In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 10-489V

(Filed: September 12, 2013)

TO BE PUBLISHED[1]

VALERIA FLORES,	*	Vaccine Act Entitlement;
	*	Causation-in-fact; Human
Petitioner,	*	Papilloma Virus (HPV)
	*	Vaccine/Spinal Cord Infarction
v.	*	
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
	*	
	*	
Respondent.	*	

Clifford Shoemaker, Vienna, Virginia, for Petitioner.
Debra Begley, U.S. Department of Justice, Washington, D.C., for Respondent.

DECISION

HASTINGS, ***Special Master.***

This is an action in which the Petitioner, Valeria Flores, seeks an award under the National Vaccine Injury Compensation Program (hereinafter "the Program"[2]), on account of a spinal cord infarction that Petitioner believes was caused by a human papilloma virus (hereinafter "HPV") vaccination. For the reasons set forth below, I conclude that Petitioner is not entitled to an award.

[1] Because I have designated this document to be published, this document will be made available to the public unless petitioner files, within fourteen days, an objection to the disclosure of any material in this decision that would constitute "medical files and similar files the disclosure of which would constitute a clearly unwarranted invasion of privacy." See 42 U.S.C. §300aa-12(d)(4)(b).

[2] The applicable statutory provisions defining the Program are found at 42 U.S.C. § 300aa-10 *et seq*. (2000 ed.). Hereinafter, for ease of citation, all "§" references will be to 42 U.S.C. (2000 ed.).

I

APPLICABLE STATUTORY SCHEME AND CASELAW

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showings that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-lasting injury; and has received no previous award or settlement on account of the injury. Finally--and the key question in most cases under the Program--the petitioner must also establish a *causal link* between the vaccination and the injury. In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table Injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table" corresponding to the vaccination in question, within an applicable time period following the vaccination also specified in the Table. If so, the Table Injury is presumed to have been caused by the vaccination, and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. §300aa-13(a)(1)(A); §300aa-11(c)(1)(C)(i); §300aa-14(a); §300aa-13(a)(1)(B).

In other cases, however, the vaccine recipient may have suffered an injury *not* of the type covered in the Vaccine Injury Table.[3] In such instances, an alternative means exists to demonstrate entitlement to a Program award. That is, the petitioner may gain an award by showing that the recipient's injury was "caused-in-fact" by the vaccination in question. §300aa-13(a)(1)(A); §300aa-11(c)(1)(C)(ii). In such a situation, of course, the presumptions available under the Vaccine Injury Table are inoperative. The burden is on the petitioner to introduce evidence demonstrating that the vaccination actually caused the injury in question. *Althen v. HHS*, 418 F. 3d 1274, 1278 (Fed. Cir. 2005); *Hines v. HHS*, 940 F. 2d 1518, 1525 (Fed. Cir. 1991). The showing of "causation-in-fact" must satisfy the "preponderance of the evidence" standard, the same standard ordinarily used in tort litigation. §300aa-13(a)(1)(A); *see also Althen*, 418 F. 3d at 1278; *Hines*, 940 F. 2d at 1525. Under that standard, the petitioner must show that it is "more probable than not" that the vaccination was the cause of the injury. *Althen*, 418 F. 3d at 1279. The petitioner need not show that the vaccination was the sole cause or even the predominant cause of the injury or condition, but must demonstrate that the vaccination was at least a "substantial factor" in causing the condition, and was a "but for" cause. *Shyface v. HHS*, 165 F. 3d 1344, 1352 (Fed. Cir. 1999). Thus, the petitioner must supply "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury;" the logical sequence must be supported by "reputable medical or scientific explanation, *i.e.*, evidence in the form of scientific studies or expert medical testimony." *Althen*, 418 F. 3d at 1278; *Grant v. HHS*, 956 F. 2d 1144, 1148 (Fed. Cir. 1992).

The *Althen* court also provided additional discussion of the "causation-in-fact" standard, as follows:

[3] No Table Injury is alleged in this case. Petitioner's theory in this case is solely one of "actual causation."

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F. 3d at 1278 (citations omitted). The *Althen* court noted that a petitioner need not necessarily supply evidence from *medical literature* supporting the petitioner's causation contention, so long as the petitioner supplies the *medical opinion* of an expert. *Id*. at 1279-80. The court also indicated that, in finding causation, a Program factfinder may rely upon "circumstantial evidence," which the court found to be consistent with the "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." *Id*. at 1280.

Since *Althen*, the Federal Circuit has addressed the causation-in-fact standard in several additional rulings, which have affirmed the applicability of the *Althen* test, and afforded further instruction for resolving causation-in-fact issues. In *Capizzano v. HHS*, 440 F. 3d 1317, 1326 (Fed. Cir. 2006), the court cautioned Program factfinders against narrowly construing the second element of the *Althen* test, confirming that circumstantial evidence and medical opinion, sometimes in the form of notations of treating physicians in the vaccinee's medical records, may in a particular case be sufficient to satisfy that second element of the *Althen* test. Both *Pafford v. HHS*, 451 F. 3d 1352, 1355 (Fed. Cir. 2006), and *Walther v. HHS*, 485 F. 3d 1146, 1150 (Fed. Cir. 2007), discussed the issue of which party bears the burden of ruling out potential non-vaccine causes. *DeBazan v. HHS*, 539 F. 3d 1347 (Fed. Cir. 2008), concerned an issue of what evidence the special master may consider in deciding the initial question of whether the petitioner has met her causation burden.

Another important aspect of the causation-in-fact case law under the Program concerns the factors that a special master should consider in evaluating the *reliability* of expert testimony and other scientific evidence relating to causation issues. In *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), the Supreme Court listed certain factors that federal trial courts should utilize in evaluating proposed expert testimony concerning scientific issues. In *Terran v. HHS*, 195 F. 3d 1302, 1316 (Fed. Cir. 1999), the Federal Circuit ruled that it is appropriate for special masters to utilize *Daubert's* factors as a framework for evaluating the reliability of causation-in-fact theories presented in Program cases. One of the factors listed in *Daubert* is whether the scientific theory "has been subjected to peer review and publication." 509 U.S. at 593. The Court noted that while publication does not "necessarily" correlate with reliability, since in some instances new theories will not yet have been published, nevertheless "submission to the scrutiny of the scientific community is a component of 'good science,'" so that the "fact of publication (or lack thereof) in a peer reviewed journal thus will be a relevant, though not dispositive, consideration in assessing the scientific validity" of a theory. *Id*. at 593-94.

II

FACTS AND PROCEDURAL HISTORY

A. Facts

Valeria Flores ("Valeria" or "Petitioner") was born on September 6, 1993, and was 14 years old at the time of the vaccination here at issue. (Petition at p. 1.) Though she had a few significant illnesses, Valeria's medical history prior to 2008 is not relevant here.[4] At the time of her vaccination, she had experienced no recent illnesses or injuries. (Ex. 20,[5] P. 3.)

On April 28, 2008, Valeria was seen for a school physical. (Ex. 7, p. 4.) During that exam, she was given her first meningococcal and HPV vaccinations. (Ex. 6, p. 1; Ex. 7, p. 6.) There are no medical records that suggest that Valeria reported any concerns following her first HPV vaccination. On June 27, 2008, Valeria received her second HPV vaccination. (Ex. 6, p. 1; Ex. 7, p. 10.)

The medical records make it clear that Valeria's symptoms began the following day, on June 28, 2008, although there is a discrepancy regarding the exact timing of symptom progression. According to the ambulance records, she *awoke* with left-sided weakness that progressed to shortness of breath. (Ex. 1, p. 5.) Similarly, records from the first hospital, Mt. Sinai, reflect that she awoke with a severe headache and left arm weakness. (Pet. Ex. 8, pp. 7, 28.) However, the records from Rush University Medical Center, to which she was later transferred, contain a statement from Valeria's mother reporting that Valeria had no symptoms until 12:30 in the afternoon, when she complained of a sudden, severe headache, followed by left arm pain and weakness. (Ex. 20, p. 35.) The notes from the emergency medical technicians ("EMTs") who arrived at Valeria's home at 1:22 in the afternoon state that Valeria had difficulty breathing and that her symptoms had begun approximately ninety minutes earlier. (Ex. Ex. 4, p. 3.)

In any event, it is clear that, at some time on June 28, Valeria experienced symptoms including left-sided weakness, headache, and shortness of breath. (Ex. 1, p. 5; Ex. 4, p. 3; Ex. 8, pp. 7, 28; Ex. 20, p. 35.) When the emergency medical service ("EMS") arrived, Valeria developed bradycardia and suffered a cardiac arrest. (Ex. 4, p. 4.) She was intubated and responded to cardiopulmonary resuscitation and atropine. (*Id*.) By the time she arrived at the hospital, her blood pressure had returned to 102/74, and she was no longer asystolic. (*Id*.)

