government responded, agreeing with petitioner that the "*Stevens* standard" is contrary to law. *See* Response to Pet. Motion for Review at 8-11. Assuming *arguendo* that the "*Stevens* standard" is lawful, however, the government contended that petitioner's suggestion that a more relaxed causation standard should be applied has been "waived, has no merit, and is based on a non-precedential decision." *Id.* at 7-8. Instead, the government argues that the court should affirm the Chief Special Master's decision because the petitioner failed to demonstrate that the tetanus toxoid vaccination caused her injuries. *Id.* at 3-8.

STANDARD OF REVIEW

Congress requires the judges of this court to analyze conclusions of law made by a special master under the Vaccine Act *de novo*, under a "not in accordance with law" standard. *See* 42 U.S.C.§ 300aa-12(e)(2)(B). "The 'not in accordance with the law' aspect of the standard of review is . . . involved . . . [where there is] dispute over statutory construction or other legal issues." *Hines* v. *Sec'y Dep't of Health and Human Servs*., 940 F.2d 1518, 1527 (Fed. Cir. 1991); *see also Saunders Sec'y Dep't of Health and Human Servs*., 25 F.3d 1031, 1033 (Fed. Cir. 1994) (quoting *Munn* v. *Sec'y Dep't of Health and Human Servs.,* 970 F.2d 863, 870 n.10 (Fed. Cir. 1992)).

Factual findings of a special master, however, should not be set aside unless they are found to be "arbitrary and capricious" or a special master has abused his or her discretion in determining such findings. *See* 42 U.S.C. § 300aa-12(e)(2)(B). The United States Court of Appeals for the Federal Circuit ("Federal Circuit"), recognizing that "no uniform definition of this standard has emerged," has instructed the court that the decision of a special master may be found to be "arbitrary and capricious" only if he or she:

> relied on factors which Congress has not intended [the special masters] to consider, entirely failed to consider an important aspect of the problem, offered an explanation for its decision that runs counter to the evidence . . . or is so implausible that it could not be ascribed to a difference in view or the product of agency expertise.

Hines, 940 F.2d at 1527 (quoting *Motor Vehicle Mfrs. Ass'n* v. *State Farm Mut. Auto Ins. Co.,* 463 U.S. 29 (1983) (discussing a similar standard of review for agency rulemaking under the Administrative Procedure Act). Discretionary rulings are reviewed under an "abuse of discretion standard." *Munn*, 970 F.2d at 870 n.10.

THE ELEMENTS AND BURDEN OF PROOF IN VACCINE ACT CASES

The Vaccine Act provides that a petitioner may qualify to receive compensation and other relief under the Vaccine Injury Compensation Program ("Program") if injury can be established either by causation in law or causation in fact. Causation in law is established if one of the vaccines, listed in the Vaccine Injury Table at 42 U.S.C. § 300aa-14(a) ("Table"), was administered to a

petitioner and the "first symptom or manifestation of onset or of the significant aggravation of such injuries, disabilities, illnesses, conditions, and deaths"of specific adverse medical conditions associated with the use of each vaccine and listed in the Table occurred within a time period specified in the Table. *See* 42 U.S.C. § 300aa-14(a); 42 C.F.R. §100.3(a). The Table is to be read and interpreted by reference to "Qualifications and aids to interpretation," that define the key terms used in the Table. *See* 42 U.S.C. § 300aa-14(b); 42 C.F.R. § 100.3(b).

Congress also decided to afford a petitioner the opportunity to receive relief under the Program even if the time period for the first symptom or manifestation of a specified injury is not satisfied. *See* 42 U.S.C. § 300aa-11(c)(1)(C)(ii); § 300aa-13. Under these circumstances, however, a petitioner must establish causation in fact under a traditional tort analysis, *i.e.*, first, by establishing a *prima facie* case offering evidence of sufficient facts to establish each element of the claim and then, by meeting a burden of proof as to each element of the claim under a "preponderance of the evidence" standard. Thus, a non-Table Vaccine Act petitioner must proffer at least some evidence as to each element of the claim, but also sufficient evidence to persuade the special master or court by a preponderance or "greater weight" of evidence that each fact asserted is more probable than not.

