In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: October 15, 2015

* * * * * * * * * * * * * * * *	PUBLISHED DECISION
DWAYNE COZART and MICHELE HAMILTON, as representatives of the Estate of C.A.C.,	No. 00-590V
	Special Master Dorsey
Petitioners,	
v.	Denial of Entitlement; Hepatitis B (Hep B), Diphtheria-Tetanus-Acellular-Pertussis (DTaP); Inactivated Polio (IPV); Haemophilus Influenzae Type B (Hib) Vaccines; Sudden Infant Death Syndrome (SIDS); Death.
SECRETARY OF HEALTH AND HUMAN SERVICES,	
Respondent.	
* * * * * * * * * * * * * * * *	

Ronald Craig Homer, Conway, Homer & Chin-Caplan, Boston, MA, for petitioners.
Ryan Daniel Pyles, U.S. Department of Justice, Washington, DC, for respondent.

DECISION[1]

I. INTRODUCTION

Petitioners, Dwayne Cozart and Michele Hamilton, filed a petition under the National Childhood Vaccine Injury Act ("Vaccine Act" or the "Program"),[2] 42 U.S.C. § 300aa-10 et seq. (2012), as the representatives of the estate of their son, C.A.C. Petitioners alleged that C.A.C.

[1] Because this published decision contains a reasoned explanation for the action in this case, the undersigned intends to post this decision on the website of the United States Court of Federal Claims, in accordance with the E-Government Act of 2002, Pub. L. No. 107-347, 116 Stat. 2899, codified as amended, 44 U.S.C. § 3501 (2012). In accordance with the Vaccine Rules, each party has 14 days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted decision. If, upon review, the undersigned agrees that the identified material fits within the requirements of that provision, such material will be deleted from public access.

[2] The National Vaccine Injury Compensation Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755, codified as amended, 42 U.S.C. §§ 300aa-10 - 34 (2012) ("Vaccine Act"). Individual section references will be to 42 U.S.C. § 300aa of the Vaccine Act.

"experienced an adverse reaction to [his October 19, 1998] inoculations which resulted in his death on October 19, 1998." Petition at 1. Petitioners filed an amended petition alleging that as a result of the administration of the hepatitis B ("Hep B"), Diphtheria-Tetanus-acellular-Pertussis ("DTaP"), inactivated polio ("IPV"), and haemophilus influnezae ("Hib") vaccines on October 19, 1998, C.A.C. died on October 19, 1998. Amended Petition at 1, filed Oct. 24, 2011. Respondent recommended against awarding compensation to petitioners. See Respondent's Report, filed July 15, 2013, at 13.

After a review of the entire record, the undersigned finds that petitioners have failed to provide preponderant evidence that the vaccinations C.A.C. received on October 19, 1998, caused his death. Accordingly, petitioners are not entitled to compensation.

II. BACKGROUND

A. Procedural History

Petitioners filed a petition on October 2, 2000, pursuant to the Vaccine Act, alleging that C.A.C. had "an adverse reaction to [his October 19, 1998 vaccinations], which resulted in his death . . . ." See Petition at 1. On October 24, 2011, petitioners filed an amended petition setting forth additional factual support for their claim.[3] See Amended Petition. Petitioners filed the expert report of Dr. Douglas C. Miller, a neuropathologist, on August 6, 2012. In addition to the expert report, petitioners filed Dr. Miller's curriculum vitae and seven exhibits of medical literature referenced in Dr. Miller's report.

On September 26, 2012, respondent filed a motion for summary judgment, arguing that "on the current record, there is a lack of evidence as a matter of law for the Court to find that petitioners are entitled to compensation under the terms of the [Vaccine] Act," and the petition must be dismissed. See Respondent's Motion for Summary Judgment ("MSJ") at 8, 12. On October 15, 2012, petitioners filed an opposition to respondent's motion for summary judgment. In their opposition, petitioners contended that "respondent has not shown that a 'genuine issue as to any material fact' does not exist, and therefore, [respondent's MSJ] must be denied." See Petitioners' Opposition to Respondent's Motion for Summary Judgment ("Opp. to MSJ"), at 8 (emphasis in original). The undersigned denied respondent's motion for summary judgment on February 12, 2013, reasoning that summary judgment would be inappropriate because petitioners' expert reports raised issues of fact as to causation. See Order Denying Respondent's Motion for Summary Judgment at 4.

[3] This case became part of an omnibus proceeding in which all participating petitioners alleged that thimerosal in pediatric vaccines caused or contributed to death. See Order dated Sept. 27, 2011 (indicating that this case was part of the omnibus proceeding). On November 23, 2010, a decision was entered denying entitlement in the test case in that proceeding, Kolakowshi v. Sec'y of Health & Human Servs., No. 99-625V, 2010 WL 5672753 (Fed. Cl. Spec. Mstr. Nov. 23, 2010).

Respondent filed an expert report from Dr. Hart G.W. Lidov, a neuropathologist, on April 30, 2013. On June 21, 2013, respondent filed an expert report from Dr. Christine McCusker, an immunologist. Petitioners subsequently filed an expert report from Dr. James Oleske, also an immunologist. On February 10, 2014, respondent filed a supplemental report from Dr. McCusker.

The undersigned encouraged the parties to discuss whether an informal resolution of this case was possible prior to proceeding to a hearing. The parties made several attempts, but were ultimately unable to resolve the case before the hearing. An entitlement hearing was held on September 25 and 26, 2014, in Washington, D.C. After the experts testified and the hearing concluded, the undersigned again encouraged the parties to discuss informal resolution. On December 5, 2014, the parties filed a joint status report stating that they were unable to resolve the case. Based on this status report, the undersigned held one more status conference in an attempt to provide any needed assistance to the parties to resolve this case. At the conclusion of this status conference, the undersigned requested that the parties make one final attempt to resolve the case. See Order dated January 7, 2015, at 1. Those efforts were unsuccessful. The undersigned then ordered the parties to each file their post-hearing briefs by February 23, 2015. See Order dated Jan. 23, 2015.

This matter is now ripe for adjudication.

B. Summary of Relevant Facts

C.A.C. was born on August 17, 1998. Petitioner's Exhibit ("Pet. Ex.") 1 at 40. At his two week well-child visit to the pediatrician, C.A.C. was noted to be developing normally. Id. at 3. On September 29, 1998, C.A.C.'s mother called the pediatrician regarding a red bumpy rash on C.A.C. that had persisted and worsened since August 25, 1998. Pet. Ex. 9 at 14. The pediatrician saw C.A.C. later that same day and concluded that the rash was likely eczema and prescribed Eucerine cream. Id.

On October 19, 1998, C.A.C. saw the pediatrician for his two month well-child visit. Pet. Ex. 9 at 14. The pediatrician noted that C.A.C. was a well-child. Id. At approximately 10:15 a.m., C.A.C. received the Hep B, DTaP, IPV, and Hib vaccinations. Id. at 14, 18. After the visit, C.A.C.'s mother took him to the babysitter. Pet. Ex. 46 at 3.[4] The babysitter put C.A.C. down for a nap. Id. At 2:57 p.m., emergency medical services ("EMS") were dispatched to the babysitter's house because C.A.C. was unresponsive. Pet. Ex. 5 at 1. When the Duncanville Fire Department EMS arrived, C.A.C. was pulseless and apneic. Cardiopulmonary resuscitation ("CPR") was performed, and C.A.C. was intubated and given epinephrine. Id.

C.A.C. was taken to the Charlton Methodist Hospital. Upon arrival at approximately 3:30 p.m., C.A.C. had no pulse and was asystolic. Pet. Ex. 8 at 7. The endotracheal tube in his esophagus was removed and placed in his trachea and CPR was continued. Id. C.A.C. received atropine and epinephrine. Id.

[4] Several of petitioners' exhibits are not paginated. For those exhibits, the undersigned cites to the PDF page number.

At the hospital, Dr. Joe Tsou documented the child's "history of present illness." Pet. Ex. 8 at 7. In the history, Dr. Tsou wrote that the child presented to the Emergency Department ("ED") with CPR in progress after being found unresponsive at the babysitter's home. Id. Dr. Tsou noted that the child had received immunizations earlier that morning at the pediatrician's office. After receiving the immunizations, C.A.C.'s mother had given the child Tylenol and then left him at the babysitter's home. Id. Dr. Tsou noted that the infant went to sleep and "afterwards . . . was found unresponsive." Id. The babysitter called 911, but paramedics "reported no signs of life." Id. CPR with advanced cardiac life support ("ACLS") had been instituted without a response from the child. Id. Dr. Tsou documented that the infant had a rectal temperature of 94.7 degrees indicating that "significant time had elapsed since the time of arrest." Id. The nurse who recorded the resuscitation efforts was Donald Jesmer, RN. Id. at 3. In addition to documenting the child's medical history, Dr. Tsou performed a physician exam. Id. at 8. He noted "coffee ground vomitus around [the] mouth," congested chest, distended abdomen, and paleness. Id. Resuscitative efforts were not successful and the infant was pronounced dead at 15:47 [3:47 p.m.]. Id. at 7. Nurse Jesmer reported the case to the medical examiner's office. Id. at 11.