Upon arrival in the Mt. Sinai Hospital emergency room on June 28, Valeria was awake, but unable to feel or move her extremities. (Ex. 8, p. 7.) At that emergency room, Valeria's parents reported that she had been suffering from a severe headache and left arm weakness, followed by

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[4] In 1998, Valeria had a positive reaction to a tuberculin skin test and was treated with nine months of Isoniazid. (Ex. 3, p 28.) She was also followed for crystals in her urine. (*Id.* at pp. 8, 10.) She had measles at the age of 3. (Ex. 20, p. 3.)

[5] Petitioner filed Exhibits 1 through 15 on September 17, 2010, and has since filed a number of additional consecutively-numbered exhibits. Respondent has filed Exs. A through O at various times.

shortness of breath.[6] (*Id.* at 9.) They also reported that she had received her HPV vaccination the day before. (*Id.*) Coagulation studies were normal, and a urinalysis showed high levels of protein. (*Id.* at 18, 20.) A brain CT, without contrast, was normal. (*Id.* at 24.) Valeria was transferred to Rush University Hospital that same day for further medical treatment. (Ex. 1, p. 5; Ex. 20, p. 3.)

Upon arrival at Rush, further evaluation was conducted. In an admission note, Valeria's mother reported that earlier that day Valeria began to complain of a headache so painful that she was in tears. (Ex. 20, p. 35.) Valeria's mother noted that about five minutes after the headache started, Valeria began having left arm pain that developed into paralysis and loss of sensation. (*Id*.) By the time the EMS arrived, Valeria had developed flaccid paralysis of her upper and lower extremities and slurred speech. (*Id*.) An MRI showed changes in the cervical cord at C2 through C4, which was thought to possibly indicate "ischemic change . . . myelitis, or acute demyelination." (Ex. 20, p. 1079.) A cerebral angiogram showed no evidence of aneurysms, arterial venous malformations, or arterial venus fistulae. (*Id*. at 813.) The potential diagnoses, as of June 29, 2008, included "ischemia/thrombotic event, myelitis, acute demyelination, vascular abnormalities, toxins (lead, heavy metals), infectious disease, and autoimmune." (*Id.* at 42.)

Valeria underwent an extensive workup while at Rush, in an attempt to determine the cause of her symptoms, including her paralysis. An echocardiogram did not reveal a patent foramen ovale;[7] cerebral spinal fluid cultures were negative; all autoimmune studies – rheumatoid factor, antinuclear antibodies, double-stranded DNA, Sjogren's syndrome and SSB antibodies – were negative. (Ex. 20, pp. 883, 891, 899, 904-905, 1002.) A coagulopathy workup, including proteins C and S, Antithrombin III, and Factor V Leiden, were negative. (*Id.* at 884-886, 897, 949-950.) However, a MTHFR A1298C heterozygous mutation, a common genetic abnormality, was found during Valeria's genetic work-up. (*Id*. at 944.) An infectious disease workout was also negative. (*Id*. at 980-81, 1001-08, 1031-34.)

The records from Rush indicate a shift in the analysis of her condition away from possible heart-related causes, so that Valeria was then given a working diagnosis of transverse myelitis. (Ex. 20, p. 23.) On July 3, 2008, she was started on a five-day course of solumedrol, without improvement. (Ex. 20, p. 20.) She then received one dose of cyclophosphamide, and was started on a five-day course of blood plasma exchange. (*Id*.) She again showed no improvement. (*Id*. at 24.)

On August 6, 2008, Valeria's case was reviewed by two neurologists, Drs. Tilwalli and Stefofski. Dr. Tilwalli, a neurology fellow, opined that given Valeria's quick onset, absence of inflammatory markers, and lack of response to anti-inflammatory treatment, he favored a vascular

[6] It should be noted that Valeria was fluent in English and her father spoke "adequate" English at the time of the injury. The records reveal that her parents communicated with hospital staff through an interpreter. (Ex. 8, p. 5; Ex. 9, p. 1; Ex. 20, pp. 6, 26.)

[7] Patent foramen ovale is a congenital condition in which there is a small opening between the chambers of the heart.

etiology. (Ex. 20, p. 29.) He also noted that he thought Valeria's HPV vaccination was too close to symptom onset to induce an inflammatory response. (*Id.*) Similarly, a neurologist, Dr. Stefofski, opined that Valeria's quick symptom onset "strongly favors a vascular etiology over immune mediated/inflammatory (definitely too soon for Gardasil or even for a remote preceding myelitogenic trigger)." (*Id.* at 488.) He also noted that due to the lack of response to corticosteroids and cyclophosphamide, he doubted an autoimmune etiology. (*Id.*)

Valeria continued to have flaccid paralysis throughout her hospitalization. (Ex. 9, p. 1.) Ultimately, it was determined, as all the experts in this litigation agreed, that the cause for her paralysis and other symptoms was a *spinal cord stroke*.

Due to continuous mechanical ventilation throughout her stay, Valeria understandably experienced significant anxiety. (*Id.* at 5.) As a result, she was started on anti-anxiety medication. (*Id*.) Valeria was hospitalized until August 7, 2008, when she was transferred to an inpatient rehabilitation center.[8] (Ex. 9, p. 5; Ex. 20, p. 820.)

Valeria was an inpatient at the Rehabilitation Institute of Chicago from August 7, 2008, through December 16, 2008. (Ex. 11, p. 30.) During her stay, she remained ventilator-dependent, and experienced headaches, anxiety, and spasticity. (*Id*.) Valeria's physical abilities did not improve during rehabilitation, and she required total assistance for mobility and all activities of daily living at the time of discharge. (*Id.* at 30-32.) She was also noted to have cognitive communication deficits, severe dysphagia and dysarthria, and aphonia as a result of her ventilator dependence. (*Id.* at 32.)

During discharge from inpatient rehabilitation, Valeria returned home and was cared for by her mother and a home health nurse. (Ex. 5, p. 4.) On January 22, 2009, her family reported that the transition home had gone well, and that Valeria would soon start home-based tutoring for school. (*Id*.) On February 19, 2009, Valeria was evaluated at Rush Medical Center, and it was reported that she was starting to feel sensation in her extremities. (Ex. 13, p. 6.) On March 23, 2009, during a neurological evaluation, Valeria exhibited some voluntary movement in her right index finger and left thumb, and again reported a subjective increase in sensation in her extremities. (Ex. 9, p. 4.) Despite these improvements, Valeria is still dependent on a full-time ventilator. (*Id.*)

Although Valeria is still dependent on a wheelchair and ventilator, at the time of the evidentiary hearing she was completing her senior year of high school, and was optimistic about attending college in the fall. (Tr. 5-6.)

[8] During her hospitalization, Valeria developed complications, including haemophilus influenza and streptococcus pneumonia. (Ex. 20, p. 4.) She also had a persistent yeast infection, a positive klebsiella titer, and a positive enterobacter urine culture. (*Id*.) These conditions lengthened her hospital stay at Rush.

B. Procedural History

The petition was filed on July 29, 2010, and the case was assigned to my docket. Petitioner submitted an expert report and medical records, as Exhibits 1-15, on September 17, 2010. Respondent filed expert reports in December 2010 and May 2011. Status conferences were held in January and June of 2011, and an evidentiary hearing was scheduled for January 31, 2012. At the evidentiary hearing, Petitioner relied on the testimony of one expert witness, while Respondent relied on two expert witnesses. At the conclusion of the hearing, Petitioner's counsel requested that the parties file post-hearing briefs. The last of the post-hearing briefs has been filed, so that the case is ripe for a ruling concerning the issue of whether Petitioner has met her burden of demonstrating that her injury was, more probably than not, caused by her HPV vaccination.

III

ISSUE TO BE DECIDED

In this case, Petitioner seeks a Program award, contending that she suffered a stroke that was "caused-in-fact" by her HPV vaccination received on June 27, 2008. After careful consideration, I conclude that Petitioner has *failed* to demonstrate vaccine causation of her injury.[9]

Petitioner's theory of the case, as asserted by her expert, Dr. Douglas Kerr, may be briefly summarized as follows. As all of the three testifying experts agree, Valeria experienced a spinal cord stroke, also known as a spinal cord "infarct" or spinal cord "infarction," shortly after her second HPV vaccination, which she received on June 27, 2008. In a spinal cord stroke, spinal cord tissue suffers a permanent injury due to lack of oxygen. As also agreed by all the testifying experts, Valeria's stroke was caused by a blood clot, also known as a "thrombus," which became lodged in a spinal blood vessel, obstructing the oxygen flow and leading to the spinal cord injury. (The occurrence of a blood clot causing damage to body tissue is also described in the record of this case as a "thrombosis" or a "thromboembolic event.")