In interpreting the Vaccine Act, the Federal Circuit has explained that a petitioner must proffer evidence that meets a "preponderance of evidence" burden of proof in non-Table causation in fact cases: "a proximate temporal association alone does not suffice to show a causal link between the vaccination and the injury. To prove causation in fact, petitioners must proffer a medical theory that explains the causal connection between the vaccination and illness manifested. Causation in fact requires 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* v. *Sec'y Dep't of Health & Human Servs*., 956 F.2d 1144, 1148 (Fed. Cir. 1992) (citation omitted); *Bunting* v. *Sec'y Dep't of Health and Human Servs.,* 931 F.2d 867, 873 (Fed. Cir. 1991) ("petitioner's burden is not to show a generalized 'cause and effect relationship' with listed illnesses, but only to show causation in the particular case[.] [Otherwise,] a different and greater burden [would be placed] on petitioners than was enacted by Congress."). Subsequently, the Federal Circuit has clarified that *Grant* requires satisfaction of two separate elements to make out a *prima facie* case in a non-Table case: petitioner must prove, "by a preponderance of the evidence, that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." *Shyface* v. *Sec'y Dep't of Health and Human Servs*., 165 F.3d 1344, 1352 (Fed. Cir. 1999) (adopting RESTATEMENT (SECOND) OF TORTS 431 (1977) standard for determining the "legal cause" of the harm). Thus, evidence of a similarity to a Table injury, Table time periods, or the elimination of other potential causes of injury all have been held to be insufficient to establish causation in fact as a matter of law in non-Table cases. *See Grant*, 956 F.2d at 1148.

If petitioner is able to establish legal causation or causation in fact, then the burden of proof shifts to the government under 42 U.S.C. § 300aa-13(a)(1)(B) to establish that a factor unrelated to the vaccine was the actual cause of the petitioner's illness or injury. *See Jay* v. *Sec'y Dep't of Health and Human Servs*., 998 F.2d 979, 984 (Fed. Cir. 1993); *see also Strother* v. *Sec'y Dep't of Health and Human Servs.,* 21 Cl. Ct. 365, 374 (1990) (Rader, J.).

DISCUSSION

Neither the United States Court of Federal Claims nor the United States Court of Appeals for the Federal Circuit has had an occasion to review the *Stevens* decision. Nevertheless, the Chief Special Master advises that "The only issue the court must resolve [on review of the instant case] is whether petitioner satisfied the standard established in *Stevens.*" *Althen,* at *9. The court disagrees. The *Stevens'* causation in fact "analytical framework" does not bind the court. The Chief Special Master's adoption and utilization of that "framework" in deciding the instant case, however, is ripe for the court's *de novo* review.

A. The Chief Special Master's Utilization of the *Stevens* "Analytical Framework" to Decide the Instant Case Was Contrary to Law.

The limited duties of a special master are defined in the Vaccine Act with clarity and specificity:

> **(d) Special masters**
>
> (2) The special masters *shall recommend rules* to the Claims Court. . .
> (3)(A) A special master to whom a petition has been assigned *shall issue* a decision . . .*[that] shall*—
> (i) *include findings of fact and conclusions of law*, and
> (ii) be issued as expeditiously as practicable. . . .

42 U. S.C. § 300aa-12(d) (emphasis added).

In addition, the Act requires that special masters:

> shall consider, in addition to all other relevant medical and scientific evidence *contained in the record* –
>
> (A) any diagnosis, conclusion, medical judgment . . . which is *contained in the record* regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death, and
>
> (B) the results of any diagnostic or evaluative test which are *contained in the record* and the summaries and conclusions.