Medical examiner and pathologist Dr. Lauri S. Holley of the Dallas County Medical Office, Dallas County Institute of Forensic Sciences, handled the case. Pet. Ex. 12 at 30. Field Agent Gaylor documented the following investigative reports taken from the infant's pediatrician and the ED nurse:

> Per Dr. Davison – Decd [decedent] has been healthy, born at Columbia Arlington, no problems in pregnancy for mother . . . Saw about 1030, 10-19-98, normal exam, noted decd was in 85th percentile on growth chart. Decd had two-month's immunization consisting of DTAP, Hep B, Hemophalus B [Hib vaccine] Flu and injectable Polio. Notes no problems [after] admin of shots.
>
> Per RN Jesmer, CMH-ER – Decd was at the babysitters, Marilyn Davis . . . NOK [next of kin]/sitter relate decd appeared fine [after] visit to the doctor. Decd was fed and put down for a nap (time unclear at this point). Ca. 1515, Ms. Davis checked on decd and [found] him unresponsive in bed and called 911. Decd was noted face down by EMS, and some purge was noted from the nares/os. No trauma evident. App nat. (SIDS) [Sudden Infant Death Syndrome] r/o rxn to immunizations. Gaylor, FA.
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> Pet. Ex. 12 at 31.

Dr. Holley performed an autopsy on the child on October 20, 1998. Pet. Ex. 9 at 19. The external examination revealed "posterior lividity[5] [that was] partially fixed" and "lividity of the right side of the face with blanching over the pressure areas." Pet. Ex. 9 at 19. Lividity was also

[5] Lividity is defined as "the quality of being livid; discoloration, as of dependent parts, by the gravitation of the blood." Dorland's Illustrated Medical Dictionary 1069 (32nd ed. 2012) ("Dorland's).

seen on the right ear and neck. Pet. Ex. 12 at 17. The internal examination revealed petechiae[6] of the epicardium, petechiae of the pleural lung surfaces, with moderately congested parenchyma of the lung. Pet. Ex. 9 at 20. A chest x-ray showed a right pneumothorax.[7] Id. The remainder of the external examination was unremarkable. Id. A microscopic examination of lung tissue showed atelectasis[8] of tissue from the right lung, and "intra-alveolar hemorrhage in the right middle and left upper lobes." Pet. Ex. 12 at 4. A microscopic examination of the thymus revealed "minimal focal involution" and an increase in "Hassall's corpuscles." Id. at 4. The "[h]istologic sections of [the] medulla at multiple levels reveal[ed] scant arcuate nuclei neurons bilaterally." Id. at 5. Dr. Holley noted that "Arcuate nucleus hypoplasia has been reported in association with infants dying of SIDS." Id. at 6. The toxicology results on blood and vitreous fluid were normal as were the results from serology tests on the cerebrospinal fluid. Id. The medical examiner concluded that the child's death should be classified as SIDS. Id. "This category is used when complete autopsy, investigation and additional studies fail to yield a definite cause of death. Although there was recent immunization, a connection to the death could not be established." Id.

C. Sudden Infant Death Syndrome

SIDS is defined as "the sudden death of an infant less than 1 year of age that remains unexplained after a complete autopsy, death scene investigation, and review of the clinical history." Pet. Ex. 27 at 2. Its "distinctive features" include "a peak incidence at 2 to 4 months of age, male predominance, and the presence of intrathoracic petechiae." Respondent's Exhibit ("Resp. Ex.") A-6 at 1. The death is linked to "a sleep period," which is "the time when the majority of death occurred." Id. It is not clear "whether SIDS occurs during sleep itself or during the many transitions between sleep and arousal that occur . . . since [] deaths are typically not witnessed." Id.

SIDS is the leading cause of infant mortality in the United States, with an incidence of .53 per 1,000 infants. Resp. Ex. C-10 at 3; Pet. Ex. 27 at 2. Japan has the lowest rate of SIDS at 0.09 per 1,000 and New Zealand has the highest, at 0.80 per 1000 infants. Resp. Ex. A-6 at 1. Research into the causes of SIDS revealed that the risk of death was twofold in infants who were put to sleep in the prone position. Resp. Ex. C-10 at 3. In 1994, the National Institute of Child Health and Development began the "Back-to-Sleep" ("BTS") Campaign, educating parents and child care providers to place infants on their backs for sleep. Id. The BTS campaign was a success, reducing the rate of SIDS by more than 50% within ten years. Id. Unfortunately, the rate of SIDS has plateaued, and it still remains the leading cause of postneonatal infant mortality in the US. Id.

As research progressed, other risk factors for SIDS related to the "sleeping environment" were recognized, including "over-bundling, bed sharing, face down position and soft bedding."

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[6] Petechia (plural petechiae) is defined as "a pinpoint, nonraised, perfectly round, purplish red spot caused by intradermal or submucous hemorrhage." Dorland's at 1422.

[7] Pneumothorax is defined as "an accumulation of air or gas in the pleural space." Dorland's at 1476.

[8] Atelectasis is the "incomplete expansion of a lung or a portion of the lung." Dorland's at 171.

Pet. Ex. 27 at 3. These factors were thought to contribute to "asphyxia due to airway compression or rebreathing of exhaled gases in the face-down position." Resp. Ex. A-6 at 2. In 1994, Dr. Hannah C. Kinney and her colleagues proposed the Triple Risk Model as a way to conceptualize the "emerging multidisciplinary data." Resp. Ex. A-6 at 2. "According to this model, SIDS occurs when three factors are present simultaneously. The first factor is an underlying vulnerability in the infant; the second, a critical developmental period; and the third, an exogenous stressor." Id. The Venn diagram below shows an illustration of the Triple Risk Model.

Pet. Ex. 25 at 3, Figure 1.

Risk factors may be extrinsic and intrinsic. "Extrinsic risk factors are physical stressors that [] place a vulnerable infant at risk for asphyxia or other homeostatic derangement." Pet. Ex. A-6 at 3. These factors include "prone and side-sleeping positions, bedclothes that cover the head, sleeping on sofas or other soft furniture in which the infant could become wedged, a high ambient temperature . . . soft bedding, and bed sharing." Id. The prone sleeping position is still associated with 30% to 50% of SIDS cases and another 50% occur where infants are "sharing a bed, sofa, or sofa chair with another person." Id. Another extrinsic risk factor is mild infection, including "upper respiratory tract infection." Resp. Ex. A-6 at 3; Resp. Ex. C-10 at 4.

"The occurrence of extrinsic risks in virtually all SIDS cases implies that SIDS is precipitated by a 'trigger' at the time of death. These extrinsic risk factors are consistent with asphyxia-generating conditions, e.g., face-down position, prone position, and adult mattress." Resp. Ex. C-10 at 5. Studies have also shown that having multiple risk factors significantly increases the risk of SIDS. In a 2012 article[9] by Kinney, et al., the authors studied 568 SIDS deaths from the San Diego Medical Examiner's Office from 1991 to 2008 and found that the "majority of SIDS infants were subject to at least 2 extrinsic risk factors." Id.

[9] Hannah C. Kinney et al., Risk Factor Changes for Sudden Infant Death Syndrome After Initiation of Back-to-Sleep Campaign, 129 Pediatrics 630, 630-38 (2012).

"An intrinsic risk factor is defined as a genetic or environmental factor" that "affects the underlying vulnerability of the infant." Resp. Ex. A-6 at 3; Resp. Ex. C-10 at 3. These include "developmental factors, such as prematurity . . . genetic factors, such as familial SIDS (i.e., a recurrence of SIDS in subsequent siblings), male sex (by a 2:1 ratio), and race or ethnic group . . . [and] environmental conditions extrinsic to the infant, such as poverty, and prenatal exposure to . . . cigarette smoke and alcohol or illicit drugs." Id.

The mechanism of death of SIDS has been thought to be related to a failure of the "autonomic regulation of cardiovascular or respiratory activity or both." Resp. Ex. A-6 at 4 (quoting Daniel C. Shannon & Dorothy H. Kelly, SIDS and Near-SIDS, 306 New Eng. J. Med. 959, 959-65 (1982)). There is "compelling evidence for a respiratory pathway in the majority of SIDS deaths." Id. The "respiratory pathway to SIDS" can be described in five steps. Id. The infant first has a "life-threatening event" that causes "severe asphyxia, brain hypoperfusion, or both." Id. Examples of life-threatening events include "rebreathing exhaled gases in the face-down position" and "obstructive apnea due to gastric regurgitation." Id. Second, the "vulnerable infant does not wake up and turn his or her head in response to asphyxia . . . resulting in rebreathing or an inability to recover from apnea." Id. "Third, progressive asphyxia leads to a loss of consciousness and areflexia" and "hypoxic coma." Id. Fourth, the infant develops extreme bradycardia and hypoxic gasping." Id. Fifth, and finally, there is a failure of autoresuscitation due to ineffective gasping that leads to "uninterrupted apnea and death." Id. The increased risk of SIDS in infants younger than six months is probably due to "immature homeostatic systems . . . [d]evelopmental motor mechanisms" (such as when the infant is in the prone position), because at this age, the infant is unable to lift and turn his or her head. Id.