The experts in this case differ as to what *caused* the blood clot to form. Dr. Kerr, for reasons to be detailed below, testified that Valeria's HPV vaccination caused the formation of the blood clot. Respondent's two experts, Dr. Peter Bingham, and Dr. Joan Gill, on the other hand, find it improbable that Valeria's HPV vaccination had anything to do with the formation of the blood clot. They do not claim to know what caused the clot, but note that the cause of most spinal cord strokes is unknown, and argue that there is no good evidence to support either the proposition that an HPV vaccination could cause such a blood clot *in general*, or that it *did* cause a blood clot in Valeria.

[9] Petitioner has the burden of demonstrating the facts necessary for entitlement to an award by a "preponderance of the evidence." §300aa-13(a)(1)(A). Under that standard, the existence of a fact must be shown to be "more probable than its nonexistence." *In re Winship*, 397 U.S. 35 8, 371 (1970) (Harlan, J., concurring).

After carefully considering all of the evidence in the record, I must *reject* Petitioner's claim that her stroke was caused by her HPV vaccination. There are several reasons for this ultimate conclusion, which I will discuss separately in the pages below.

IV

SUMMARY OF EXPERT WITNESSES' CREDENTIALS AND OPINIONS

A. Petitioner's expert Dr. Douglas Kerr

1. Qualifications

Dr. Douglas Kerr received a degree in biology from Princeton University in 1988, and graduated from Thomas Jefferson University in 1995 with a medical degree and a Ph.D. in biochemistry and molecular biology. He completed a one-year residency in the Department of Internal Medicine at the Graduate Hospital in Philadelphia in 1997, followed by a neurology residency at The Johns Hopkins Hospital from 1996 to 1999. Dr. Kerr is certified by the American Board of Psychiatry and Neurology. From 1999 until 2005, he served as an Assistant Professor at The Johns Hopkins School of Medicine in the Department of Neurology, as well as The Johns Hopkins School of Public Health in the Department of Molecular Microbiology and Immunology. Thereafter Dr. Kerr taught as an Associate Professor in both departments until 2010. He was also an Associate Professor in the Department of Cellular and Molecular Medicine from 2006 until 2010. In 1999, Dr. Kerr founded the Johns Hopkins Transverse Myelopathy Center, for which he served as the Director until 2010. Dr. Kerr became the Director for Neurodegeneration at the biotechnology company Biogen-Idec in 2010, a position that he continues to hold. He has published more than 100 professional abstracts, presentations and papers. (Ex. 17 pp. 1-21; Tr. 8-25.)[10]

2. Summary of opinion of Dr. Kerr

As noted above, Dr. Kerr testified that the blood clot that caused Valeria's stroke was a result of the HPV vaccination that Valeria received the day prior to her injury. (Tr. 32.) Dr. Kerr testified that Valeria had a genetic predisposition making her susceptible to blood clotting, involving multiple genes, and that "genetic loading" conferred a risk of adverse vaccine response. (Tr. 33.) Dr. Kerr asserted that Valeria's first HPV vaccination, which she received on April 28, 2008, sensitized Valeria's immune system, and that the second dose, received on June 27 of that same

[10] Dr. Kerr left Johns Hopkins after the institution determined that he had engaged in professional and research misconduct. (Tr. 19-20.) Dr. Kerr testified, on the other hand, that the action by Johns Hopkins was unwarranted. (Tr. 25-29.) I have reached no conclusion whatsoever about this issue, and it has played no role in my resolution of this case. I have assumed the sincerity of Dr. Kerr's opinion, and have evaluated his testimony in light of his prestigious academic credentials. My resolution of this case is based simply on the fact that despite Dr. Kerr's credentials, I found that the testimony of Respondent's experts was substantially more persuasive than that of Dr. Kerr in this case.

year, then elicited an "exuberant" and rapid immune response. (Tr. 41-42.) Dr. Kerr testified that one of two reactions occurred, resulting in the blood clot. His first theory was that the HPV vaccination received on June 27, 2008, created *inflammation* due to an exuberant immune response, thereby resulting in the blood clot that caused Valeria's spinal cord stroke. (Tr. 35-36.) Dr. Kerr's second theory was that the same vaccination caused *platelet aggregation* in Valeria's blood, which also could have resulted in the blood clot. (Tr. 36.) (In his expert report, Dr. Kerr offered a *third* alternative theory, that the HPV vaccination triggered an "antiphospholipid syndrome" that led to the clot. (Ex. 22, p. 4.) He withdrew that third alternative, however, during the evidentiary hearing. (Tr. 147-48.)[11])

B. Respondent's experts

1. Dr. Peter Bingham

Dr. Bingham received a B.A. from Harvard College in 1981, and a medical degree from the Columbia College of Physicians & Surgeons in 1987. From 1987 through 1992 he served as a pediatric resident, and then a neurology resident, at the Children's Hospital of Philadelphia. Dr. Bingham was also a neurology resident at the University of Pennsylvania Hospital from 1989 until 1992. He was trained in a fellowship for neuromuscular disease at the University of Pennsylvania Hospital from 1993 through 1994. Dr. Bingham has held multiple teaching positions at the University of Pennsylvania School of Medicine, first as an Instructor of Clinical Neurology from 1990 to 1994, and then as an Assistant Professor of Neurology and Pediatrics until 2000. He concurrently worked as a collaborating scientist at the Monell Chemical Senses Center in Philadelphia from 1999 through 2000. In 2000, Dr. Bingham became a Clinical Associate Professor of Neurology and Pediatrics at the University of Vermont, a position that he currently holds, in which he treats children with neurological disorders. He has published over 50 abstracts, presentations, and papers. (Ex. B, pp. 1-6; Tr. 188-93.)

2. Dr. Joan Gill

Dr. Joan Gill received her B.S. from St. Norbert College in West De Pere, Wisconsin, in 1965, and her medical degree from the Medical College of Wisconsin in 1976. She was a pediatrics intern at Milwaukee Children's Hospital in the Medical College of Wisconsin from 1976 to 1977, where she also served a pediatric residency from 1977 until 1979. Dr. Gill further

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[11] Concerning that third theory, Dr. Kerr wrote as follows:

> The term antiphospholipid syndrome describes an autoantibody-induced hypercoagulable state, whose hallmarks are recurrent thrombosis. Research shows the central role of endothelial cells, monocytes, platelets, and complement in induction of thrombosis in antiphospholipid syndrome and that vaccines may contribute to the development or activation of antiphospholipid antibodies resulting in thrombosis. * * * Thus several investigators have noted that vaccinations can trigger the generation and/or activation of antiphospholipids that interact with blood vessel inflammation and platelet aggregation to induce thrombosis. (Ex. 22, p. 4.)

specialized in pediatric hematology and oncology through a fellowship at the Medical College of Wisconsin and the Blood Center of Southeastern Wisconsin from 1978 to 1981. She is board-certified in both Pediatrics and Pediatric Hematology/Oncology. Dr. Gill has served in multiple faculty positions at the Medical College of Wisconsin, beginning as a Clinical Instructor of Pediatrics from 1981 to 1982. She became an Assistant Professor of Pediatrics in 1982, an Associate Professor of Pediatrics in 1988, and a Professor of Pediatrics in 1994, a position that she still holds. Additionally, Dr. Gill has served at the Medical College of Wisconsin as a Professor of Medicine since 2002, and as a Professor of Pollution Health-Epidemiology since 2009. She presently holds a position as an Investigator at the Blood Center of Southeastern Wisconsin. Her medical practice focuses on blood disorders in children, in which she commonly treats children with genetic predispositions for bleeding and clotting disorders, as well as children with immune-related blood disorders. (Tr. 124-26.) Within her field of expertise, Dr. Gill has published more than 80 professional articles, and has presented over 80 lectures. (Ex. J, pp 2-42; Tr. 123-28.)

3. Summary of opinions of Respondent's experts

Dr. Bingham agreed with Dr. Kerr's general conclusion that Valeria suffered an infarction of her spinal cord as a result of a blood clot. (Tr. 194.) However, Dr. Bingham disagreed with Dr. Kerr's proposed theories of vaccine-causation. Dr. Bingham testified that Valeria's HPV vaccination did not cause a blood clot by means of *inflammation*, because Valeria's clinical tests showed no evidence of inflammation. (Tr. 196, 199-200.) He further testified that there exists no established association between the HPV vaccination and spinal cord infarction, nor is that vaccine known to be a probable cause of blood clots. (Tr. 200, 216.) He opined that it is not probable that Valeria's HPV vaccination had any causal connection to her stroke. (Tr. 195, 214, 216.)