42 U.S.C. § 300aa-13(b)(1) (emphasis added); Rule 3(b), VACCINE RULES OF THE UNITED STATES COURT OF FEDERAL CLAIMS.

The purview of the special masters, therefore, was limited by Congress to making case-by-case determinations based solely on evidence "contained in the record." 42 U.S.C. § 300aa-13(b)(1). In direct contravention of the language of the Vaccine Act, however, the Chief Special Master proclaims that the special masters now *"must move beyond case-by-case decision-making toward*

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." *Althen,* at *16 (emphasis added). Not a word in the Vaccine Act, however, authorizes the Chief Special Master to impose any particular "analytical framework" in a causation in fact case; nor is the Chief Special Master charged with determining "the" framework. If a question of law arises regarding the interpretation or implementation of the Vaccine Act, that is a matter for the courts, not the special masters. *See Knudsen* v. *Sec'y Dep't of Health and Human Servs*., 35 F.3d 543, 549 (Fed Cir.1994) ("The *sole* issues for the special master are, based on the record evidence as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the . . . injury or that the . . . injury is a table injury, and whether it has not been shown by a preponderance of the evidence that a factor unrelated to the vaccine caused the . . . injury. *See* 42 U.S.C.§ 300aa-13(a)(1), (b)(1).") (emphasis added); *Hodges* v. *Sec'y Dept. of Health and Human Servs.,* 9 F 3d. 958, 961 (Fed. Cir. 1993) ("Congress assigned to a group of specialists, the Special Masters . . . the unenviable job of sorting through these painful cases and, based upon their accumulated expertise in the field, *judging the merits of the individual claims*.") (emphasis added). That the parties in *Stevens* invited the Chief Special Master to opine on such a framework does not change this analysis.

Of course, a special master properly may propose an "analytical framework" in *dicta. See, e.g., Wagner* v. *Sec'y Dept. of Health and Human Servs*., 1997 WL 617035, at *9 ("[M]y own thoughts on this legal issue constitute pure dicta, not essential to my task [.]") A special master's views also may be of general public interest and make a valuable contribution to the academic and scholarly commentary about the Vaccine Act and its administration. A special master, however, is an adjudicative fact finder charged with applying *existing* legal precedent to decide a particular case based on the record before him or her; a special master ultimately is not the maker nor the interpreter of the law.[21] *See, e.g., La Buy* v. *Howe's Leather Co.,* 352 U. S. 249, 256 (1957) ("The use of master is 'to aid judges in the performance of specific judicial duties'. . . and not to displace the court.") (citation omitted); *In re Bituminous Coal Operators Ass'n Inc.*, 949 F.2d 1165, 1666 (D.C. Cir. 1991) (Ginsburg, J.) (requiring a district judge "to reserve . . . and not delegate to the special master, the *core [judicial] function* of making dispositive rulings, including . . . conclusions of law on issues of liability.") (emphasis added). Although the constitutional issues implicit in *La Buy* and explicitly raised in *Bituminous Coal Operators* are not at issue here because of the court's Article I status and the fact that petitioner voluntarily initiated proceedings under the Vaccine Act, the concern that special masters confine their role to one of *assisting* the court, rather than usurping its authority and proper role to determine dispositive issues of law, is no less relevant in this case.

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[21] *See, e.g.,* Brazil, Wayne D., *Special Masters in Complex Cases: Extending the Judiciary or Reshaping Adjudication,* 53 U. CHI. L. REV. 394, 396 (Spring 1986) (observing "even [special] masters with clearly limited mandates seem pressured or tempted to gravitate into larger spheres. With broader duties, masters might contribute more, but they also may invade the proper preserve of the judiciary[.]")

B. The Application of the *Stevens* "Analytical Framework" In This Case Contravenes the Vaccine Act and Supreme Court and Federal Circuit Precedent.