Research on the "underlying vulnerability" present in infants who die of SIDS has focused on the area of the brainstem responsible for autonomic function and respiration. Resp. Ex. A-6 at 7. This research suggested that 50% to 75% of infants who die of SIDS may have a neurochemical abnormality in the "medullary 5-hydroxytryptamine system," which modulates and integrates many different homeostatic functions, including "ventilation and gasping . . . responses to carbon dioxide and oxygen, [and] arousal from sleep." Id. at 7. This vulnerability has also been described as a deficiency "in the neurotransmitter serotonin (5-HT) in [the] brainstem [] that help mediate protective responses to homeostatic stressors such as asphyxia." Resp. Ex. C-10 at 5, 7. The researchers referred to this as the "medullary 5-HT system," which is comprised of "5-HT neuronal cell bodies" located in the medulla, including the ventral surface of the medulla in an area called the arcuate nucleus. Pet. Ex. 27 at 4. Animal research indicated that 5-HT "influences multiple homeostatic functions mediated by the medulla," including "central chemoreception to carbon dioxide and/or oxygen . . . cardiovascular function . . . upper airway control . . . [and] respiratory rhythm generation." Id. Autopsies of SIDS infants have revealed that some infants with SIDS have "hypoplasia of the arcuate nucleus at the ventral medullary surface and 5-HT receptor binding abnormalities in the arcuate and other medullary nuclei." Id. at 5. Kinney and her colleagues believed that there is a "subclinical autonomic dysfunction associated with SIDS" related to abnormalities of the "medullary 5-HT system," which is seen at autopsy. Pet. Ex. 27 at 5. They hypothesized that the medullary 5-HT defect originates in utero during the period of development and differentiation of the brainstem. Id. at 7. They also believed that "sudden death in SIDS likely results from a complex interaction of

several/multiple dysfunctional neurotransmitter systems in the brainstem, and that death is triggered by homeostatic stressor during sleep in a vulnerable developmental period." Id. at 8.

III. STANDARDS FOR ADJUDICATION

The Vaccine Act was established to compensate vaccine-related injuries and deaths. § 300aa-10(a). "Congress designed the Vaccine Program to supplement the state law civil tort system as a simple, fair and expeditious means for compensating vaccine-related injured persons. The Program was established to award 'vaccine-injured persons quickly, easily, and with certainty and generosity.'" Rooks v. Sec'y of Health & Human Servs., 35 Fed. Cl. 1, 7 (1996) (quoting H.R. Rep. No. 908 at 3, reprinted in 1986 U.S.C.C.A.N. at 6287, 6344).

Petitioners' burden of proof is by a preponderance of the evidence. § 300aa-13(a)(1). The preponderance standard requires a petitioner to demonstrate that it is more likely than not that the vaccine at issue caused the injury. Moberly v. Sec'y of Health & Human Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Human Servs., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, petitioners must prove that that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner who satisfies this burden is entitled to compensation unless respondent can prove, by a preponderance of the evidence, that the vaccine's injury is "due to factors unrelated to the administration of the vaccine." § 300aa-13(a)(1)(B).

IV. EXPERT OPINIONS AND CAUSATION ANALYSIS

A. Issue

The parties agree that the sole issue to be resolved is "whether the vaccines that [C.A.C.] received on October 19, 1998, caused or substantially contributed to his death." (citations omitted). See Joint Prehearing Submission ("Jt. Sub."), filed August 25, 2014, at 2.

B. Legal Framework

To receive compensation under the Program, petitioners must prove either: (1) that C.A.C. suffered a "Table Injury"—i.e., an injury listed on the Vaccine Injury Table—corresponding to a vaccine that he received, or (2) that C.A.C. suffered an injury that was actually caused by vaccination. See §§ 300aa-13(a)(1)(A) and 11(c)(1); Capizzano v. Sec'y of Health & Human Servs., 440 F.3d 1317, 1319-20 (Fed. Cir. 2006). Petitioners must show that the vaccine was "not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Moberly, 592 F.3d at 1321 (quoting Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)).

Because petitioners do not allege that C.A.C. suffered a Table injury, they must prove that the vaccines C.A.C. received caused his death. To do so, they must establish, by preponderant evidence: (1) a medical theory causally connecting the vaccine and his injury ("Althen Prong One"); (2) a logical sequence of cause and effect showing that the vaccine was the reason for his injury ("Althen Prong Two"); and (3) a showing of a proximate temporal relationship between the vaccine and his injury ("Althen Prong Three"). § 300aa–13(a)(1); Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005).

The causation theory must relate to the injury alleged. Thus, petitioners must provide a reputable medical or scientific explanation that pertains specifically to this case, although the explanation need only be "legally probable, not medically or scientifically certain." Knudsen v. Sec'y of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994). Petitioners cannot establish entitlement to compensation based solely on their assertions. Rather, a vaccine claim must be supported either by medical records or by the opinion of a medical doctor. § 300aa-13(a)(1). In determining whether petitioners are entitled to compensation, the special master shall consider all material contained in the record, § 300aa-13(b)(1), including "any . . . conclusion, [or] medical judgment . . . which is contained in the record regarding . . . causation." § 300aa-13(b)(1)(A). The undersigned must weigh the submitted evidence and the testimony of the parties' offered experts and rule in petitioners' favor when the evidence weighs in their favor. See Moberly, 592 F.3d at 1325-26 ("Finders of fact are entitled—indeed, expected—to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence"); Althen, 418 F.3d at 1280 ("close calls" are resolved in petitioner's favor).

Another important aspect of the causation-in-fact case law under the Vaccine Act 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 Pharm., 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. Sec'y of Health & Human Servs., 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.

C. Althen Analysis

(1) Althen Prong One: Petitioners' Medical Theory

Under Althen Prong One, petitioners must set forth a medical theory explaining how the vaccines could have caused C.A.C.'s death. Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009); Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355-56 (Fed. Cir. 2006).

Petitioners' theory of causation must be informed by a "sound and reliable medical or scientific explanation." Knudsen, 35 F.3d at 548; see also Veryzer v. Sec'y of Health & Human Servs., 98 Fed. Cl. 214, 223 (2011) (noting that special masters are bound by both § 300aa-13(b)(1) and Vaccine Rule 8(b)(1) to consider only evidence that is both "relevant" and "reliable"). If petitioners rely upon a medical opinion to support their theory, the basis for the

opinion and the reliability of that basis must be considered in the determination of how much weight to afford the offered opinion. See Broekelschen v. Sec'y of Health & Human Servs., 618 F.3d 1339, 1347 (Fed. Cir. 2010) ("The special master's decision often times is based on the credibility of the experts and the relative persuasiveness of their competing theories."); Perreira v. Sec'y of Health & Human Servs., 33 F.3d 1375, 1377 n.6 (Fed. Cir. 1994) (stating that an "expert opinion is no better than the soundness of the reasons supporting it.") (citing Fehrs v. United States, 620 F.2d 255, 265 (Ct. Cl. 1980)).

a. Petitioners' Expert Dr. James Oleske

Dr. James Oleske received his medical degree from the Seton Hall Medical School (now Rutgers New Jersey Medical School) in 1971. Tr. 5. From 1971-1976, Dr. Oleske served as both a pediatric resident and a pediatric ambulatory care fellow with the College of Medicine and Dentistry of New Jersey. Tr. 6. He was also a pediatric infectious disease and immunology fellow at Emory University. Tr. 6-7. Dr. Oleske received his master's degree in Public Health from Columbia University in 1974. Tr. 5. He is licensed to practice medicine in New Jersey with specialties in pediatrics and diagnostic laboratory immunology. See Curriculum Vitae of Dr. James Oleske, Pet. Ex. 48 at 2.

Dr. Oleske is certified by the American Board of Pediatrics and the American Board of Allergy and Immunology. Pet. Ex. 48 at 2; tr. 7. He worked with the Brighton Group, which is a group led by the Centers for Disease Control and Prevention ("CDC") that focuses on issues of vaccine safety. Tr. 7. Currently, Dr. Oleske serves as the Director of the Division of Allergy, Immunology, and Infectious Diseases and Pediatric Palliative Care at Rutgers New Jersey Medical School. Tr. 5. His duties include teaching medical students as well as seeing patients. Tr. 5-6.

Dr. Oleske's proposed medical theory for explaining how the vaccines at issue can cause death was premised on the Triple Risk Model proposed by Dr. Kinney and her colleagues.[10] Pet. Ex. 47 at 3. Dr. Oleske explained that the first element in the Triple Risk Model refers to an infant's underlying vulnerability, also called an intrinsic risk factor. Id. at 3. Intrinsic risk factors include a defect in the "medullary serotonergic system . . . [the] area of the brain [that] controls autonomic functions of the body including [] blood pressure, heart rate and respiration." Id. at 4. Another intrinsic risk factor is hypoplasia[11] of the arcuate nucleus. Tr. 11. Without an intrinsic risk factor, a child can be exposed to the other SIDS factors and not be affected. Tr. 116. However, if a child has such an abnormality, it can affect how that child's immune system deals with external stressors. Pet. Ex. 47 at 3.

The second factor of the Triple Risk Model is a critical development period, usually from age one to six months when an infant's cardiorespiratory protective mechanisms are not

[10] Pet. Ex. 25: Hannah C. Kinney et al., Medullary Serotonergic Network Deficiency in the Sudden Infant Death Syndrome: Review of a 15-Year Study of a Single Dataset, 60 J. Neuropathology and Experimental Neurology 228, 228-247 (2001).

[11] Hypoplasia is defined as "incomplete development or underdevelopment of an organ or tissue." Dorland's at 905.

fully developed. Tr. 20. The third component of the Triple Risk Model is an exogenous stressor, also known as an extrinsic risk factor.[12] Tr. 381. "The recognition of . . . extrinsic risk factors for SIDS, can lead to effective preventative strategies, as has been identified in the context of sleep position (prone[13] versus supine) of the infant and the infant's sleeping environment." Pet. Ex. 47 at 3.