Dr. Gill testified that although Valeria suffered a spinal cord infarction, Valeria's MTHFR gene mutation was not a contributing factor. (Tr. 138.) She also disagreed with Dr. Kerr's conclusion that the HPV vaccine caused inflammation that resulted in a blood clot. (Tr. 138-50, 154.) Dr. Gill stated that Valeria's lab results did not show any evidence of inflammation (Tr. 140, 142-46, 177), *or* platelet aggregation (Tr. 149-50). She additionally noted that a clotting response to the vaccination, produced by inflammation, would have taken at least four days after vaccination to develop, whereas Valeria suffered the onset of her stroke symptoms approximately one day post-vaccine. (Tr. 139-40, 179-80.)

V

DR. KERR FAILED TO DEMONSTRATE THAT A COMBINATION OF GENETIC FACTORS MADE VALERIA SUSCEPTIBLE TO BLOOD CLOTTING OR STROKES

Dr. Kerr stressed that *both* of his causation theories are based on the assumption that Valeria must have had a "genetic predisposition" that caused her to be susceptible to such an unusual reaction to the HPV vaccine, which vaccine he acknowledged to be "very safe" in general, and which is routinely administered without any adverse consequences. (Tr. 33; Ex. 22, p. 1.) He testified that the assumption of such a genetic predisposition is "absolutely critical" to his

causation theories. (Tr. 33.) He explained that such a genetic predisposition would require a *combination* of several genes--"six or seven or maybe 10 genes." (Tr. 33; see also Tr. 72-73.)

However, Dr. Kerr acknowledged that he did *not* know what that combination of genes might be. (Tr. 74.) In the final analysis, I conclude that Dr. Kerr was engaging in mere *speculation* or *guesswork* in concluding that Valeria must have had such a cluster of genes. Thus, this part of his theory, which he himself claimed as "absolutely critical" to his overall theories (Tr. 33), has *not* been shown to be probable.

In this regard, it should be noted that, as all of the testifying experts agree, Valeria *does* have a *particular* mutation in the portion of her genetic code known as "MTHFR." (MTHFR stands for methylenetetrahydrofolate reductase--Tr. 132.) In an earlier written expert report, Dr. Kerr specifically asserted, without qualification, that Valeria's "mutation in the MTHFR gene" gives her a "genetic predisposition to thrombosis." (Ex. 22, p. 1.) During the evidentiary hearing, however, Dr. Kerr backed off quickly from that assertion, acknowledging that Valeria's MTHFR mutation "alone" could not make her susceptible to blood clotting and stroke. (Tr. 74.) While asserting that Valeria must have some unknown "cluster" of genes that made her susceptible, Dr. Kerr acknowledged that her MTHFR mutation may *not* have been any part of that unspecified gene cluster. (Tr. 73-74.) He stated that the MTHFR mutation "may" have been "one of many factors genetically" that contributed to her alleged predisposition. (Tr. 74, lines 17-19.)[12]

In contrast, the only hematologist (blood specialist) to testify,[13] Dr. Gill, testified that Valeria's *particular* type of MTHFR mutation, known as the MTHFR - 1298 mutation, does *not* cause blood clotting.[14] (Tr. 132-38.) Dr. Gill explained that conclusion in detail, and pointed to a medical study supporting that conclusion. (Tr. 135-137; Ex. K.)

Dr. Kerr, in contrast, did not point to any problems with the reasoning of Dr. Gill described in the prior paragraph. Instead, he pointed to two other medical articles to support the proposition that MTHFR mutations might cause an increased risk of clotting. (Tr. 50-51; *see* Exs. 27 and 45.) However, on cross examination, Dr. Kerr admitted that those two articles did *not* deal with the *specific* type of MTHFR mutation which *Valeria* has, the MTHFR - 1298 mutation. (Tr. 112-13.)

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[12] Moreover, respondent's expert, Dr. Gill, explained that testing of Valeria did *not* reveal any other genetic mutations beyond her MTHFR mutation. (Tr. 149.)

[13] Dr. Kerr acknowledged that if in his medical practice he had a patient with a spinal cord clot, he would consult with a hematologist or oncologist to determine the *cause* of the clot. (Tr. 23.)

[14] In one of petitioner's post-hearing briefs, filed on August 27, 2012, petitioner's counsel states that Valeria's MTHFR-1298 mutation "*is* associated as a risk factor for venous thrombosis--a fact acknowledged by Respondent's expert. Tr. at 171." (Brief at p. 3, emphasis in original.) But this grossly misrepresents what Dr. Gill said. Dr. Gill, in fact, stated clearly that while *some* types of MTHFR mutations might be a risk factor, the *MTHFR-1298* mutation, which Valeria has, is *not* a risk factor for any type of blood clotting or stroke. (Tr. 136-38.) Unfortunately, this misrepresentation of an expert's testimony reflects poorly on petitioner's counsel.

Moreover, Dr. Gill explained that the mechanism by which *some* types of MTHFR mutations might increase the risk of clotting would be by increasing "homocysteine" levels (Tr. 132), but Valeria's testing indicated that Valeria did *not* have increased homocysteine levels (Tr. 137).

In sum, I find that Dr. Kerr totally failed to establish a factor what he himself called a "critical factor" in his analysis--that Valeria had some type of *genetic predisposition* that made her susceptible to have blood clots. In this regard, I reiterate that Dr. Kerr first asserted, without qualification (Ex. 22, p. 1), that Valeria's MTHFR - 1298 mutation made her susceptible to blood clotting; but later, upon being contradicted by a blood specialist concerning this point, he abandoned that assertion. Instead, he could do no more than propose that Valeria *might* have had a cluster of several different genes that made her susceptible, but could not even propose what any of those genes might have been.

In short, in my view, this "critical factor" of Dr. Kerr's appears to be no more than sheer speculation. This speculation was also firmly rebutted by Dr. Gill's testimony, as explained above. Accordingly, *both* of Dr. Kerr's causation theories, which were *both* based on this flawed assumption of genetic susceptibility, have not been established as probable, for this reason alone.

VI

DR. KERR FAILED TO DEMONSTRATE THAT VALERIA'S STROKE WAS VENOUS RATHER THAN ARTERIAL

Dr. Kerr also based his causation theories on the assertion that Valeria's spinal cord stroke was *venous* (*i.e.*, in a vein) rather than *arterial* (*i.e.*, in an artery). (*E.g.*, Tr. 238-40.) However, the evidence indicates that Valeria's stroke was likely arterial, not venous.

First, concerning this issue, I note that Dr. Kerr simply gave very little explanation concerning *why* he believes that Valeria's stroke was venous rather than arterial. He failed to make a coherent argument on that issue. (*See* Tr. 238-40.)

Dr. Gill, on the other hand, explained the difference in presentation between an arterial stroke and a venous stroke. (Tr. 129-30.) She explained that an arterial stroke would cause a sudden, dramatic onset of symptoms, while a venous stroke would not. (*Id*.) And Valeria's own sudden presentation on June 28, 2008, seems to fit Dr. Gill's description of an *arterial* stroke, rather than a venous stroke.

Similarly, a medical article filed by respondent, the Novy article (Ex. F), supports Dr. Gill's testimony on this point. That article studied 27 victims of arterial spinal cord strokes, all of whom suffered an acute, sudden onset of neurological symptoms, with symptoms proceeding from non-existent to very serious "usually within about 2 minutes" but always within "a few hours." (Ex. F, p. 1115) The medical histories of those 27 *arterial* spinal cord stroke victims seem similar to that of Valeria. In contrast, the Novy article stated that in the case of a *venous*

spinal cord stroke, the victim has a "subacute progressive course" (*i.e.*, a slower, less dramatic course) of symptoms. (*Id*. at p. 1119, first column.)

Further, Dr. Gill explained how the results of a "D-dimer" test on Valeria make it "very, very unlikely" that Valeria's stroke was venous. (Tr. 164.)

Dr. Gill, accordingly, opined that Valeria's stroke was likely arterial rather than venous. (Tr. 131, 170-71.) Dr. Bingham stated the same opinion. (Tr. 194.)

Comparing the explanation of Dr. Gill and the Novy article described above, to the largely unexplained opinion of Dr. Kerr on this point, I find it likely that Valeria's stroke was arterial, not venous. This is another point that militates in favor of rejecting Dr. Kerr's causation opinion in this case, which is based upon the assumption that Valeria's stroke was venous.

VII

DR. KERR FAILED TO DEMONSTRATE THAT THE HPV VACCINATION CAUSED *INFLAMMATION* LEADING TO VALERIA'S BLOOD CLOT

A. Dr. Kerr's "inflammation" theory in general

As noted above, Dr. Kerr alternatively presented *two different* theories as to how Valeria's HPV vaccination may have contributed to Valeria's blood clot that caused her stroke. First, he theorized that the HPV vaccination created *inflammation*, thereby resulting in the blood clot that caused Valeria's stroke. (Tr. 35-36.) Dr. Kerr's second theory was that the same vaccination caused *platelet aggregation*, again resulting in the blood clot. (Tr. 36.)