The court's analysis of the *Stevens* "analytical framework" begins with an examination of whether the language of the Vaccine Act is clear. If so, "that is the end of the matter." *Chevron U.S.A., Inc.* v. *Natural Res. Def. Council, Inc.*, 467 U.S. 837, 842-43 (1984). In determining the clarity of the statute, the court "relies on a commonsense consideration of the words[.]" *See Shalala* v. *Whitecotton*, 514 U. S. 268, 277(1995) (O'Connor, J., concurring opinion). Only if the statute is "silent or ambiguous" is any further inquiry required. *See Chevron,* 467 U. S. at 843. In *Stevens*, however, the Chief Special Master erroneously observed: "Unfortunately, Congress imparted little guidance as to what proof would be necessary to show causation." *Stevens,* at *7. To the contrary, the language of 42 U.S.C. § 300aa-13(a)(1) could not be more clear: Congress specified that the petitioner must prove causation in fact by a "preponderance of the evidence" as to each factor set forth in 42 U.S.C. § 300aa-11(c)(1). In the instant case, the Chief Special Master, perhaps recognizing the flawed premise of *Stevens,* now has re-characterized it as a proposed "analytical framework" consisting of a "five-prong analysis as a *means* of meeting the preponderance of evidence standard[.]" *Althen,* at *12 n.29 (emphasis added). The *Stevens* "analytical framework," however, is much more than a "means." *Id.* In fact and in operation, three of the five *Stevens* elements either significantly change the statutory burden of proof or directly contravene the language of the Vaccine Act and therefore are erroneous as a matter of law. *See Althen,* at *15 ("*Stevens* attempts to guide the experts by defining 'preponderance[.]'") As discussed *infra*, the Supreme Court already has defined "preponderance," and the Federal Circuit has provided ample guidance as to how to weigh evidence in Vaccine Act cases.

1. The "Medical Plausibility" Element

The Supreme Court has defined a preponderance of the evidence to require "the trier of fact 'to believe that the existence of a fact is more probable than its nonexistence before [he or she] may find in favor of the party who has the burden to persuade the [judge] of the fact's existence.'" *Concrete Pipe and Prod. of California, Inc.* v. *Constr. Laborers Pension Trust for Southern California*, 508 U.S. 602, 622 (1993) (quoting *In re Winship*, 397 U.S. 358, 371-372 (1970) (Harlan, J., concurring)). "[J]udges often express [preponderance of evidence] mathematically by saying the plaintiff must establish the facts necessary to her [or his] case by a probability greater than 0.5 or greater than 50%. That is to say the facts claimed by the plaintiff must be more likely than not to exist." DOBBS, DAN B., THE LAW OF TORTS 360 (2000) ("DOBBS").

In the context of Vaccine Act cases, the Federal Circuit has summarized this evidentiary burden as follows: "The claimant must prove by a preponderance of the evidence that the vaccine, and not some other agent, was the actual cause of the injury." *Munn*, 970 F.2d. at 865. A preponderance of evidence, however, does not require proof of scientific certainty. *Bunting,* 931 F.2d at 873 ("The standard of proof required by the Act is simple preponderance of evidence; not scientific certainty."). *Steven's* "medical plausibility" element, however, changes and lowers the petitioner's burden of proof from the preponderance of the evidence standard required by 42 U.S.C. § 300aa-11(c)(1). To be "plausible" a fact need only be "*superficially* fair, reasonable, or valuable." MERRIAM-WEBSTER'S COLLEGIATE DICTIONARY 890 (10th ed. 2001) (emphasis added). Therefore,

by definition, a medical "plausibility" does not achieve the level of reliability expected in a medical record or medical opinion. *See* 42 U.S.C. § 300aa-13(a)(1) (specifically prohibiting a special master or the court from making "a finding based on the claims of a petitioner alone, unsubstantiated by medical records or by medical opinion"); RULE 8(C), VACCINE RULES OF THE UNITED STATES COURT OF FEDERAL CLAIMS (Appendix J to the RCFC) ("The special master will consider all *relevant, reliable* evidence, governed by principles of fundamental fairness to both parties.") (emphasis added); *Daubert* v. *Merrill Dow Pharm., Inc.* 509 U.S. 579, 590 (1993) ("[T]he requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability.") Indeed, even the Chief Special Master acknowledged the inherent vagueness attendant to using a "plausibility" standard: "Plausibility is different things to different people. [The1994 IOM REPORT had] to explain how they were using plausibility because they used it several different ways throughout the report. It's . . . difficult to get a grasp on.") (TR 142-43). And Dr. Martin, one of the government's experts, observed: "Plausible . . . is a very vague term. It's a hypothetical possibility." (TR 111).

