In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 09-284V
September 30, 2010
To be Published

MARQIANO JAMES, deceased, by and through his natural mother, COLLEEN CHEE, and his natural father, MARCO JAMES,	*	
Petitioners,	*	DTaP; incomplete brain more vulnerable to apnea; cardiac arrest; death
v.	*	
SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Stephen I. Leshner, Phoenix, AZ, for petitioners.
Heather L. Pearlman, Washington, DC, for respondent.

MILLMAN, Special Master

DECISION[1]

Petitioners filed a petition on May 5, 2009 under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10 *et seq*., alleging that their son Marqiano James (hereinafter,

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

Marqiano) died on December 12, 2007 as a result of the vaccinations administered to him on December 11, 2007, in particular the pertussis component of DTaP.

The disagreement between the parties concerns whether Marqiano, born prematurely and without a neocortex, died from apnea and cardiac arrest because he had a vaccine reaction or because he was medically fragile from birth. There was no autopsy in this case.

A hearing was held on July 21, 2010. Testifying for petitioners were Marqiano's mother and petitioners' expert Dr. Steven Pike. Testifying for respondent was Dr. Mary Ann Guggenheim.

FACTS

On August 12, 2007, Marqiano was born at 34 weeks gestation by caesarean section at Maricopa Medical Center (MMC). CHEE/MMC 101.[2] Dr. Kim H. Manwaring recommended early delivery because Marqiano had severe fetal hydrocephalus[3] and hydronephrosis.[4] *Id*. at 101, 339-40. At birth, Marqiano had major brain malformation with massive head enlargement due to the severe hydrocephalus, dysmorphic facial features, hypogonadism, and cystic enlargement of a kidney. *Id*. at 909, 918, 920.

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[2] Petitioners' method of pagination includes initials of providers. For example, Maricopa Medical Center records are paginated as MMC and the number of the page. Phoenix Indian Medical Center records are paginated as PIMC and the number of the page. Hacienda Healthcare records are paginated as HH and the number of the page. Sometimes these abbreviations are preceded by CHEE, the last name of Marqiano's mother.

[3] Hydrocephalus is "a condition marked by dilatation of the cerebral ventricles, most often occurring secondarily to obstruction of the cerebrospinal fluid pathways...and accompanied by an accumulation of cerebrospinal fluid within the skull." Dorland's Illustrated Medical Dictionary, 30th ed. (2003) at 870.

[4] Hydronephrosis is distention of the pelvis and calices of the kidney with urine, as a result of obstruction of the ureter." Dorland's, *supra* note 3, at 872.

Dr. Manwaring operated on Marqiano to place an external ventricular drain for the temporary remediation of his hydrocephalus. MMC 1181. Marqiano was diagnosed with aqueduct stenosis. *Id*. at 573. On August 19, 2007, Dr. Manwaring removed the external ventricular drain and implanted a left frontal lobe pressure ventriculoperitoneal shunt. MMC 1183. The diagnosis was severe near end-stage hydrocephalus, congenital, secondary to aqueductal stenosis. *Id*.

On August 21, 2007, a brain MRI showed Marqiano had marked hydrocephalus involving the lateral ventricles and the third ventricle. MMC 707. The study suggested stable, marked hydrocephalus, lobar holoprosencephaly[5] with septo-optic dysplasia,[6] and a kinking of the cervicomedullary junction, likely related to Marqiano's abnormal brain anatomy. *Id*. at 708.

Marqiano had difficulty feeding and also reflux. Therefore, on September 7, 2007, a gastrostomy tube was placed in him to provide nutrition. MMC 813, 827, 830, 833, 901, 1185.

On September 26, 2007, Marqiano was evaluated at the Phoenix Indian Medical Center (PIMC) where he received his first series of vaccinations: DTaP, inactivated polio, HiB (haemophilus B influenza), hepatitis B, and pneumococcal vaccines. PIMC 006.