As to Dr. Kerr's *inflammation* theory, his presentation failed to show that it is probable either that the HPV vaccination in general *can* contribute to the type of inflammation that would cause a blood clot/stroke, or that Valeria's HPV vaccination *did* contribute to her blood clot by causing inflammation.

In support of his theory that Valeria's HPV vaccination contributed to her stroke by causing inflammation, Dr. Kerr asserted that the vaccination caused "massive microglial activation in Valeria's central nervous system," which caused the inflammation. (Tr. 242-43.) But Dr. Kerr later acknowledged, however, that he was unaware whether the HPV vaccine even contained any agents that *can* cause microglial activation. (Tr. 248-49.)

Dr. Kerr theorized that Valeria had *systemic inflammation* caused by the vaccination. He opined that such systemic inflammation caused a series of symptoms, and that those symptoms were "part of a *systemic* inflammatory response." (Tr. 41, lines 7-8, emphasis added.) He stated that Valeria's arm pain was "the first manifestation of *systemic* inflammation" (Tr. 244, lines 3-4, emphasis added), and reiterated that she suffered from "*systemic* inflammation" (Tr. 246, lines 8-9, emphasis added).

Dr. Gill, however, provided persuasive arguments against Dr. Kerr's inflammation theory. Dr. Gill explained that a number of different tests done on Valeria demonstrated that she did *not* have systemic inflammation at the time that she developed the blood clot. (Tr. 140, 142-46, 177.) Dr. Bingham also interpreted the testing of Valeria as showing no signs of inflammation. (Tr. 199-200.)

Dr. Kerr also asserted that the HPV vaccine caused inflammation in Valeria's *central nervous system*, but Dr. Bingham explained that testing of her spinal cord fluid did *not* show inflammation. (Tr. 195, 199; Ex. 20, p. 100.)

Dr. Gill also testified that systemic inflammation caused by a vaccination, even by a *second* HPV vaccination when Valeria had previously received an initial dose of that vaccine, would take at least *four days* to develop, whereas Valeria's stroke symptoms began only *one day* post-vaccine. (Tr. 138-40, 179-80.) Dr. Kerr argued that the one-day time period was sufficient for a *second* vaccination to cause very rapid inflammation, but Dr. Gill's testimony was supported by the notes of Valeria's actual treating physicians at the time. For example, one of Valeria's treating neurologists, Dr. Tilwalli, expressed the opinion that due to the onset of stroke symptoms just one day after the HPV vaccination, the stroke could not have been the result of an inflammatory response to that vaccine. (Ex. 20, p. 9.) And another neurologist who treated Valeria, Dr. Stefofski, also indicated that the cause of the stroke could not have been "immune mediated inflammatory," adding that the timing of Valeria's stroke symptoms was "definitely too soon for Gardasil" to have been the cause. (Ex. 20, p. 488.) (Gardasil is the brand name of the HPV vaccine that Valeria received.) I found that Dr. Gill's testimony on this point, as supported by the notations of both Dr. Tilwalli and Dr. Stefofski, was substantially more persuasive than that of Dr. Kerr.

In this regard, Dr. Kerr, to be sure, did point out that *any* vaccination, in order to produce the immunity that is its purpose, does produce *some* type of inflammation in the vaccinee. (Tr. 241-42.) Dr. Kerr argued that one part of the body's immune system, the "innate" immune system, would produce inflammation *soon* after vaccination (Tr. 42-43), and he seemed to suggest that such inflammation, produced by the innate immune system, resulted in Valeria's blood clot. But Dr. Gill testified that she saw no likelihood that the *innate* immune system could produce *localized* inflammation causing a blood clot, in the absence of *systemic* inflammation that would have shown up on the testing of Valeria. (Tr. 140.)

Dr. Gill also testified that she knew of no medical literature supporting Dr. Kerr's opinion that the HPV vaccine *could*, in general, cause the type of inflammation that might cause a blood clot. (Tr. 146.) And Dr. Kerr, on cross-examination, acknowledged that he had *not* submitted any literature showing that HPV vaccination could cause the type of inflammation that could lead to a stroke. (Tr. 79.)

B. Dr. Kerr's reliance on medical literature concerning inflammation

In support of his inflammation theory, Dr. Kerr relied upon certain medical literature. He relied upon medical articles by Petersdorf and Beeson (Ex. 52) and Ghose (Ex. 50), as well as letters to medical journals written by Perez (Ex. 29) and Finsterer (Ex. 39). (See Ex. 22, p. 2; Tr.

47-49.) According to Dr. Kerr, these papers "noted a link between vaccinations and the subsequent development of blood vessel inflammation and thrombosis," thereby suggesting "that vaccines may cause immune activation which triggers thrombosis." (Ex. 22, p. 2.)

Respondent's experts, however, argued that those four papers do *not* offer significant support for the general proposition that vaccines can cause the type of serious inflammation that could lead to a stroke.

Significantly, as I analyze those four papers, only one of the patients described in those four papers suffered a *stroke*, and none of them received an *HPV* vaccination. Instead, a few of the described patients suffered a different condition, known as "giant cell arteritis," after *influenza* vaccination. (Exs. 29, 39, 50, 52.) Giant cell arteritis, Dr. Gill explained, is a condition in which the victims suffer a certain type of inflammation of the temporal artery, involving strong evidence of "systemic immune activation." (Tr. 153.) Thus, those articles do offer at least some support for the proposition that the *influenza* vaccination might lead to systemic immune activation and the type of severe inflammation involved in giant cell arteritis.

Valeria, however, received the *HPV* vaccination, not an influenza vaccination. Moreover, there was *no evidence* in Valeria either of giant cell arteritis or of systemic immune activation. (*See* discussion at pp. 13-14, above.) Thus, for that reason alone, the four papers cited by Dr. Kerr, which describe "giant cell arteritis" after influenza vaccination, offer scant support for the very different proposition that the *HPV* vaccination can cause the type of inflammation that could lead to a stroke.

Moreover, Dr. Gill also explained that if Valeria had experienced systemic immune activation, as is involved in giant cell arteritis, her testing results would have been *quite different* than they actually were, concerning *several different* tests. (Tr. 153-54.) Dr. Kerr did not attempt to refute that point.

Accordingly, Dr. Kerr's reliance on Exs. 52, 50, 29, and 39 again did not constitute persuasive evidence for his theory that *HPV* vaccination can contribute in general to the causation of *strokes* by causing inflammation.

VIII

DR. KERR FAILED TO DEMONSTRATE THAT THE HPV VACCINATION CAUSED *PLATELET AGGREGATION* LEADING TO VALERIA'S BLOOD CLOT

As noted above, Dr. Kerr's second theory was that the HPV vaccination caused *platelet aggregation* resulting in Valeria's blood clot. (Tr. 36.) "Platelet aggregation" means that the platelets in the blood become "sticky," and become attached to each other. (Tr. 149.)

However, Dr. Gill, the only testifying hematologist (blood specialist), testified that she saw no evidence of platelet aggregation in Valeria's medical records. (Tr. 149.) She noted that

persons who develop platelet aggregation[15] also develop low platelet counts (also known as thrombocytopenia), because when "platelets are clumping together, they get removed from circulation" (Tr. 149-50); Valeria's blood testing, however, indicated a *normal* platelet count (Tr. 150; Ex. 8, p. 15).

I found Dr. Gill's explanation concerning this point to be persuasive, in part because of her superior credentials, as a hematologist, in this area concerning blood components; and in part because the testing results in the record support her testimony.

Concerning this issue of platelet aggregation, Dr. Kerr in his expert report relied upon several medical articles. (Ex. 22, pp. 2-4.) Dr. Gill, however, persuasively explained why Dr. Kerr's reliance in this regard was misplaced. First, Dr. Kerr relied on Ex. 40, an article about five Finnish conscripts who died after vaccinations, during the years 1948-72. (Ex. 22, p. 3; Ex. 40, p. 1414.) It is unclear why Dr. Kerr relied upon Ex. 40, however. None of the five victims received a *HPV* vaccination. (Tr. 82; Ex. 40, p. 1414.) The article did not reveal the cause of death of the victims--it did not say that any had suffered *strokes*. (Tr. 83; Ex. 40, p. 1414.) None of the victims were said to have had genetic anomalies, which Dr. Kerr said was a "critical factor" in Valeria. (Tr. 84; Ex. 40.) Most importantly, the article did not even mention *platelet aggregation*. For all those reasons, I cannot find that Ex. 40 offers any support to Dr. Kerr's theory that Valeria's HPV vaccination caused *platelet aggregation* leading to her blood clot.