For purposes of this case, Dr. Oleske expanded on the Triple Risk Model in a novel way. He argued that vaccinations act as extrinsic risk factors under the Triple Risk Model, analogous to the way that infections act as extrinsic risk factors. Pet. Ex. 47 at 4. Dr. Oleske testified that an infant who has an infection is exposed to an antigen, which leads to an inflammatory response. Tr. 23. The inflammatory response "may appear only as a little nasal discharge or cough or fever." Id. The infant then goes through the process of developing an immunity to that infection. Tr. 23. With infection, cytokines are released, which "cross from the systemic circulation to the central nervous system circulation." Tr. 25. "[T]he triple-risk theory sees those cytokines. . . as a regulator . . . in a beneficial way that prevents a baby from not breathing and seems to modulate an upregulation of the serotonin system." Tr. 26. "[I]n a vulnerable infant … [the] cytokine balance . . . becomes negative and can lead to SIDS death." Tr. 26-27. Thus, Dr. Oleske argued that vaccines provoke the release of pro-inflammatory cytokines, which adversely affected homeostasis and contributed to SIDS death. Tr. 28. Dr. Oleske opined that when an infant with an intrinsic vulnerability, such as hypoplasia of the arcuate nucleus, and who is younger than six months of age, receives vaccines, the infant's immune system releases a "cytokine storm," which ultimately causes a SIDS death. Tr. 85. "[I]n the vulnerable infant . . . the antigen load of vaccines and adjuvants, can become neurodamaging and provide the 'perfect storm' for SIDS." Pet. Ex. 47 at 5.

To support his opinions, Dr. Oleske cited research[14] performed by Hazim Kadhim and his colleagues that revealed increased levels of certain cytokines in the brains of infants who died of SIDS. Pet. Ex. 47 at 4. This research, according to Dr. Oleske, suggested that in SIDS, cytokines may act as mediators in the failure of "respiratory/arousal functions in a susceptible infant." Id. at 3-5.

Although Dr. Oleske testified that the Triple Risk Model is generally accepted in the medical community as a reliable model for SIDS, he conceded that Kinney has never postulated that vaccines are extrinsic factors, nor has she researched the issue. Tr. 57, 75-76. Dr. Oleske also conceded that there is no way to measure cytokines or to obtain evidence to support his proposed mechanism. Tr. 71-73. While there is no evidence to support his opinion, Dr. Oleske testified that the "state of the art is rapidly advancing" and he is optimistic that in the future there

[12] Extrinsic risk factors include prone sleeping, co-sleeping, soft bed clothing, warm, ambient environment, male gender, and mild infection. Pet. Ex. 30 at 4: HC Kinney et al., The Brainstem and Serotonin in the Sudden Infant Death Syndrome, 4 Annu Rev Pathol Mech Dis 517-550, 519 (2009).

[13] Prone sleeping is lying face-down. Dorland's at 1526.

[14] Pet. Ex. 37: Hazim Kadhim et al., Interleukin-2 as a Neuromodulator Possibly Implicated in the Physiopathology of Sudden Infant Death Syndrome, 480 Neuroscience Letters 122, 122-26 (2010).

will be improved neuropathology analysis that will shed light on the mechanism of "overstimulation of cytokines" relative to SIDS deaths. Tr. 72.

b. Petitioners' Expert Dr. Douglas C. Miller

Dr. Douglas C. Miller earned his medical degree from the University of Miami School of Medicine in 1978. Curriculum Vitae of Dr. Douglas C. Miller, Pet. Ex. 22 at 1. He also received a Ph.D. in physiology and biophysics from the University of Miami in 1980. Id. Dr. Miller was a resident at Massachusetts General Hospital from 1980-1984, focusing in the areas of anatomic pathology and neuropathology. Id. Dr. Miller's most recent position is serving as a clinical professor of pathology and anatomical sciences at the University of Missouri School of Medicine and he is also the program director of pathology residency. Id. at 3. In addition, he is an associate medical examiner for Boone, Callaway, and Greene Counties. Id.

Like Dr. Oleske, Dr. Miller used the Triple Risk Model for SIDS as a framework for his proposed theory of causation. Tr. at 284. With the Triple Risk Model, the infant is thought to have an intrinsic vulnerability. Pet. Ex. 21 at 4. Infants may be vulnerable, or at risk, because of "brainstem abnormalities which lead to deficiencies in serotonin mediated synoptic activity, from the arcuate nuclei or other brainstem serotoninergic nuclei." Id. A "significant proportion of SIDS cases have histopathological abnormality in the medulla, the lowest part of the brainstem." Id. This area of the brain is "responsible for intuition and regulation . . . breathing" and regulation of heart rate. Id. The vulnerable infant is then put at "extra risk by environmental factors such a prone sleeping position . . . or some other stress and then [the infant] suffer[s] from some kind of event from which [he or she] fail[s] to arouse and breathe, ending in a SIDS death." Id. at 4-5.

Dr. Miller explained that based on Kinney's model of SIDS, "the ultimate mechanism [of death] is apnea and the failure to restart breathing." Tr. 369. "SIDS is almost always an asphyxial phenomenon." Tr. 370. In SIDS, asphyxia is "produced by potential nervous system deregulation," which in this instance, Dr. Miller opined, was caused by the vaccinations. Tr. 370. However, Dr. Miller noted that there is no way to distinguish between asphyxia caused by an extrinsic factor such as a prone sleeping position versus asphyxia caused by a central nervous system dysfunction. Tr. 372.

Reaching outside of the traditional extrinsic risk factors listed in the Triple Risk Model of SIDS, and like Dr. Oleske, Dr. Miller argued that vaccines are analogous to upper respiratory infection as an extrinsic risk factor. Tr. 297. Dr. Miller testified that vaccines administered in the thigh of an infant (peripherally), stimulate the release of cytokines, which cross the blood brain barrier[15] ("BBB"), resulting in fever, and can lead to the same outcome as an external stressor. Tr. 296-99. Dr. Miller posited that the

[15] Technically speaking, Dr. Miller testified that cytokines may not cross the BBB, but the BBB may have some sort of transport system allowing cytokines to cross it. Tr. 297-98. According to Dr. Miller, the process is somewhat "obscure." Tr. 299. Moreover, "it may not be necessary to cross the blood-brain barrier to result in central nervous system effects." Tr. 300.

> [C]ombination of vaccine-induced cytokine release and cytokine-mediated abnormal brainstem responses in . . . infants with abnormal medullary serotoninergic respiratory control and arousal systems represents a scientifically, medically plausible mechanism whereby such infants . . . can die from the indirect effects of the vaccine.
>
> Pet. Ex. 21 at 5.

When an infant is made vulnerable by hypoplasia of the arcuate nucleus, Dr. Miller argued that inflammatory cytokines provoke "an abnormal brainstem response." Pet. Ex. 21 at 5. Dr. Miller explained that the arcuate nucleus is the "carbon dioxide sensor in the medulla that . . . drives respiration if carbon dioxide levels become elevated." Tr. 274-75. When levels of carbon dioxide rise above a certain level, the arcuate nucleus stimulates the body to "breathe off the carbon dioxide and breathe in more oxygen." Tr. 277-78. Hypoplasia of the arcuate nucleus may result in a failure of the medulla to properly stimulate arousal and respiration in the face of elevated carbon dioxide. Id.

In summary, Dr. Miller believed that cytokines communicate and interact with the central nervous system (CNS), leading to irregular breathing and episodes of apnea. Tr. 288-89. Apnea leads to hypoxemia, or low levels of oxygen. Id. The defect in the infant's medulla results in a failure to arouse the infant. Id. The failure to stimulate respiration results in elevated carbon dioxide, progressively low levels of oxygen, and ultimately leads to death. Id.

To support his opinion, Dr. Miller cited an article[16] published in 2000 by Froen that describes a study in which nicotine and IL-1 beta (a pro-inflammatory cytokine that is released during infection) were given to pigs and then apnea was induced by artificial means. Tr. 302. Dr. Miller testified that while the study did not exactly focus on the human condition, it suggests that inflammatory cytokines may inhibit an infant's ability to respond to apnea. Tr. 301.

Notably, Dr. Miller conceded that neither Kinney nor her colleagues have ever described or identified vaccines as exogenous stressors in the Triple Risk Model of SIDS. Tr. 348. When asked if he were aware of anyone else who had identified vaccination as an exogenous stressor applicable to the Triple Risk Model, Dr. Miller answered that he did not know anyone else other than Dr. Oleske. Tr. 350.

During the hearing, Dr. Miller discussed and criticized a number of the epidemiological studies cited by respondent's experts. Dr. Miller stated that he did not believe that there was any epidemiological study that has been conducted in what he feels is the "necessary right way." Tr. 329. Dr. Miller testified that "if you don't do the study right, then the answers you get are worthless." Tr. 331.