This is more than an exercise in semantics. The Vaccine Act, as most legislation, was the product of considerable compromise. As part of that compromise, the vaccine manufacturers acceded to those interests that wanted to allow petitioners who did not have Table injuries the opportunity to receive compensation under the Vaccine Act. The *quid pro quo* was that the manufacturers wanted to be able to rely on the fact that a non-Table petition would be required to meet a traditional tort causation in fact standard, which was and is settled as a matter of law. *See, e.g.,* DOBBS at 360 ("A lesser standard of persuasion than preponderance of evidence [in tort cases] is almost unheard of."). *Stevens'* "medical plausibility" element, however, unlawfully changes the standard of proof that Congress determined was appropriate and, therefore, disturbs settled expectations that reflect "not only the weight of the public and private interest affected, but also a societal judgment about how the risk of error should be distributed between the litigants." *Santosky* v. *Kramer,* 455 U.S. 745, 754-55 (1982) (quoting *Vitek* v. *Jones*, 445 U.S. 480,491 (1980)) (holding that the 'minimum requirements [of procedural due process] being a matter of federal law. . . are not diminished by the fact that the State may have specified its own procedures[.]"). Therefore, the Chief Special Master's findings regarding "medical plausibility" are contrary to law and should be reversed and vacated.

2. The "Confirmation of Medical Plausibility From the Medical Community and Literature" Element

Stevens' second element requires "confirmation of *medical plausibility* from the medical community *and* literature." *Stevens*, at *23 (emphasis added). The Chief Special Master explains that this "Prong" requires petitioner to "establish that peer-reviewed literature is reporting that the vaccine is *related in some sense* to the injury alleged." *Stevens,* at * 24 (emphasis in original deleted in part). As a threshold matter, the Vaccine Act does not preclude causation in fact from being established by a petitioner in the absence of peer reviewed literature. Accordingly, this element changes and increases a petitioner's burden of proof. Moreover, this "Prong" is not faithful to *Daubert*, which does not require that an expert's theory be supported by scientific literature; instead, scientific literature is only one of several factors to be considered by the court in determining the reliability of an expert's opinion. *See Daubert*, 509 U.S. at 594 ("The fact of publication (or lack thereof) in a peer-reviewed journal thus will be relevant, *though not dispositive*, consideration in assessing the

scientific validity of a particular technique or methodology on which an opinion is premised.") (emphasis added).

Accordingly, the Federal Circuit in Vaccine Act cases requires evidence of a strong temporal relationship *and either* reliable medical opinion *or* scientific theory explaining a logical sequence of cause and effect to establish causation in fact. *See Grant*, 956 F.2d at 1148 ("Causation in fact requires 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.") (emphasis added); H.R. Rep. No. 99-908, pt. 1, at 15 (1986) ("evidence in the form of scientific studies *or* expert medical testimony is necessary to demonstrate causation[.]") (emphasis added). In addition, the mere suggestion in peer-reviewed literature that a vaccine is only "*related in some sense*" to the injury falls far short of the reliability required by a "preponderance" standard in an individual case. *See Stevens*, at *24 (emphasis added). At the same time, the lack of such literature, as a matter of law, does not preclude a petitioner from meeting a preponderance standard, based on the totality of evidence in a particular case. Therefore, the Chief Special Master's findings regarding "Prong" two of the *Stevens* "analytical framework" are contrary to law and should be reversed and vacated.

The Chief Special Master found that petitioner in the instant case did not satisfy the burden of proof regarding the second *Stevens* "Prong" and ended his analysis without any discussion about the three additional "Prongs"of the "framework."[22] Therefore, no further review is required here, other than to note that "Prong" three suffers from the same deficiencies as elements one and two of the "analytical framework," because it requires proof of an injury based on the plausibility standard set out in "Prongs" one and two.