Dr. Kerr also seemed to rely, in his written expert report, on several other articles to support his platelet aggregation theory. (Ex. 22, pp. 3-4.) Some of those articles were later filed as Ex. 33, a CDC article; Ex. 24, the Baker article;[16] Ex. 37, the Rivard letter; and Ex. 47, the Granel article.[17] However, in his oral testimony on direct examination in this case, Dr. Kerr made

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[15] I note that in the hearing transcript, and several places the transcript states "platelet *activation;*" however, I believe, from the context, that the witness said "platelet *aggregation*." *See* Tr. 151, lines 5 and 16; Tr. 152, line 23.

[16] Regarding the Baker article, Dr. Kerr wrote:

> [I]nvestigators studied thirty-two army apprentices aged 16 and 17 years, undergoing standard immunization, and found that the heparin thrombin clotting times were significantly reduced after vaccination, indicating the development of a temporary hypercoagulable state due to platelet aggregation. This hypercoagulable state was apparent within 24 hours of the vaccination, a finding of some relevance to Ms. Flores, since her thrombosis occurred quickly after her vaccination as well. This transient hypercoagulable state was not observed in elderly individuals given vaccinations and returned to normal by 14 days after vaccination. Interestingly, the subjects of this study were 16 and 17 years old, quite close to the age of Ms. Flores when she received her Gardasil vaccine. (Ex. 22, p. 3.)

[17] In the transcript, an article cited in Dr. Kerr's report, by Kacerik, is misspelled as "Casterick." (Tr. 101.) The article, however, was never filed into the record of this case. (Tr. 101.)

no reference to those articles. (See Tr. 8-55.) And most of those articles, like Ex. 40, do not even *mention* platelet aggregation.

In contrast, Dr. Gill did comment upon two of those articles cited by Dr. Kerr--the two articles (Ex. 24 and Ex. 37) that did mention platelet aggregation. Dr. Gill argued persuasively that those articles do *not* support Dr. Kerr's platelet aggregation theory in this case. (Tr. 150-53.) There is no need for me to repeat here Dr. Gill's discussion of these articles. It is sufficient to say that Dr. Gill convincingly explained why those articles do not offer support to Dr. Kerr's platelet aggregation theory. In contrast, Dr. Kerr in his rebuttal testimony (Tr. 239-250) made no effort to explain why Dr. Gill's analysis of Ex. 40, Ex. 24, or Ex. 37 was flawed in any way.

In short, Dr. Kerr's presentation fell far short of demonstrating that it is probable that Valeria even suffered *any* platelet aggregation, much less that platelet aggregation contributed to her blood clot or stroke.

IX

DR. KERR'S RELIANCE UPON THE SLADE ARTICLE

Dr. Kerr also seemed to rely heavily on the Slade article, which he offered to support the *general* principle that HPV vaccines raise the risk of stroke in a vaccinee. (See Ex. 22, pp. 4-5; Tr. 43-46.) (The Slade article is filed, in the record of this case, as both Ex. 34 and as Ex. L.)

After studying that article and the experts' discussion of it, however, I conclude that it does not offer significant support for Dr. Kerr's general proposition that the HPV vaccine can contribute to causing strokes.

The Slade article analyzed reports to the "VAERS" system concerning the HPV vaccine. VAERS, the Vaccine Adverse Event Reporting System, was created to collect data concerning incidents in which a person suffers an adverse health event soon after receiving a vaccination. (42 U.S.C. §300aa-25(b)(1).) Under the VAERS system, vaccine administrators and manufacturers are required to report any adverse health event suffered by a person soon after a vaccination, without regard to whether there is reason to believe that the vaccination *caused* the injury. (*Id*.) VAERS reports, however, can be submitted by anyone, whether a medical or health official or not. (*Id*.)

The VAERS system, therefore, is useful chiefly as a way of sending a "signal" or "alert" to the medical community that there is a possibility that a vaccine *might* be causing a certain condition or disease. In other words, if a number of VAERS reports are filed describing a certain type of condition as occurring after a certain type of vaccine, the medical community might decide to take steps to *investigate* whether there might be a *causal* connection between the vaccine and the condition. (Tr. 200-02; see also Ex. O, p. 1, which states that the "primary function of VAERS is to detect early warning signals and generate hypotheses about possible new vaccine adverse events.")

However, an analysis of VAERS reports *by themselves* is *not* very useful as evidence of whether a causal connection does exist. That is because, among other reasons, the VAERS system does not provide information as to the "background rate" of a certain condition in a certain population. As a hypothetical example, suppose that Condition A is known to occur in one-year-olds at a rate of about 10 cases per million one-year-olds, for unknown reasons. In that situation, if VAERS reports show *a few* cases of Condition A occurring in one-year-olds shortly after receiving Vaccine B, when in fact millions of one-year-olds are routinely receiving Vaccine B every year, those VAERS reports would not shed any significant light on the question of whether Vaccine B *causes* Condition A. If, on the other hand, the VAERS system were to receive *hundreds* of reports of Condition A after Vaccine B, and Vaccine B is a new type of vaccine, then the medical community would likely take that as an "alert" to set up *systematic studies* testing whether in fact there are proportionally more occurrences of Condition A in one-year-olds receiving Vaccine B than would be the case in one-year-olds who do *not* receive Vaccine B. Only such *systematic studies*, rigorously comparing populations who do and do not receive a certain vaccine, can yield significant evidence as to whether Condition A is associated with Vaccine B. In contrast, any analysis of VAERS reports themselves can only yield a rough "signal" as to whether systematic studies should be done.

Indeed, in the Slade article itself, the authors caution that, for the reasons explained above, "VAERS data must be interpreted cautiously, and cannot generally be used to infer causal associations." (Ex. L, pp. 756-57.) And numerous judges and special masters of this court have explained that VAERS data is of very limited utility in resolving causation issues, and cannot offer strong support to a causation conclusion.[18]

With reference to the specifics of the Slade article, Dr. Kerr stated that HPV vaccines ("Gardasil") "have been associated with disproportionately high reporting of thromboembolic events." (Ex. 22, p. 4.) Dr. Kerr relies on this allegedly "disproportionately high" reporting of strokes after HPV vaccination in the Slade article, as evidence that the HPV vaccine *can* contribute, in general, to the causation of strokes. (Ex. 16, p. 5; Ex. 22, pp. 4-5; Tr. 43-45, 79-80.)[19]

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[18] *See, e.g., Analla v. HHS*, 70 Fed. Cl. 552, 558 (2006) (affirming the special master's conclusion that certain VAERS reports were not sufficient to justify a causation-in-fact finding); *Ryman v. HHS*, 65 Fed. Cl. 35, 40 (2005) (affirming special master's election not to accord substantial weight to VAERS data); *Capizzano v. HHS*, 63 Fed. Cl. 227, 231 (2004) (affirming special master's statement that VAERS data has limited value), *vacated on other grounds*, 440 F. 3d 1317 (Fed. Cir. 2006); *Manville v. HHS*, 63 Fed. Cl. 482, 494 (2004) (not error for the special master to discount VAERS reports); *Nance v. HHS*, No. 06-730V, 2010 WL 3291896 at *9 (Fed. Cl. Sp. Mstr. July 30, 2010) (indicating that reliance on VAERS data was not persuasive).

[19] Dr. Kerr noted that the Slade article--

> concluded that "there was disproportional reporting of syncope and venous thromboembolic events….the significance of these findings must be tempered with the limitations (possibly underreporting) of a passive reporting system." (Ex. 22, pp. 4-5): Dr. Kerr proposed that the significance of Dr. Slade's parenthetical is

However, evidence provided by the respondent persuasively indicated that the Slade article does *not* provide significant evidence that the HPV vaccine adds to the risk of the type of stroke that *Valeria* suffered. For example, Dr. Gill analyzed the Slade article, and concluded that it did not support Dr. Kerr's analysis. (Tr. 154-157; Ex. I, pp. 2-3.) The Slade article analyzed VAERS reports filed during the first 2 ½ years during which the HPV vaccination was administered in the U.S., a period during which about 23 million doses of the HPV vaccination were distributed. (Ex. L, pp. 750-51.) Dr. Gill noted that during that period, there were 31 strokes or stroke-like events reported to VAERS after HPV vaccination. (Tr. 155; Ex. L, p. 754, third column.) However, Dr. Gill noted, *none* of those 31 events were similar to the stroke suffered by Valeria--that is, none were *spinal cord* strokes. (Tr. 155.) Further, of the victims of those 31 events, 90% had known risk factors for stroke. (Tr. 156.) That 90% figure is confirmed in the Slade article itself, which notes that "twenty-eight of the 31 cases (90%) had a known risk factor" for stroke. (Ex. L, p. 754, third column.) Also, Dr. Gill noted that in the 30 events which occurred after HPV vaccination alone (*i.e.*, no other vaccination was administered at the same time as the HPV vaccine), the average ("mean") time between vaccination and the event was 41.5 days. (Tr. 157; Ex. L, p. 754, third column.) This timing factor in Slade is in sharp contrast to *Valeria's* stroke, the first symptoms of which occurred on the *first day* after her HPV vaccination.