On October 4, 2007, certified nurse practitioner Kathleen Klas discuss with Marqiano's family his very grim prognosis because of severe damage to his brain tissue due to hydrocephalus. MMC 526. Marqiano's family stated they wanted Marqiano to receive

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[5] Holoprosencephaly is a "failure of cleavage of the prosencephalon with a deficit in midline facial development." Dorland's, *supra* note 3, at 859. The prosencephalon is "the part of the brain developed from the anterior of the three primary vesicles of the embryonic neural tube; it comprises the diencephalon and telencephalon..... Called also *forebrain*." *Id*. at 1520.

[6] Dysplasia is "abnormality of development." Dorland's, *supra* note 3, at 577.

everything that could be done for him. *Id*. Marqiano's gastrostomy button was leaking. *Id*. at 527.

Marqiano was frequently evaluated at PIMC for failure to thrive and his leaking gastrostomy tube. PIMC 11-17. On October 27, 2007, he was taken to the MMC emergency room after he turned blue from coughing and vomiting while receiving a tube feeding. MMC 306. He had not gained weight for a month. *Id*. at 314. Admitted to the hospital, Marqiano had multiple episodes of vomiting, apnea, hypoxia, and bradycardia. *Id*. at 323-45. He was discharged from the hospital on November 5, 2007 with a diagnosis of aspiration pneumonia, multiple congenital anomalies, holoprosencepahly, gastric tube dependence, hydrocephalus, and blindness. MMC 308.

The next day, November 6, 2007, Marqiano was admitted to MMC because of his continuing gastrostomy tube leakage. MMC 171. The tube was replaced twice while he was hospitalized. *Id*. at 168. He was discharged on November 13, 2007. *Id*. at 169.

On November 17, 2007, Marqiano returned to the MMC emergency room because of the leaking gastrostomy tube and an intermittent fever. MMC 37. A replacement tube was on order and not yet available. *Id*. Therefore, Marqiano was discharged to the Hacienda Medical Facility, which is a skilled nursing facility, to await the new gastrostomy tube delivery. MMC 37. Hacienda evaluated him as having a good discharge potential but a bad rehabilitation potential and prognosis. *Id*. at 52-53.

On December 11, 2007, Dr. Tom Herr evaluated Mariqano during a general pediatric visit. HH 245. Marqiano received his second series of vaccinations: DTaP, hepatitis B, and

inactivated polio combined as Pediarix, HiB, Prevnar, RotaTeq, and Synagis (respiratory syncytial virus) vaccines. *Id*. (Synagis is not on the Vaccine Injury Table.)

On December 12, 2007, Marqiano died in his sleep in the Hacienda Medical Facility. The nurse's entry at midnight reflects that a report from the night nurse at 10:00 p.m. was that Marqiano was stable, asleep in his crib, without signs of distress. HH 78. At the 3:10 a.m. nurse's check-up, he was gray. *Id*. At 3:15 a.m., the nurse got a respiratory therapist who detected that Marqiano had no pulse and was not breathing. *Id*. at 77. Paramedics arrived at 3:25 a.m. Marqiano was pronounced dead at Maricopa Medical Center at 4:21 a.m. *Id*. The death certificate listed the cause of death as cardiopulmonary arrest due to or as a consequence of aspiration due to or as a consequence of congenital brain malformation. Ex. 1, p. 1.

TESTIMONY

Marqiano's Mother

Marqiano's mother testified first for petitioners. Tr. at 4. Marqiano was born prematurely and had hydrocephalus. Tr. at 5-6. Marqiano was placed at Hacienda Skilled Nursing because his gastrotube was leaking. Tr. at 6. Marqiano responded to her when she spoke to him by opening his eyes and smiling. Tr. at 7. She took Marqiano to see Dr. Sipperly, a retinal consultant, on the day of his vaccinations because Marqiano could not see. Tr. at 7-8. She also took him to Dr. Herr at the Phoenix Indian Medical Center for Marqiano's four-month well baby check-up. Tr. at 8-9. Marqiano had no sign of illness. Tr. at 9. Marqiano received his immunizations. *Id*. She took Marqiano back to Hacienda at 4:30 p.m. *Id*.