C. The Petitioner Carried the Statutory Burden of Proving Causation in Fact.

The Federal Circuit held in *Jay* that petitioner was entitled to "judgment as a matter of law" if the petitioner carried its statutory burden of proving causation under 42 U.S.C. § 300aa-11(c)(1)(C)(ii) and 42 U.S.C. § 300aa-13(a)(1)(A). *See Jay*, 998 F.2d at 984. The undisputed facts in *Jay* on which the Federal Circuit relied in reversing the decision of the United States Court of Federal Claims and awarding petitioner relief in that case include that: "an otherwise healthy child received a DPT shot; the DPT shot caused fever, directly or indirectly limpness, and intermittent inconsolable extended screaming; the child missed his normal nightly feeding; the child died within 18 hours of the shot; the autopsy was inconclusive; and a medical expert testified, uncontradicted, that the DPT shot caused the death, the medical theory being that an encephalopathy occurred." *Jay*, 998 F.2d at 983. The record in this case shares many similarities.

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[22] Although the Chief Special Master's Entitlement Decision states that petitioner was denied relief based on the "totality of the evidence," *Althen,* at * 1, this representation is belied by the fact that the Chief Special Master's Entitlement Decision ended its analysis with petitioner's failure to satisfy "Prong Two." *See Althen*, at *14 ("[T]he 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].").

In the instant case, petitioner's medical records evidence that she was generally in good health before she received a tetanus toxoid vaccine on March 28, 1997. (P. Ex. 20 at 1). Both of the government's experts agreed that the initial symptom of petitioner's illness, *i.e.,* optic neuritis, occurred within a medically appropriate time period.[23] Optic neuritis is widely recognized as a symptom of "diffuse demyelinating diseases such as ADEM and multiple sclerosis." 1994 IOM REPORT at 83; *see also id.* Glossary Exhibit C at 340 ("Optic Neuritis represents a central demyelinating disease of the optic nerve anterior to the optic chiasm. It can occur as a solitary unexplained monophasic disease or it may be an early sign of multiple sclerosis.").[24] In addition, the petitioner established a logical sequence of cause and effect, in that within 18 days after receiving a tetanus toxoid vaccine and until the trial, petitioner evidenced some form of continuing and worsening demyelinating disease, which is "characterized pathologically by diffuse foci of perivenular inflammation[.]" 1994 IOM REPORT at 83. This record is replete with incident after incident of worsening inflammatory disease during this period. *See infra* at 3-6.

The law in the Federal Circuit is well established that once a petitioner establishes a strong temporal relationship between receiving the vaccine and first symptoms of illness, a logical sequence of cause and effect, supported by a reliable medical opinion *or* scientific theory, also must be proffered to explain the causal link. *See Grant*, 956 F.2d at 1148. Petitioner's expert presented a reliable medical opinion linking petitioner's medical records and progressing illness to the established medical theory of "degeneracy" and "epitope spreading" to establish causation. Both "degeneracy" and "epitope spreading" were known to and not disputed by Dr. Martin, one of the government's expert witnesses.[25] Moreover, Dr. Martin's theory of "degeneracy" and "epitope spreading" appears to be supported by a pathology report, dated September 1, 2000, indicating that:

> The deep cortex shows increasing abnormalities in relation to marked tissue destruction with secondary demyelination . . . . The tissue destruction appears to be due to inflammation involving the small and medium size blood vessels, many of which are surrounded and infiltrated by lympho-plasmaytic infiltrates extending into the adjacent tissue. . . . IP studies, however, show

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[23] Dr. Martin testified: "Something in the range between seven (days) and four weeks would be an appropriate temporal relationship for an autoimmune response." (TR 119). Dr. Safran concurred that the temporal relationship here is appropriate. (TR 159).

[24] Optic neuritis is not a "vasculitis "illness, as Dr. Safran, one the government's experts testified. *See Althen*, at*6.