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[16] Pet. Ex. 33: J. Frederik Froen et al., Adverse Effects of Nicotine and Interleukin-1β on Autoresuscitation After Apnea in Piglets: Implications for Sudden Infant Death Syndrome, 105 Pediatrics 1, 1-5 (2000).

c. Respondent's Expert Dr. Christine McCusker

Dr. Christine McCusker earned a Master of Science at McMaster University in 1988 followed by a Medical Degree at McMaster University in Hamilton, Ontario (Canada) in 1993. Tr. 121; Curriculum Vitae of Dr. Christine McCusker, Resp. Ex. D at 1. Her residency training was in pediatrics at Montreal Children's Hospital, McGill University from 1993-1996. Resp. Ex. D at 2. She was then a clinical fellow in allergy and immunology at McGill University from 1996-1999. Id. Dr. McCusker is board certified in pediatrics and in allergy and immunology. Id. at 2-3; tr. 122. She now treats pediatric patients at an allergy clinic. Tr. 123. In addition, she teaches medical students in the areas of immunology, dermatology, and malignant hematology. Tr. 123. She also works as an emergency room physician approximately once a month. Id.

Dr. McCusker disagreed with petitioners' experts that vaccines may act as an extrinsic risk factor under the Triple Risk Model of SIDS. Dr. McCusker testified that vaccines do not affect the mechanics of breathing, unlike the other extrinsic risk factors such as prone sleeping position, bed-sharing, or over bundling. Tr. 166. Moreover, neither Kinney nor other researchers have identified vaccines as an extrinsic risk factor for SIDS. Tr. 166, 170. Further, Dr. McCusker disagreed with petitioners' experts' comparison of vaccination to an upper respiratory infection. Tr. 196-97. With SIDS, the infant is not breathing properly and does not arouse. Tr. 174. Upper respiratory infections in infants create an effect on the infant's ability to breathe. Tr. 170-71. Infants breathe through their noses, and congestion created by an upper airway infection impairs their ability to breathe through their noses, which may contribute to a mechanical obstruction. Tr. 167, 225. Dr. McCusker explained that vaccines do not contribute to a mechanical obstruction of the airway or problem with gas exchange. Tr. 225.

As described above, the role of cytokines is fundamental to petitioners' proposed theory of causation. Dr. McCusker disagreed with petitioners' experts regarding cytokines because current research suggests that cytokines operate as signals instead of causing inflammation as petitioners argue. Tr. 132-33, 160. Dr. McCusker described the evolution in the understanding of the role of cytokines in the brain based on research by Kinney and her colleagues. Tr. 162-64. In the brain, cytokines are called neurokines.[17] Tr. 222. Early research focused on the pro-inflammatory role of cytokines and their contribution to causing pathology. Tr. 159. Ongoing research, however, has shown that cytokines are constantly being produced in the brain, and researchers now believe that cytokines must be doing something other than causing pathology. Tr. 159-65.[18] Cytokines are now thought to be "communication molecules" important for neuroregulation. Tr. 164, 223. "In normal brain function [] cytokines are . . . involved in things like neuro-protection [and] neuro-modulation." Tr. 150. Thus, cytokines are indicators of stress (signals) not causes of illness or pathology. Tr. 154, 203.

[17] The word cytokines is used throughout this decision, regardless of whether referencing cytokines in the brain, in order to be consistent with the testimony of the experts, who generally used the word cytokines instead of other words such as neurokines.

[18] For a more complete discussion, see Dr. McCusker's expert report, Resp. Ex. C at 2-4 and her testimony, Tr. 135-66.

A 2011 article by Kinney[19] articulated the current thinking on cytokine regulation. In SIDS, infants do not properly respond to hypercapnia (elevated CO2) and there is a failure of arousal and respiration. Tr. 154-55. In the presence of hypercapnia, there is an increase or upregulation of cytokines in the brain. Tr. 154. Dr. McCusker testified that "something [bad is] going on, so [the brain] releases [the cytokine] IL-6." Tr. 154-55. Thus, the cytokines signal stress. Id.

Moreover, the view that cytokines found in the brain are pro-inflammatory has changed. The current thinking is set forth in an article[20] by Noga Ron-Harel, et al. In this article, the authors explained that pro-inflammatory cytokines are abundant in the normal healthy brain and are thought to modulate "neuroendocrine and behavioral responses" to stress. Resp. Ex. C, Tab 3 at 3. Current research shows that the cytokine IL-6 is involved in the development of memory and behavior, and that its presence does not indicate a pathological inflammatory process. Tr. 157, 165. In 2010, Hugo Besedovsky, et al.,[21] reported that brain cytokines, such as IL-1 and IL-6, are produced in a healthy brain "induced by both peripheral immune signals and by central neuronal signals." These cytokines may function as "mediators" of the "relay system . . . capable of receiving and integrating peripheral immune signals with central neural signals." Cytokines IL-1 and tumor necrosis factor (TNFα) are also known to be involved in the regulation of sleep. Resp. Ex. C-7 at 2. Long-term or chronic increases in some cytokines (IL-6) may be related to disease, "while acute stress-induced increases . . . might be adaptive in restoring homeostasis." Resp. Ex. C-9 at 6.

Regarding the use of epidemiology studies in SIDS cases, Dr. McCusker testified that it is the goal of these types of studies to find "the small associations that are overlooked by others." Tr. 183-84. She testified that the designs of the studies are to look for rare events, and the studies look at the frequency of the events in the population and then calculate how many cases have to be accumulated in order to come to a conclusion that is sufficiently powered. Tr. 184.

d. Respondent's Expert Dr. Hart G. W. Lidov

Dr. Hart G.W. Lidov received a Ph.D. from Johns Hopkins University in 1980 followed by a medical degree in 1982. Curriculum Vitae of Dr. Hart G. W. Lidov, Resp. Ex. B at 1. From 1983-1991, Dr. Lidov was a resident in pediatrics and neurology at Massachusetts General Hospital and a neuropathy and anatomic pathology resident at Brigham and Women's Hospital. Id. He has a special qualification in child neurology from the American Board of Psychiatry and Neurology. Id. at 2. Dr. Lidov presently serves as a staff neurologist at Children's Hospital in

[19] Pet. Ex. 28: Hannah C. Kinney et al., The Serotonergic Anatomy of the Developing Human Medulla Oblongata: Implications for Pediatric Disorder of Homeostasis, 41 J. Chemical Neuroanatomy 182, 182-99 (2011).
[20] Resp. Ex. C, Tab 3 at 3: Noga Ron-Harel et al., Brain Homeostasis is Maintained by "Danger" Signals Stimulating a Supportive Immune Response Within the Brain's Borders, 5 Brain, Behavior, and Immunity 1036, 1036-43 (2011).
[21] Resp. Ex. C, Tab 5 at 1: Hugo O. Besedovsky & Adriana del Rey, Central and Peripheral Cytokines Mediate Immune-Brain Connectivity, 36 Neurochemical Research 1, 1-6 (2010).

Boston, associate neuropathologist at Brigham and Women's Hospital, and consultant in neuropathology at Beth Israel Deaconess Medical Center. Id. at 3.

Dr. Lidov viewed the Triple Risk Model of SIDS as a developing hypothesis and offered his opinion of the triple risk factors. Tr. 380-81. As to the first intrinsic risk factor, he testified that some sort of abnormal brainstem pathology "seems to be inherent" in SIDS infants. Tr. 420. Although the brainstem abnormality may not be the same in all infants, Dr. Lidov argued that "the vulnerable infant circle in that famous Venn diagram is actually covering up what's presumed always ultimately to be brainstem abnormalities." Tr. 420-21.

Unlike Drs. Oleske and Miller, Dr. Lidov did not believe that vaccines are an extrinsic risk factor for SIDS. Tr. 382-83. Dr. Lidov noted that none of the studies regarding the epidemiology of SIDS risk factors identifies vaccinations as extrinsic risk factors. Tr. 382. Dr. Lidov argued that as a hypothesis, the Triple Risk Model was not "sufficiently understood or so uniformly recognized as the mechanism underlying a definable subset of SIDS cases, let alone the foundation on which to take the next step as Dr. Miller suggests." Resp. Ex. A at 4. Dr. Lidov testified that "there is no reason to invoke a novel and previously unrecognized factor [vaccines] as a significant contributing factor to his [C.A.C.'s] death." Tr. 379-80.

Further, Dr. Lidov disagreed that the medical literature cited by Dr. Miller supports the theory that cytokines can play a causal role in SIDS associated with vaccination. Resp. Ex. A at 7. The "role for inflammatory cytokines advocated by [Dr. Miller] does not bring a novel factor to light; it simply inserts a mechanistic step" into petitioners' theory that "vaccines increase the risk of SIDS." Id. at 10.