At 3:30 a.m. the next morning, one of the nurses from Hacienda called her and told her they had found Marqiano unresponsive and CPR was being done. Tr. at 10. She went to

Maricopa Medical Center where she was informed that Marqiano died, but no one gave her a cause of death. Tr. at 11.

Petitioners' Expert Dr. Pike

Dr. Steven Pike testified next for petitioners. Tr. at 12. He is board-certified in toxicology, emergency medicine, occupational and environmental medicine, and industrial hygiene. Tr. at 13. He practices emergency medicine and medical toxicology primarily. *Id*. Dr. Pike's opinion is that Pediarix (which Marqiano received) contains acellular pertussis components that can cause acute and chronic persistent and severe neurological dysfunction. This view is consistent with the medical literature and with the Institute of Medicine (IOM) opinions on DPT vaccine. Tr. at 14.

Dr. Pike continued that Pediarix can also cause post-immunization apnea, cardiopulmonary arrest, and death (mentioned in the manufacturer's product insert). Tr. at 15. Dr. Pike opined that Marqiano's post-immunization apnea, cardiorespiratory arrest, and death were the kind of consequences that Pediarix or DTaP can cause in premature infants. *Id*. His opinion is that Pediarix was more likely than not the proximate cause of Marqiano's apnea, cardiorespiratory arrest, and death. *Id*.

In explaining the mechanism of pertussis vaccine injury, Dr. Pike testified that the most serious component is pertussis toxin itself even though, in the acellular formulation, there is an attempt to neutralize its toxicity. Tr. at 16. The mechanisms to neutralize pertussis toxin's toxicity are imperfect and some residual toxicity can exist. There are also idiosyncratic reactions that can occur in individuals. *Id*.

Pertussis toxin can increase the permeability of the blood-brain barrier, allowing fluid and material to enter the brain, stimulating T-cells which can release certain types of proteins called cytokines that can attract other forms of inflammatory cells. *Id*. The activated T-cells and inflammatory cells can produce swelling and edema around the nerve cells and glial cells, producing numerous clinical effects: encephalopathy, seizure activity, anaphylaxis, or sudden apnea. Tr. at 17. Apnea in premature infants such as Marqiano can lead to death and Dr. Pike believes this is what happened to Marqiano. Tr. at 17-18.

Dr. Pike believes Marqiano's death certificate is incorrect in listing aspiration as a cause of his death. The death certificate is correct in listing cardiopulmonary arrest. Tr. at 20. The reason he believes there was no aspiration is that the Hacienda nurses were monitoring Marqiano and did not report him to have any evidence of vomiting when they discovered him to be apneic. *Id*. There was no vomit reported in his mouth, on the crib, or in his vicinity. *Id*.

When the paramedics arrived, they did not report any evidence of vomiting or aspiration. This would be routine and very important information for paramedics to give emergency physicians. Tr. at 20-21. Dr. Pike has experience as an emergency physician. The paramedics will almost always inform him if there is any evidence of vomiting or aspiration because they know the importance of starting certain types of antibiotics early and the possible need for bronchoscopy to remove foreign material from the bronchus to the main stem or branching bronchi. Tr. at 21. When the paramedics intubated Marqiano, they did not report that they had to suction his oral pharynx, providing further proof that Marqiano had not aspirated. *Id*. They had no problem inserting the endotracheal tube other than Marqiano's congenital facial deformities. *Id*. Furthermore, after intubation, the paramedics did not report that any vomit

came out of the endotracheal tube. Typically, after an endotracheal intubation, if a person has aspirated, vomit would come through the tube and have to be suctioned out. But this was not observed with Marqiano. Tr. at 21-22.