[25]Dr. Martin testified, "I do not agree with the conclusions [of Dr. Smith that it is likely or probable that tetanus toxoid triggered petitioner's disability], but it is correct that *degeneracy* . . . moves T lymphocytes . . . [which] can respond to one antigen . . . and are able to recognize large numbers, probably in the range of 10 to the six[th] of one million different antigens by one T cell receptor. Among these many antigens that stem from, a pattern as this *cannot be excluded as a theoretically possibility* . . . ." (TR 83) "*I agree with the theoretical possibility* [that tetanus toxoid caused petitioner's demeylinating illness], but I . . . currently do not have the evidence supporting it."). (TR 122) (emphasis added).

> a marked predominance of T cells and insufficient atypia of B cells to sustain a diagnosis of lymphoma. . . . Absent any demonstrable cause of the vascular inflammation and absent systemic vasculitis, this case falls into the category of primary angiitis of the central nervous system. . . . Clinically and pathologically, this is an unusual presentation and evolution of cerebral vasculitis, and no agreement was reached on the nature of the disease [but] [m]orphologically, the features are those of a primary vasculitis of the brain.

(P. Ex. 26 at 126).

Finally there is no evidence in this record that petitioner's injuries were caused by some factor other than the tetanus toxoid vaccine. There is also no evidence of a virus or other explanation for petitioner's onset and deteriorating condition other than the tetanus toxid vaccine, which is made from a bacterial agent. (TR 57). Notably, Dr. Vollmer early on identified an infection as a potential cause of petitioner's illness. (P. Ex. 4 at 23) ("small abnormalities scattered throughout the white matter, suggestive of vasculitis or sarcoid or parainfectious disease"). Neither Dr. Vollmer nor the government's experts, knew or seemed to appreciate that petitioner's hypothyroid condition likely was autoimmune disorder that would have made her T cells more sensitive to the effects of the vaccine and the potential for both degeneracy and epitode spreading. Nor did the Chief Special Master. As the Federal Circuit observed in *Jay*, "The special master losing sight of the forest for the trees, ignored entirely the fact of [a child's] death. [Petitioner's expert physician] did not assume that an encephalopathy occurred. Rather, he testified that an encephalopathy occurred based on [the child's] *entire history*[.]" *Jay*, 998 F. 2d at 983 (emphasis added). Based on petitioner's entire medical history and the record in this case, the court believes that the petitioner satisfied the statutory requirements for recovery.

Petitioner proffered reliable medical records, a reputable medical opinion, a logical sequence of cause and effect, and a medical theory causally connecting the vaccination to the onset and development of her demyelinating illness. In other words, petitioner established that but for the vaccine, it is more likely than not (greater than 50%) that she would not have incurred optic neuritis and subsequent symptoms of demyelinating illness. Moreover, petitioner has established that it is more likely than not (greater than 50%) that the vaccine was a substantial factor in causing her demyelinating illness. Therefore, the Chief Special Master erred as a matter of law because the petitioner met the statutory burden to establish causation in fact under 42 U.S.C. § 300aa-11(c)(1)(C)(ii) and 42 U.S.C. § 300aa-13(a)(1)(A), albeit that causation was not established to a medical certainty. *See Knudsen,* 35 F.3d at 548-49 ("The determination of causation in fact under the Vaccine Act involves ascertaining whether a sequence of cause and effect is 'logical' and legally probable, not medically or scientifically certain."); *Bunting*, 931 F.2d at 873 ("The standard of proof required by the Act is simple preponderance of the evidence, not *scientific certainty*.") (emphasis added). Petitioner, therefore, is entitled to relief under the Vaccine Act.

CONCLUSION

For the foregoing reasons, Petitioner's Motion for Review is **GRANTED**, the June 3, 2003 Entitlement Decision of the Chief Special Master is hereby **REVERSED** and **VACATED**, and the case is remanded to the Chief Special Master for an award of compensation to the petitioner, reasonable attorneys fees, and other costs. The Clerk of the Court shall enter judgment accordingly.

IT IS SO ORDERED.

____

Susan G. Braden
Judge