Dr. Lidov's expert report analyzed many of the articles cited by petitioners' experts and explains in detail the problems with the experts' conclusions.[22] As for petitioners' argument that vaccines trigger the release of pro-inflammatory cytokines, which contribute to SIDS deaths, Dr. Lidov cited the Jacques Banchereau article,[23] which involves a review of 37 types of cytokines, for the proposition that cytokines may be anti-inflammatory and not just pro-inflammatory. Dr. Lidov also cited the 2012 Mechtild Vennemann article [24] to establish that research does not support the conclusion that cytokines contribute to SIDS. The purpose of the Vennemann study was to "evaluate the role of cytokines as a possible factor triggering or influencing the risk of sudden death of infants." Resp. Ex. A, Tab 11 at 1. Cytokine (IL-B, IL-6 and TNFα) levels were compared in four groups of infant deaths (total of 119 deaths). Id. at 1. The four groups were SIDS deaths without evidence of infection, SIDS deaths with evidence of infection, explained natural death (severe pneumonia, congenital heart disease, respiratory infections), and unnatural death (suffocation, severe brain injury). Id. at 1-2. The researchers found that cytokine levels in the four groups were not significantly different. Id. at 1. The results did show

[22] To review Dr. Lidov's complete discussion of his analysis of the medical literature cited by Dr. Miller, see Dr. Lidov's expert report, Resp. Ex. A at 4-10.
[23] Resp. Ex. A, Tab 4: Jacques Banchereau et al., From IL-2 to IL-37: The Expanding Spectrum of Anti-inflammatory Cytokines, 13 Nature Immunology 925, 925-31 (2012).
[24] Resp. Ex. A, Tab 11. Mechtild M. T. Vennemann et al., Cytokines and Sudden Infant Death, 126 Int. J. Legal Med. 279, 279-84 (2012).

that when compared with normal values, serum cytokine levels were elevated in all of the four groups studied. Id. This finding of elevated cytokine levels in all causes of death, not just SIDS deaths, suggested that the elevated cytokine levels were possibly due to "agonal or post-mortem changes." Id. In three cases, there were very high levels of cytokines; in two of these deaths, there was evidence of infection, and in the third case, the infant died of hemorrhagic shock and a severe lung infection. Id. at 3-4. The authors posited that the increased concentration of cytokines in these three cases "could be the expression of an overwhelming activation of the cytokine system indicating a cytokine storm, which may explain the death in the two infants with infection." Id. at 5. In summary, the authors concluded that there was no significant difference in "cytokine levels between SIDS cases and non-SIDS cases." Id.[25]

Regarding the use of epidemiological studies in general, Dr. Lidov testified that these types of studies are "a well-established way of refining epidemiologic information, particularly in a situation like SIDS, where . . . doing the epidemiologic studies is extremely challenging . . . ." Tr. 391. He testified that it is "an absolutely desirable thing" to enlarge groups by taking the smaller studies that have been conducted and analyze these studies in a way that draws out larger groups. Id. Dr. Lidov stated that a meta-analysis study is the best way to conduct a study in SIDS cases. Tr. 391-92.

e. Evaluation of the Evidence

Althen Prong One requires petitioners to set forth a reliable medical theory explaining how the received vaccines could have caused the alleged injury. Althen, 418 F.3d at 1278. While scientific certainty is not required to establish causation under the Vaccine Act, id. at 1279, the theory must be supported by a "sound and reliable" medical or scientific explanation. Knudsen, 35 F.3d at 548.

Here, petitioners failed to prove Althen Prong One for two fundamental reasons. First, while petitioners showed by testimony and medical literature that the Triple Risk Model may be an accepted mechanism to explain some SIDS cases, they failed to show that their interpretation of the Triple Risk Model, as it relates to vaccines, is a sound and reliable medical theory. Both Dr. Oleske and Dr. Miller conceded that vaccines have not been identified as an extrinsic risk factor for SIDS. Tr. 57, 348. Dr. Miller was unable to identify any medical professional, other than Dr. Oleske, who identified vaccines as exogenous stressors implicated in the Triple Risk Model. Tr. 350. Moreover, neither Dr. Oleske nor Dr. Miller produced evidence that other professionals in the medical community support the opinion that vaccinations operate like infections as exogenous stressors for purposes of the Triple Risk Model of SIDS.

[25] In the Vennemann article, the authors recognized that their results differed from those reached by Vege et al., where researchers found that IL-6 cerebrospinal fluid (CSF) levels were higher in cases of infectious death as compared to SIDS deaths. Resp. Ex. A. Tab 11 at 4-5; A. Vege et al., Are Elevated Cerebrospinal Fluid Levels of IL-6 in Sudden Unexplained Deaths, Infectious Deaths and Deaths Due to Heart/Lung Disease in Infants and Children Due to Hypoxia?, 87 Acta Paediatrica 819, 819-24 (1998).

Secondly, petitioners failed to show by a preponderance of the evidence that vaccinations cause cytokines to provoke "an abnormal brainstem serotonin response" or otherwise act in a manner that causes or contributes to SIDS death. Pet. Ex. 21 at 5. It is unclear how the Froen article cited by Dr. Miller supports his opinions, as vaccines were not studied, and the focus of the study was on the effects of nicotine, not vaccines. The testimony given by and studies cited by respondent's experts suggest that cytokines do not play any causal role in SIDS. The current understanding of the role of cytokines, as expressed by Dr. McCusker, is that cytokines act to signal the occurrence of a pathological process. Until the role of cytokines is better understood through research, the question of whether cytokines act to cause pathology, as Drs. Oleske and Miller testified, or act to signal the occurrence of a pathological process, as Dr. McCusker testified, remains unanswered. It is premature, based on the evidence presented in this case, to accept petitioners' proposed medical theory that vaccinations may act as exogenous stressors under the Triple Risk Model of SIDS.

(2) Althen Prong Two: Logical Sequence of Cause and Effect

Under Althen Prong Two, petitioners must prove by a preponderance of the evidence that there is a "'logical sequence of cause and effect showing that the vaccination was the reason for the injury.'" Capizzano, 440 F.3d at 1324 (quoting Althen, 418 F.3d at 1278). "Petitioner[s] must show that the vaccine was the 'but for' cause of the harm . . . or in other words, that the vaccine was the 'reason for the injury.'" Pafford, 451 F.3d at 1356 (citations omitted).

a. Petitioners' Expert, Dr. Oleske

Dr. Oleske opined that C.A.C. died of SIDS and that his vaccinations were extrinsic risk factors as described in the Triple Risk Model. Pet. Ex. 47 at 6. Using the Triple Risk Model of SIDS as a framework, Dr. Oleske testified that C.A.C. was a vulnerable infant because he had hypoplasia of the arcuate nucleus. Tr. 11. Further, Dr. Oleske testified that the death occurred when C.A.C. was two months and two days old, a critical time frame, which satisfies the second element of the Triple Risk Model. Tr. 21-22. Dr. Oleske opined that C.A.C.'s vaccinations operated as an exogenous stressor causing a cytokine storm, like a mild infection might, under the Triple Risk Model. Tr. 26-28. He testified that an "inflammatory cytokine storm [was]…the major cause of death." Tr. 85.

Dr. Oleske failed, however, to identify factual support in the record for his theory that the vaccines C.A.C. received triggered the release of cytokines or caused a cytokine storm in the child. For example, when asked what symptoms might be seen in a two-month-old infant who was having a pathological response to cytokines caused by vaccines, Dr. Oleske testified that in the initial six hours, an infant might not have any "discernible clinical signs or symptoms" such as inflammation at the injection site or fever. Tr. 39. The "immune reaction is . . . silent." Id. Dr. Oleske testified that C.A.C. had an irregular response to the vaccines that was "silent" or a "less obvious inflammatory response []," although he could not identify any evidence that this immune process was actually occurring in the child. Tr. 40. Moreover, he did not explain why, in the face of what he believes was a cytokine storm, or release of cytokines sufficient to cause death, there were no clinical signs or symptoms of inflammatory response. Id.

As for Althen Prong Two, Dr. Oleske testified that the following sequence of events would occur. Within three to six hours after vaccination, there would be a local inflammatory reaction at the injection site, with an "influx of inflammatory cells and immune cells to the area responding very rapidly to the foreign antigen." Tr. 73-74. The local response would then become systemic. This process generally causes symptoms such as fever and increased heart rate. Tr. 74. Dr. Oleske conceded that in another SIDS case in which he provided an expert opinion, the infant had unusual behaviors, was irritable, had loss of appetite, and had redness at the site of vaccination. Tr. 40. In contrast, C.A.C. did not exhibit these symptoms and his inflammatory response was silent. Id.

During the hearing, there was considerable focus on the question of whether C.A.C. was sleeping prone, on his back, or on his side, at the time of his death. Dr. Oleske testified that sleeping prone is a "prominent risk factor" for SIDS. Tr. 42. Dr. Oleske agreed that a nurse made an entry in C.A.C.'s records that stated that the "[infant] was noted face down by EMS." Pet. Ex. 12 at 31; Tr. 47. However, because Dr. Oleske could not find an emergency responder report in the medical record documenting the position of the child, he considered the note by the nurse to be hearsay and did not believe it. Tr. 47-48, 111.

Dr. Oleske gave inconsistent testimony about the infant's sleeping position. In his expert report, Dr. Oleske stated that C.A.C. was put to bed on his side. Pet. Ex. 47 at 3. At the hearing, he testified that there was insufficient information for him to reach a conclusion about the infant's sleeping position. Tr. 48-49. Dr. Oleske also testified that the autopsy finding of posterior lividity indicates that the infant may have been on his back, but the finding of facial lividity indicates the infant may have been on his side. Tr. 111-12, 114. As for the side position, Dr. Oleske agreed that one can make an argument that side-sleeping is problematic and may be a risk factor for SIDS. Tr. 46.

b. Petitioners' Expert, Dr. Miller

Dr. Miller testified that C.A.C. died of SIDS, and that the vaccines he received were a substantial contributing factor in his death. Pet. Ex. 21 at 2. The autopsy showed "sparse neuronal populations in the medullary ventral arcuate nuclei." Id. at 4. Otherwise, the histological examination was unremarkable. Id. Dr. Miller noted that the autopsy showed "no specific cause of death, leading to a diagnosis of SIDS." Id. at 5. The abnormal findings of the arcuate nuclei are "associated with a high risk of SIDS." Id.