Moreover, the paramedics reported hearing good breath sounds with their ventilatory efforts through the endotracheal tube. In the emergency department, there was no report of any gurgling or rhonchi (loud sounds occurring when there is a lot of phlegm). Tr. at 22. The emergency physician at Maricopa Medical did report cardiorespiratory failure. His second diagnosis was holoprosencephaly. Tr. at 22. Holoprosencephaly is a combination of Marqiano's lack of formation of the cortex of his brain, his aqueductal stenosis, and his hydrocephalus. Tr. at 24. Nowhere did the emergency physician write down aspiration. Tr. at 23. Dr. Pike has no idea why the death certificate has aspiration as one of the reasons for Marqiano's death, although it is not unusual for death certificates to be erroneous. *Id.*

Dr. Pike said he agreed with Dr. Guggenheim, respondent's expert, that Marqiano's death was caused by perturbation of brain function, but he believes that the cause of that perturbation was Pediarix vaccine which contains pertussis toxin and other pertussis components. Tr. at 25.

The undersigned asked Dr. Pike how Marqiano could seemingly be fine at night and then a few hours later be in trouble. Tr. at 26. Dr. Pike responded that inflammation in brain tissues and breaches of the blood-brain barrier can occur over hours. The rate at which a change occurs depends on the toxin's potency in the case of pertussis and the rate at which leakage of the blood-brain barrier occurs. *Id*. The exact mechanism for sudden apnea in premature infants who receive this vaccine has not been completely worked out, but there is an increased rate of apnea in these patients. Tr. at 27.

The purpose of the blood-brain barrier is not only to prevent unwanted proteins and other materials from entering the brain but also to limit the amount of fluid entering the calvarium to prevent compression of the brain or brain swelling. Tr. at 27-28. Marqiano already had swelling of the brain from his aqueductal stenosis and hydrocephalus, which required shunts to be implanted. Tr. at 28. The shunts would have protected him from increased intracranial pressure, but would not have protected him from the direct effects that pertussis toxin has on neurons. *Id*. The mechanisms are not well understood to explain how pertussis toxin causes apnea in premature infants. *Id*.

Marqiano was born at 34 weeks gestation, whereas the normal gestational age is 40 weeks. Tr. at 28-29. He was born with a congenital anomaly of his brain, hydrocephalus, and blindness, showing his premature status regarding the central nervous system was more significant. Tr. at 29. Although Marqiano was born six weeks premature, his brain maturity was much less than his gestational age. Tr. at 30. He had no developed cortex and very limited capability of brain function as evidenced by his blindness and hydrocephalus. *Id*. Brain immaturity made Marqiano more vulnerable to the effects of pertussis toxin even in a purified state. *Id*. One could argue that Marqiano's brain development arrested perhaps as early as 20 weeks gestation or even less because he did not form the significant major brain structures. Tr. at 32.

The stenosis of his aqueduct, a certain portion of the brainstem where cerebral spinal fluid flows through the ventricles that usually would be in the cortex, caused his hydrocephalus. The hydrocephalus can compress cortical neurons to create a very thin cortex. Marqiano had an absence of development of cortical tissue in addition to having hydrocephalus. *Id*.

Dr. Pike did not believe that Marqiano would have died in any event at four months. Marqiano actually seemed to be doing fairly well given his limitations. Tr. at 33. He had trouble with feeding but he was improving and getting therapy. *Id*. He had an expectation of a much less degree of functioning than most infants, but there was no reason to believe that he was not going to sustain life. *Id*. His brainstem was functioning. He could breathe on his own. His heart was strong. The centers of his brain that controlled vital functions such as ventilation, cardiac activity, and blood pressure seemed intact. *Id*.