Dr. Bingham, too, discussed the Slade article (Tr. 206-209), and opined that the Slade article does not support the general theory that the HPV vaccine increases the risk of stroke (Tr. 209). Like Dr. Gill, Dr. Bingham also noted that the average time of the stroke-like events described in Slade (about 42 days) was a far cry from the one-day onset in Valeria's case. (Tr. 208.)

In addition, while all of the stroke-like events described in Slade were *venous* events, Valeria's stroke was likely an *arterial* stroke. (*See* discussion at pp. 12-13 above).[20]

> that there may be still greater reason to accept causation than the data from a passive reporting system might suggest. (Ex. 22, p. 5.)

[20] Dr. Kerr also pointed to the fact that the Slade article indicates the possibility of an increased risk of "syncope," or fainting, after HPV vaccination. He asserted that Valeria suffered from syncope, and seemed to argue that such circumstance would add to a likelihood that HPV vaccination contributed to Valeria's stroke. (See Ex. 22, p. 5; Tr. 45.) However, Dr. Kerr did not explain why he believes that syncope can contribute to causing a spinal cord stroke. Moreover, a close review of the Slade article indicates that none of the syncope events described in Slade seem to have been associated with a stroke. The syncope events described in Slade were mostly classified as "nonserious" events. (Ex. L, p. 753, first column.) (*See* Ex. N, p. 8283, noting that adolescents receiving vaccines faint fairly frequently after vaccination.) The "serious" syncope events seem to have been when a vaccinee *fell* after fainting, suffering a head injury as a result of the fall. (Ex. L, p. 753, first column.) Valeria, however, did not suffer from any falling event produced by fainting. To be sure, Valeria's medical records do indicate that in the ambulance, she may have lost consciousness, which might qualify as a case of syncope. (See Tr. 55.) But Dr. Kerr did not explain how that circumstance supports a conclusion that Valeria's stroke was caused by her HPV vaccination.

Accordingly, after full analysis of the Slade article, I do not find that it provides significant support to the proposition that Valeria's HPV vaccination contributed to causing her stroke.

X

THE MEDICAL LITERATURE ANALYZING ADVERSE EVENTS REPORTED AFTER HPV VACCINATION ADDS REASON TO DOUBT DR. KERR'S THEORY

The Vaccine Act case law makes it clear that in order to show causation under the Act's "more probable than not" standard, a petitioner need *not* supply epidemiologic or other medical literature supporting causation. (See, *e.g.*, *Capizzano v. HHS*, 440 F. 3d 1317, 1325 (Fed. Cl. 2006); *Andreu v. HHS*, 569 F. 3d 1367, 1378 (Fed. Cir. 2009).) However, when epidemiologic literature concerning the vaccine in question is placed into the record of the case, the special master may give such literature weight, as appropriate, if such literature either offers support for, or tends to contradict, the petitioner's causation theory. (*See, e.g.*, *Taylor v. HHS*, 108 Fed. Cl. 807, 819-821 (Fed. Cl. 2013) (the special master did not err in considering epidemiological evidence); *Andreu v. HHS*, 569 F. 3d 1367, 1379 (Fed. Cir. 2009) (a special master may assess epidemiological evidence in "reaching an informed judgment as to whether a particular vaccination likely caused a particular injury.")).

In this case, certain medical literature in the record, which analyzes reports of adverse events after HPV vaccination, adds slightly to the reasons for *rejecting* Dr. Kerr's causation theory.

First, as noted above, the Slade article analyzed VAERS reports filed during the 2 ½ years during which the HPV vaccination was administered in the U.S., a period during which 23 million doses of the HPV vaccine were distributed. (Ex. L, pp. 750-51.) During that period, there were 31 strokes or stroke-like events reported to VAERS after HPV vaccination. (Tr. 155; Ex. L, p. 754, third column.) However, as Dr. Gill noted, *none* of those 31 events were similar to the stroke suffered by Valeria--that is, none were *spinal cord* strokes. (Tr. 155.) In addition, while all the stroke events described in Slade were *venous* events, Valeria's stroke was likely an *arterial* stroke. (*See* discussion at pp. 12-13 above.)

In short, the Slade article reviewed the VAERS reports for a 2 ½ year period in which the first 23 million doses of HPV vaccines were distributed in the United States. Yet *no* spinal cord strokes at all were reported after HPV vaccination, nor were any arterial strokes of *any* kind reported (while Valeria suffered an *arterial, spinal cord* stroke). Thus, while VAERS reports are of *very* limited utility in deciding causation issues, as discussed above (pp. 17-18), in my final analysis of the Slade article, I find that the article, if anything, adds some slight weight to the case *against* Dr. Kerr's causation theory, rather than in favor of his theory.

The record of this case also includes other epidemiologic articles directly relating to whether the HPV vaccine is statistically associated with adverse events after vaccination.

For example, the Gold study, an Australian study of adverse events after HPV vaccination, was also filed. (Ex. D.) During the period covered by that study, 5.8 million doses of HPV vaccine were administered in Australia, but the study did not find *any* reports of strokes (thrombosis) after HPV vaccination. (Ex. D; Tr. 204.) To be sure, the Gold study, as a study of adverse event reports, seems to have the same limitations as the Slade article VAERS data discussed above. However, the study's failure to find *any* strokes after 5.8 million HPV doses would seem, like the Slade article itself, to add slight additional weight to the case *against* Dr. Kerr's causation theory.

Also filed into the record was the Gee study. (Ex. N.) In that study, the authors compared about 600,000 U.S. females, who had received HPV vaccine at ages 9 to 26, to a comparison group of young females who had not received HPV vaccine. (Ex. N, pp. 1-2.) The study found no strokes at all among the 417,000 girls aged 9-17 who received the vaccine, and only two strokes among the 113,000 vaccinated females aged 18-26. (*Id*. at p. 3, Table 13.) And the two strokes among the older vaccinees were judged *not* to indicate a statistically significant increased risk of stroke compared to non-vaccinated individuals. (*Id*. at p. 4, para. 3.1.)

The Gee study authors also looked at the risk for "venous thromboembolism" ("VTE") *separately* from the risk of "stroke." (Ex. N, pp. 2-5.) In this regard, as noted above (pp. 12-13), the record of this case preponderates in favor of a conclusion that Valeria herself suffered an *arterial* stroke, not a *venous* thromboembolic event. However, even if one were to assume that Valeria's stroke was venous rather than arterial, it is noteworthy that the Gee study found *no increased risk* even for *venous* thromboembolism, among vaccinated as compared to non-vaccinated individuals. (Ex. N, p. 3, Table 3.)

In short, taken together, the medical literature described in this Section X of this Decision, which analyzes reports of adverse events after HPV vaccination, adds slightly to the reasons for *rejecting* Dr. Kerr's causation theory.

XI

THE ABSENCE OF A KNOWN CAUSE FOR VALERIA'S STROKE

One striking factor about this case is that Valeria's medical records do not identify a known cause for Valeria's stroke, nor are respondent's two experts able to point to a likely cause. Does this absence of a known cause offer any significant support to Dr. Kerr's theory that Valeria's *HPV vaccination* contributed to provoking the stroke? I conclude that it does not.

The record of this case indicates, rather, that it is *common* for the cause of spinal cord strokes *not* to be identified. For example, the Novy article (Ex. F) discusses spinal cord strokes in general, and notes that "the pathogeneses and natural history of spontaneous * * * spinal cord infarctions remain largely unknown." (Ex. F, p. 1113.) Moreover, that study looked at 27 particular spinal cord strokes, and in 20 of those cases, no cause ("etiology") was identified. (Ex. F, p. 1116; Tr. 198-99.)

Also, Dr. Bingham confirmed that in a large percentage of spinal cord strokes, no cause is identified. (Ex. A, p. 3; Tr. 196-99.)

Accordingly, the lack of an identifiable cause for Valeria's stroke does *not* offer any significant support to Dr. Kerr's speculative causation theories.

XII

PETITIONER'S CASE FAILS THE *ALTHEN* TEST

As noted above, in its ruling in *Althen*, the U.S. Court of Appeals for the Federal Circuit discussed the "causation-in-fact" issue in Vaccine Act cases. The court stated as follows:

> Concisely stated, Althen's burden is to show by preponderant evidence that the vaccination brought about her injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury. If Althen satisfies this burden, she is "entitled to recover unless the [government] shows, also by a preponderance of evidence, that the injury was in fact caused by factors unrelated to the vaccine."