"[A]bsent any other cause that could be demonstrable . . . it [is] entirely plausible that the vaccinations . . . stimulated cytokine production . . . which had, in this unfortunately vulnerable infant, the effect of suppressing arousal from elevated CO2 levels and caused SIDS." Tr. 332. Dr. Miller opined that the cytokines that contributed to C.A.C.'s death included a combination of IL-1 and IL-6, and perhaps also tumor necrosis factor alpha (TNFα). Tr. 353. He further opined that these cytokines communicated with the brain, resulting in suppressing arousal in the face of elevated carbon dioxide levels. Tr. 332. While Dr. Miller testified that these cytokines played a role in C.A.C.'s death, he also testified that there is no way to verify the presence of cytokines or to test for them. Tr. 325. Moreover, he agreed that there was "no description of any inflammation in the pathology [autopsy] report." Tr. 354. Further, Dr. Miller testified that there

was no evidence that the vaccines caused any injury based on the examination of C.A.C.'s organs at autopsy. Tr. 347.

Dr. Miller's phrase, "absent any other cause that could be demonstrable," raises the question of whether there were extrinsic factors present that could explain this SIDS death. Tr. 332. According to Dr. Miller, extrinsic risk factors include low birth weight, the prone sleeping position, soft mattress, recent illness, "mild upper respiratory infection," hyperthermia and fever. Tr. 286-87, 345. Dr. Miller, however, did not believe that any of these risk factors were present in the circumstances surrounding C.A.C.'s death. Tr. 338. Like Dr. Oleske, Dr. Miller did not believe that C.A.C. was in the prone position and, thus, he did not believe the prone position was an extrinsic risk factor that could explain C.A.C.'s death from SIDS. Id.

According to Dr. Miller, the description of lividity described in the autopsy report indicates that the infant died on his back and slightly on his right side, and that he remained in that position for an hour or more after death. Tr. 373. Dr. Miller testified that "lividity patterns are usually established before resuscitation is started." Id. Dr. Miller conceded, however, that the description of lividity could also be explained by the infant being prone at the time of death, if the caretaker noticed the infant's death quickly and resuscitation occurred rapidly. Id. Ultimately, Dr. Miller testified there was no objective way to determine the infant's position. Id.

Like Dr. Oleske, Dr. Miller testified that the statement taken from a registered nurse during the medical examiner's investigation, which described the infant's position, was erroneous. Tr. 372. The investigative narrative states that "per RN Jesmer, CMH-ER…decd [decedent] was noted face down by EMS, and some purge was noted from the Nares/OS. No trauma evident." Pet. Ex. 12 at 31. Dr. Miller testified that he did not believe Nurse Jesmer's statement because EMS did not document the infant's position. Tr. 374. Since EMS did not chart this information, "it didn't happen." Id.

c. Respondent's Expert, Dr. McCusker

Dr. McCusker disagreed with petitioners' experts' conclusion that C.A.C.'s vaccinations played a contributing role in his death from SIDS. Resp. Ex. C at 7-8. The reasons for her opinion were as follows: first, there was no evidence of pro-inflammatory cytokines or an upregulation of cytokines. Id. at 7. If C.A.C.'s vaccines caused an increase of cytokines in his brain, "the resulting effect would most likely have been increased arousal and/or fever." Id. at 4. C.A.C. had "no reported fever, the usual first clinical sign of systemic cytokine activity." Resp. Ex. E at 4.

Second, Dr. McCusker stated that there was no evidence of a "cytokine storm" as postulated by Dr. Oleske. Tr. 177. To describe the clinical course of a "cytokine storm," Dr. McCusker used the example of an adverse reaction patients experienced during a clinical trial of an anticancer drug given to stimulate the immune system. Tr. 178, 253-55. When the drug was given to six volunteer patients the first time, the drug induced a cytokine storm. Tr. 253-54. The individuals developed fever within thirty minutes to one hour, then subsequently headache, irritability, pulmonary inflammation, and adult respiratory distress syndrome, requiring intubation to support respiration. Tr. 254. Over the course of several days, the patients

developed multi-system organ failure. Tr. 178, 254. Dr. McCusker testified that she was not aware of any vaccination causing cytokine storm. Tr. 255. She explained that even assuming vaccines can cause such a reaction, there was no evidence that C.A.C. suffered a cytokine storm. Tr. 256. C.A.C. did not have fever and there was no evidence of multi-system organ failure on autopsy. Pet. Ex. 9 at 19-23. Moreover, there was no evidence of pulmonary inflammation on autopsy. Id.

Third, the extrinsic risk factors for SIDS include "prone or side sleeping, bed sharing, over-bundling, soft bedding . . . and recent history of upper respiratory tract infection." Resp. Ex. E at 2. Dr. McCusker stated that "[i]n a recent study, [26] 99% of SIDS had a least 1 risk factor for SIDS identified at the time of death." Id. Dr. McCusker concluded that "in the case of [C.A.C.], the prone sleep position in which he was found would be considered within the list of known extrinsic risk factors" which contributed to his death from SIDS. Id. at 2. Dr. McCusker based her opinion that C.A.C. was in the prone position when he died on two pieces of evidence: (1) a statement taken from a nurse reporting that EMS found the infant in the prone position, and (2) the description by the medical examiner of "lividity of the right side of the face with blanching over the pressure areas." Tr. 125, 178. Dr. McCusker stated that based on her experience of understanding how babies sleep, the lividity on the right side of the face "implies that the right side of the face must have at least been part of the dependent pooling of blood for the baby." [27] Tr. 125. She testified that when a baby sleeps in the supine position, the baby's head might be turned to the side, but it would not be side down. Dr. McCusker stated that "you wouldn't necessarily have a specific right side of the face/whole face affected." Tr. 126. She further stated that if the child was on his side, the side of the face would be down and there would have been pressure on one side of the face. If the child was prone, the head would be either turned to the right or the left. Id. Dr. McCusker testified that when in the prone position, an infant's breathing is impaired because there is less room for the chest wall to expand. Tr. 168. Further, when face down, an infant breathes expired air that has a higher content of carbon dioxide. Id.

As for the statement given by the nurse during the medical examiner's investigation stating that EMS found the baby prone, Dr. McCusker considered it to be clear evidence that the infant was in fact prone. Tr. 178-79. She explained that in all cases of SIDS, the position of the infant is one of the first questions that is asked during an investigation into the death. Tr. 178. Dr. McCusker emphasized that "especially now with the back-to-sleep campaigns," the first question asked is "how the baby was found, and . . . if the baby was found prone" then that is what is charted in the record. Tr. 178-79.

[26] Resp. Ex. C, Tab 10: Felicia L. Trachtenberg et al., Risk Factor Changes for Sudden Infant Death Syndrome After Initiation of Back-to-Sleep Campaign, 129 Pediatrics 630, 630-38 (2012).
[27] Dr. McCusker testified that she is not an expert on the issue of lividity, and the undersigned took this evidence into consideration. Here, testimony on this issue is not determinative of the outcome, and even if Dr. McCusker's testimony on this issue was excluded, the undersigned's decision would be the same.

d. Respondent's expert Dr. Lidov

Like petitioners' experts, Dr. Lidov testified that C.A.C. died of SIDS. However, Dr. Lidov disagreed that vaccinations are extrinsic risk factors for SIDS deaths. Tr. 382-83. Dr. Lidov believed C.A.C "fits perfectly in the Triple Risk Model of SIDS" without the need to implicate vaccinations. Tr. 382. C.A.C. had hypoplasia of the arcuate nucleus, and he had known risk factors for SIDS. Id. These factors include C.A.C.'s gender (male), the fact that he died during peak incidence for SIDS (between two to four months), and the fact that he was found in the prone position. Tr. 382, 425.

To support his position that C.A.C. was in the prone position, Dr. Lidov noted the nurse's statement that C.A.C. was found prone. Tr. 385. In addition, Dr. Lidov explained that the lividity observed on the right side of the infant's face suggests that he was lying on his face, and not his back, at the time of death. Tr. 385-86. Also, the description of lividity in the face, as being fixed, indicates that the infant had been on his face longer than he had been on his back. Tr. 398-99. Dr. Lidov testified that the fact that the posterior lividity was not fixed indicates that the infant was originally on his stomach and then turned over onto his back during resuscitation efforts. Tr. 386.

Dr. Lidov disagreed with Dr. Oleske that C.A.C.'s vaccinations led to a cytokine storm that caused his death. Tr. 319. Dr. Lidov explained that cytokine storms are "dramatic illnesses" seen in association with "sepsis and septic shock, influenza, acute respiratory distress, response to blood transfusion or bone marrow transplantation, toxic response to medication . . . severe acute respiratory syndrome (SARS) outbreak, and H5N1 avian influenza." Resp. Ex. A at 9. In contrast, C.A.C. "appeared well." Id. Moreover, Dr. Lidov testified that there was no evidence of any inflammatory process in the brain. Tr. 393. C.A.C.'s brain weight was slightly heavier than normal, which is also consistent with SIDS deaths. Tr. 392.

e. Evaluation of the Evidence

Althen Prong Two requires preponderant evidence of a "logical sequence of cause and effect showing that the vaccination was the reason for the injury." Althen, 418 F.3d at 1278. This prong is sometimes referred to as the "did it cause" test; i.e., in petitioners' case, the question is whether the vaccine (or vaccines) caused the alleged injury. Broekelschen, 618 F.3d at 1345 ("Because causation is relative to the injury, a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case . . . . "); Pafford, 415 F.3d at 3.