The problem with Marqiano was that he had no cortex. The neocortex was missing, meaning he was blind because he had no occipital cortex. Tr. at 33-34. He probably could not think or have any rational thoughts because he had no other form of cortical functioning. Tr. at 34. Dr. Pike thinks Marqiano could have lived for an indefinite period of time. *Id*. If the doctors had not expected him to survive, they would have had no reason to vaccinate him. *Id*. There was a reasonable expectation for Marqiano to achieve his maximum abilities, even though those may have been very severely compromised. *Id*. Had it not been for the pertussis element of his vaccinations on December 11, 2007, Marqiano would not have died on December 12, 2007. Tr. at 35-36. He had sudden apnea after his vaccination which the vaccination caused and which compromised his vital centers. Tr. at 36-37. The toxins in the vaccine affected the respiratory center to cause apnea. Apnea means total cessation of breathing. Tr. at 37.

Dr. Pike testified that there is medical literature supporting his opinion. The vaccine table itself recognizes anaphylaxis and encephalopathy as Table injuries due to pertussis. The IOM relied on a large United Kingdom study showing a relationship between pertussis toxin and severe neurological dysfunction in concluding there was a relationship between them. Tr. at 39.

That is the National Childhood Encephalopathy Study or NCES. Tr. at 40. The problem with epidemiology, however, is that we are dealing with extremely rare events. Tr. at 41. These extremely rare events require an extremely large number of individuals to be studied in order to have sufficient epidemiologic power to detect a difference. *Id*.

Dr. Pike stated there are a number of studies reporting infants with post-immunization apnea. Tr. at 43. The product insert for Pediarix cautions physicians not to administer Pediarix in premature infants. *Id*. Because of severe disability from his congenital malformations, Marqiano was highly susceptible to developing infectious disease of any type, including Bordetella pertussis, which could cause whooping cough and death from Bordetella pertussis pneumonia. Tr. at 46. Vaccination was an important component of Marqiano's well-baby care. Tr. at 47. It was reasonable to vaccinate him. *Id*.

Dr. Pike testified that Marqiano died 14 hours after vaccination, too long for anaphylaxis, but long enough for direct toxic effects from permeability, immunological response, release of cytokines, disinhibition of neuromembrane stability with gamma aminobutyric acid (GABA), and sodium channel activation. Tr. at 51. Absent the DTaP vaccination, Marqiano would not have died. Tr. at 53. The vaccination caused apnea which caused asystole, complete absence of electrical activity in Marqiano's heart. Tr. at 56-57. A perturbation of the brain is encephalopathy. Tr. at 59. The neurons that were affected were primarily in the brainstem. Tr. at 60. What was observable was that Marqiano stopped breathing (the apnea) and his heart was no longer beating (the cardiac arrest). Tr. at 61. The only evidence Dr. Pike has for the toxic effects of pertussis on Marqiano's nerve cells is circumstantial. Tr. at 62. There is obviously no way for the biomolecular events he described as the mechanisms of the toxic actions of pertussis

toxin to be directly observable, but the signs of the toxin's effect are directly observable, i.e., the apnea and cardiac arrest. Tr. at 68.

If someone had been sitting in the dark with a flashlight on Marqiano during his last night, they would have seen increasing difficulty with breathing, probably agonal ventilations, and then no breathing for a long time. Tr. at 68-69. Had the observer taken a pulse, he or she might have noted the pulse was low and also that Marqiano's color had changed. He would be starting to get blue around the lips and around his fingers and ears. Then all of his skin would turn somewhat blue. When the nurse found him eventually, Marqiano's skin color was ashen, meaning there was no circulation basically. Tr. at 69.

There was no sign in the midnight note recounting the 10:00 p.m. nurse's visit to Marqiano to indicate he had an adverse event from pertussis toxin. Tr. at 74. Because of the nature of the event Marqiano had, Dr. Pike does not think the other vaccinations Marqiano received on December 11, 2007 had anything to do with his death. *Id*. Marqiano had a catastrophic event, apnea and cardiac arrest, with which pertussis vaccine is mostly implicated. Tr. at 75.