Althen, 418 F.3d 1274, 1278 (Fed. Cir. 2005) (citations omitted). In the pages above, of course, I have already set forth in detail my analysis in rejecting Petitioner's "causation-in-fact" theory in this case. In this part of my Decision, then, I will briefly explain how that analysis fits *specifically* within the three parts of the *Althen* test, enumerated in the first sentence of the *Althen* excerpt set forth above. The short answer is that I find that Petitioner's evidence in this case clearly does not satisfy *any* of the three parts of the *Althen* test.

A. Application of Althen Prongs 1 and 2 to this case

One interpretative issue with the *Althen* test concerns the relationship between the first two elements of that test. The first two prongs of the *Althen* test, as noted above, are that a petitioner must provide "(1) a medical theory causally connecting the vaccination and the injury," and "(2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury." Initially, it is not absolutely clear how the two prongs differ from each other. That is, on their faces, each of the two prongs seems to require a demonstration of a "causal" connection between "the vaccination" and "the injury." However, a number of Program opinions have concluded that these first two elements reflect the analytical distinction that has been described as the "can cause" vs. "did cause" distinction. That is, in many Program opinions issued prior to *Althen* involving "causation-in-fact" issues, special masters or judges stated that a petitioner must demonstrate (1) that the *type* of vaccination in question *can* cause the *type* of injury in question, and also (2) that the *particular* vaccination received by the specific vaccinee *did* cause the vaccinee's *own* injury. *See, e.g., Kuperus v. HHS*, 2003 WL 22912885, at *8 (Fed. Cl. Spec. Mstr. Oct. 23, 2003); *Helms v. HHS*, 2002 WL 31441212, at *18 n.42 (Fed. Cl. Spec. Mstr. Aug. 8, 2002). Thus, a number of judges and special masters of this court have concluded that Prong 1 of *Althen* is the

"can cause" requirement, and Prong 2 of *Althen* is the "did cause" requirement. *See, e.g.*, *Doe 11 v. HHS*, 83 Fed. Cl. 157, 172-73 (2008); *Nussman v. HHS*, 83 Fed. Cl. 111, 117 (2008); *Banks v. HHS*, 2007 WL 2296047, at *24 (Fed. Cl. Spec. Mstr. July 20, 2007); *Zeller v. HHS*, 2008 WL 3845155, at *25 (Fed. Cl. Spec. Mstr. July 30, 2008). And, most importantly, the *Federal Circuit itself* confirmed that interpretation in *Pafford*, ruling explicitly that the "can it?/did it?" test, used by the special master in that case, was equivalent to the first two prongs of the *Althen* test. *Pafford v. HHS*, 451 F.3d at 1352, 1355-56 (Fed. Cir. 2006). Thus, interpreting the first two prongs of *Althen* as specified in *Pafford*, under Prong 1 of *Althen* a petitioner must demonstrate that the *type* of vaccination in question *can* cause the *type* of condition in question; and under Prong 2 of *Althen* that petitioner must then demonstrate that the *particular* vaccination *did* cause the *particular* condition of the vaccinee in question.

A few decisions of judges and special masters have discussed issues with respect to the *precise* interpretation of Prongs 1 and 2 of *Althen*. *E.g.*, *Doe 11*, 83 Fed. Cl. at 173-74; *Scott v. HHS*, 2006 WL 2559776, at *18 (Fed. Cl. Spec. Mstr. Aug. 21, 2006); *Nussman v. HHS*, 2008 WL 449656, at *12-13 (Fed. Cl. Spec. Mstr. Jan. 31, 2008), *aff'd*, 83 Fed. Cl. 111 (2008); *Fields v. HHS*, 2008 WL 2222141, at *7 n.5 (Fed. Cl. Spec. Mstr. May 14, 2008). However, it is *not* necessary, in this case, to delve into any such potential interpretative issues, since under any reasonable interpretation of *Althen*, the Petitioner's causation evidence put forward in this case could *not* satisfy either of the first two prongs of the *Althen* test.

That is, as set forth in detail above, I have concluded that Petitioner has fallen far short of demonstrating either that the HPV vaccine *can* contribute, in *general*, to the causation of spinal cord strokes, or that Valeria's HPV vaccination of June 27, 2008, *did* cause Valeria's own stroke. Thus, Petitioner's causation arguments in this case would fail under *any* interpretation of *Althen's* Prongs 1 and 2.

Moreover, there can be no doubt whatsoever that the *Althen* test ultimately requires that, as an *overall matter*, a petitioner must demonstrate that it is "more probable than not" that the *particular* vaccine was a substantial contributing factor in causing the *particular* injury in question. That is clear from the statute itself, which states that the elements of a petitioner's case must be established by a "preponderance of the evidence." (§ 300aa-13(a)(1)(A).) And, whatever is the precise meaning of Prongs 1 and 2 of *Althen*, in this case the overall evidence falls far short of demonstrating that it is "more probable than not" that the HPV vaccine contributed to the causation of Valeria's stroke.

B. Application of Prong 3 of the Althen test to this case

Since I have concluded that Petitioner has failed to satisfy either of the *first two* prongs of *Althen*, I need not determine whether Petitioner's case satisfies the *third* prong. But in the interest of completeness, I will add a brief discussion of Prong 3.

To be sure, a striking aspect of this case is that Valeria suffered the first symptoms of her tragic spinal cord stroke on the *next day* after her HPV vaccination in question; that temporal relationship would naturally cause any lay person to consider whether a *causal* relationship exists. However, for the reasons detailed above, the evidence in this case failed, by a large margin, to provide any reason to believe that HPV vaccinations *can* cause spinal cord strokes (or any type of stroke) *in general*, or that Valeria's HPV vaccination *did* cause her own tragic stroke.

Moreover, as noted above, Dr. Gill testified persuasively that systemic inflammation caused by a vaccination, even by a *second* HPV vaccination when Valeria had previously received the first dose of that vaccine, would take at least *four days* to develop, whereas Valeria's stroke symptoms began only *one* day post-vaccine. (Tr. 139.) Similarly, the medical records show that one of Valeria's treating neurologists, Dr. Tilwalli, also expressed the opinion that due to the onset of stroke symptoms just one day after the HPV vaccination, the stroke could *not* have been the result of an inflammatory response to that vaccine. (Ex. 20, p. 9.) And another neurologist who treated Valeria, Dr. Stefofski, likewise indicated that the cause of the stroke could not have been "immune mediated inflammatory," adding that the timing of Valeria's stroke symptoms was "definitely too soon for Gardasil" to have been the cause. (Ex. 20, p. 488.) (Gardasil is the brand name of the HPV vaccine that Valeria received.)

Thus, while upon first impression to the layman, the occurrence of Valeria's first stroke symptoms only one day post-vaccine might suggest a causal relationship, in fact the timing of Valeria's symptom onset constitutes strong evidence *against* Dr. Kerr's inflammation/causation theory.[21]

C. This is not a close case

As noted above, in *Althen* the Federal Circuit indicated that the Vaccine Act involves a "system created by Congress, in which close calls regarding causation are resolved in favor of injured claimants." (418 F. 3d at 1280). Accordingly, I note here that this case ultimately is *not* a close case. As set forth in detail in the sections above, I find that the testimony of the respondent's experts was *much* more persuasive than that of Petitioner's expert Dr. Kerr, concerning all of the issues raised by Dr. Kerr's causation theories. Overall, I found the evidence in this case to be quite one-sided.

XIII

CONCLUSION

The record of this case demonstrates plainly that Valeria Flores has been through a tragic and painful medical ordeal. She and her family are certainly deserving of great sympathy. Congress, however, designed the Program to compensate only the individuals whose injuries can be linked causally, either by a Table Injury presumption or causation-in-fact evidence, to a listed

[21] One of Petitioner's post-hearing briefs states that Respondent's other expert, Dr. Bingham, "testified that the timing [of Valeria's symptoms] appears medically appropriate." (Br. Filed 8-27-12, p. 15.) But once again (*see* fn. 14 above), Petitioner's counsel has grossly distorted the testimony of a witness. Dr. Bingham (at Tr. 232) was acknowledging only the obvious fact, which I myself noted above, that the timing of Valeria's stroke symptoms, only one day after vaccination, is a reason a lay person might intivitively wonder if a causal connection exists (*i.e.*, "the whole reason we're here" (at trial)). He was certainly *not* conceding that the timing was "medically appropriate" for a vaccine causation finding.

vaccine. In this case, as described above, no such link has been demonstrated. Accordingly, I conclude that Petitioner in this case is *not* entitled to a Program award.[22]

/s/ George L. Hastings, Jr.

George L. Hastings, Jr.
Special Master

[22] In the absence of a timely-filed motion for review of this Decision, the Clerk of the Court shall enter judgment accordingly.