The basic problem with petitioners' argument regarding Althen Prong Two is that there is no evidence to support petitioners' theory that C.A.C.'s vaccinations acted as an extrinsic stressor, similar to that of an infection under the Triple Risk Model. First, petitioners did not proffer any evidence to support their position that the peripheral cytokines released in response to the vaccines administered to C.A.C. communicated with the central nervous system to invoke

an abnormal brain response in the manner described by Dr. Oleske and Dr. Miller.[28] In fact, there is no evidence of cytokines in C.A.C.'s brain, by indirect or circumstantial evidence. If Dr. Oleske is correct and cytokines caused a pro-inflammatory response, then it is likely that there would be evidence of inflammation in the brain, but Dr. Miller testified that there was no such evidence. Tr. 354.

Second, there is no evidence that C.A.C. suffered from a fever, illness, or other clinical sign or symptom after vaccination that would support a finding that cytokines played a causal role in his death. Dr. Oleske testified that C.A.C.'s death was caused by a cytokine storm. Tr. 85. Based on the evidence presented, if there had been a cytokine storm, there should have been some evidence at autopsy of a profound systemic process. Moreover, Dr. Oleske's opinion that C.A.C. had a cytokine storm, in spite of the fact that there is no evidence of such a process occurring, is in stark contrast to Dr. McCusker's testimony about the clinical presentation of patients who experience a cytokine storm.[29] Dr. McCusker presented testimony describing patients who actually developed an abnormal cytokine response. These patients developed fever, headache, and respiratory failure requiring admission to the ICU within hours of receiving the offending drug. Tr. 254. Dr. McCusker described the clinical course of the patients who develop cytokine storm as a "massive, uncontrolled pulmonary inflammation as a result of viral-induced cytokine storm in the airways." Tr. 255. Here, there is not even a suggestion of evidence that C.A.C. experienced a cytokine storm.[30]

Finally, based upon the statement taken from the nurse that paramedics found C.A.C. in the prone position, along with the findings on autopsy of lividity and blanching of the child's face, the undersigned finds that C.A.C. was lying on his face, either in the prone or the side position, both of which are strongly associated with SIDS. As Dr. Lidov explained, C.A.C met the criteria for the Triple Risk Model of SIDS without the need to consider a speculative risk factor. Tr. 382. C.A.C. had hypoplasia of the arcuate nucleus, and he had several known risk factors for SIDS. Id. These factors include C.A.C.'s gender (male), the fact that he died during peak incidence for SIDS (between two to four months), and the fact that he was found in the prone position. Tr. 382, 425.

For these reasons, the undersigned finds that petitioners failed to provide preponderant evidence of a logical sequence of cause and effect showing that C.A.C.'s vaccinations caused his death.

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[28] Note that Dr. McCusker agreed that there is communication between the peripheral body and the central nervous systems, and that cytokines played a role in the communication. But she did not agree with petitioners' experts' contention that cytokines played a pathological role. Tr. 131, 182.

[29] Resp. Ex. K: Ganesh Suntharalingam et al., Cytokine Storm in a Phase 1 Trial of the Anti-CD28 Monoclonal Antibody TGN1412, 355 New. Eng. J. Med. 1018, 1018-28 (2006).

[30] A cytokine storm is defined as a "profound systemic oversecretion of cytokines." See Institute of Medicine, Adverse Effects of Vaccines-Evidence and Causality 75 (2012). The process results in "local tissue and organ damage, and systemic symptoms." Id. There is no evidence of local tissue and organ damage here.

(3) Althen Prong Three: Proximate Temporal Relationship

Under Althen Prong Three, petitioners must provide "preponderant proof that the onset of symptoms occurred within a timeframe for which, given the understanding of the disorder's etiology, it is medically acceptable to infer causation-in-fact." De Bazan, 539 F.3d at 1352. The acceptable temporal association will vary according to the particular medical theory advanced in the case. See Pafford, 451 F.3d at 1358. A temporal relationship between a vaccine and an injury, standing alone, does not constitute preponderant evidence of vaccine causation. See, e.g., Veryzer v. Sec'y of Health & Human Servs., 100 Fed. Cl. 344, 356 (2011) (explaining that "a temporal relationship alone will not demonstrate the requisite causal link and that petitioner must posit a medical theory causally connecting vaccine and injury").

a. Petitioners' Expert, Dr. Oleske

Dr. Oleske testified that C.A.C. died sometime between three to six hours after vaccination, and that this timeframe constituted an appropriate temporal association between vaccination and death. Tr. 22. When asked about the basis for his testimony, Dr. Oleske testified that after giving the vaccination by injection, there is usually "some lag time of half an hour, an hour where there's then the beginning of a mounting systemic response." Tr. 22-23. According to Dr. Oleske, in the first six hours after vaccination, there is a local inflammatory response at the site of vaccination, with an "influx of inflammatory cells and immune cells to that area responding very rapidly to the foreign antigen." Tr. 73-74. That local response becomes systemic in "[a] fairly short period of time with mediatory releases that then travel to – for example, when fever and inflammation gets to the point where the heart rate [increases]." Tr. 74.

When Dr. Oleske was asked to explain what happens in the first three to six hours after vaccination that leads to SIDS, he stated that the local response (at the site of vaccination) becomes systemic and the "inflammatory response circulates very rapidly through the body to the central nervous system, and in the arcuate nucleus in a vulnerable infant, that kind of immunological response can, on a cellular level, cause damage that you would not see physically." Tr. 74. Ultimately, Dr. Oleske said, "[t]here are pathological mechanisms in play that we yet do not understand." Tr. 75.

b. Petitioners' Expert, Dr. Miller

Dr. Miller testified that C.A.C. died approximately five hours after his vaccinations. Tr. 307. Based on anecdotal data, Dr. Miller testified that the maximum risk period for SIDS after vaccination is 48 hours. Tr. 306-07.

With regard to the temporal relationship between vaccination and SIDS based on C.A.C.'s age, Dr. Miller stated that the literature suggests that the peak incidence of SIDS is "between two and three months" of age. Tr. 306. This age range also happens to be "when most kids get their vaccinations." Tr. 306. Whether the temporal association between vaccination and SIDS is a "coincidence or . . . related in a causal way" is the "crux of the issue." Tr. 306.

c. Respondent's Expert, Dr. McCusker

Dr. McCusker testified that when a vaccine is given, the immune response remains localized for a "significant period of time." Tr. 140. When a vaccine is given in the infant's thigh, the "initial activation event occur[s] at the thigh" and then takes "a significant amount of time to go from the thigh" to the adjacent lymph node. Id. During this time frame, cells are actively dividing "as a result of the antigen stimulation." Id. Dr. McCusker explained that it takes "several days" for the "dissemination of that information beyond the regional lymph node." Tr. 141. Although it may take days for antigen stimulation to reach beyond the local level, there can be "signs and symptoms of the pro-inflammatory response within six to 12 hours." Id. The key cytokines that are active during the first hours of an immune response . . . are implicated in the development of systemic symptoms such as fever and malaise." Resp. Ex. E at 3. C.A.C. "had no reported fever, the usual first clinical sign of systemic cytokine activity." Id.

Dr. McCusker attributed the temporal relationship between C.A.C.'s vaccination and his death to the fact that C.A.C. was just over approximately two months of age at the time of his death, an age that is high risk for SIDS. Tr. 180.

d. Respondent's expert Dr. Lidov

Like the other experts, Dr. Lidov agreed that the peak incidence for SIDS is between ages two and four months. Tr. 425. On cross-examination Dr. Lidov was questioned about the G. Ottaviani article,[31] a case report published in 2006, which questions a possible association of SIDS with hexavalent vaccines. While Dr. Lidov agreed that there are studies[32] where the authors have suggested that there is some increase in SIDS following receipt of the hexavalent vaccine, he did not find such studies persuasive because "there have been several more studies that have not found that effect." Tr. 436.

e. Evaluation of the Evidence

Neither of petitioners' experts offered any evidence to support a finding that peripheral cytokines (from the vaccination injection site) communicated to C.A.C.'s brain, triggering the mechanism described by petitioners' experts, whereby C.A.C. would succumb to SIDS within three to six hours after vaccination. There is no evidence of fever to suggest cytokine activity. There is a temporal relationship between vaccination and SIDS, but a temporal relationship alone cannot establish causation. Veryzer, 100 Fed. Cl. at 356.

Even assuming that petitioners had provided evidence that would meet their burden under Althen Prong Three, petitioners failed to establish Althen Prongs One and Two by a preponderance of the evidence, and therefore, they are not entitled to compensation.

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[31] Pet. Ex. 42: G. Ottaviani et al., Sudden infant death syndrome (SIDS) shortly after hexavalent vaccination: another pathology in suspected SIDS? 448 Virchows Arch 100, 100-04 (2006).
[32] See also Pet. Ex. 43, Traversa et al., Sudden unexpected deaths and vaccinations during the first two years of life in Italy: A case series study. PLoS ONE 2011; 6E 16363.

V. CONCLUSION

For the reasons discussed above, the undersigned finds that petitioners have not established entitlement to compensation and their petition must be dismissed. In the absence of a timely filed motion for review filed pursuant to Vaccine Rule 23, the clerk is directed to enter judgment consistent with this decision.

IT IS SO ORDERED.

s/Nora Beth Dorsey
Nora Beth Dorsey
Special Master