Anatomic brainstem abnormalities can be associated with apnea. Tr. at 75. Other than aqueductal stenosis, which caused hydrocephalus that was resolved with the placement of shunts into his ventricles to drain cerebral spinal fluid and relieve pressure, Marqiano did not have any brainstem abnormalities. Tr. at 76. Marqiano did not have any functional abnormality of his brainstem because he did not have any problem maintaining ventilation, heart rate, or blood pressure on his own. *Id*.

The MRI of August 21, 2007 showed Marqiano had kinking of the cervical medullary junction, which is part of the brainstem, but the vital centers for respiration are above it. Tr. at 77-78. If there had been a substantial functional problem, Dr. Pike would have expected some type of paralysis such as quadriparesis (paralysis of his arms and legs), but Marqiano did not have that. Tr. at 78.

Marqiano's brain abnormalities made him more vulnerable to pertussis toxin. *Id*. Those abnormalities made his brain seem more premature than his gestational age. Tr. at 78-79. A study examining apnea divided children into three groups: (1) the very premature; (2) those less than 31 weeks gestation but normal; and (3) those born after 31 weeks gestation and normal. Marqiano was more likely to fit in Group 1 because the very premature children were somewhat unstable. Tr. at 79. He did not have the central nervous system development of a normal child, but more like premature infants in terms of his neurological function. *Id*. He did not have the brain of an infant born at 34 or more weeks of gestation whose brain was normal. Tr. at 80. His brain functioned at a premature level that was perhaps much less than 31 weeks gestation. *Id*.

Marqiano's holoprosencephaly put him in the category of premature children born under 31 weeks gestation because of his compromised functional abilities. *Id*. Prematurity is an important part of Dr. Pike's opinion. Tr. at 81. Marqiano did not develop the neocortex in his brain. Tr. at 82. He was born at 34 weeks gestation but with a brain that was much more premature in its development than the age at which he was actually born. *Id*. Because pertussis toxin targets the central nervous system, Marqiano had a greater susceptibility more like those children born at 31 weeks or less of gestational age due to the prematurity of his brain. Tr. at 82-83.

Dr. Pike is neither a neurologist nor a pediatrician. Tr. at 83. He has treated over 80,000 patients, one-quarter of them children. *Id*. He has treated children with severe hydrocephalus who have also been blind. Tr. at 84. Dr. Pike's concentration is in emergency medicine. *Id*.

At the time Marqiano died, he had been improving from therapy. Tr. at 85. On November 26, 2007, the occupational therapist said Marqiano was progressing. Tr. at 88. On December 3, 2007, the therapist notes that progress was slow but significant. *Id*. These were little improvements but showed progression. Tr. at 89.

Respondent's Expert Dr. Guggenheim

Dr. Mary Anne Guggenheim, a board-certified pediatric neurologist, testified for respondent. Tr. at 92, 93. She is also board-certified in pediatrics. Tr. at 93. The last time she had a private clinical practice was in 1995. Tr. at 94. Five years ago, she stopped all clinical child neurology. *Id*. Her opinion is that there is no evidence of Marqiano having an adverse reaction to his vaccination. She thinks his death was due to his underlying condition. Tr. at 98. Children with very complex brain malformations seem stable until they die and doctors usually do not know a precise cause of death, as we do not know in this case. *Id*.

Marqiano was delivered at 34 or 36 weeks gestational age, depending on the record, by caesarean section due to concern that his hydrocephalus might further compromise his brain function if it were not shunted. Tr. at 99. He had an enlarged head circumference and was very infantile. *Id*. He had only reflex behaviors. *Id*. Marqiano had holoprosencephaly which is a complex malformation of the forebrain. *Id*. "Prosencephalon" means the frontal part of the brain or forebrain. Tr. at 99-100. The anterior portion of the brain failed to develop and, consequently, the lateral and third ventricles fused. Tr. at 100. His holoprosencephaly was of

moderate severity but not the most severe. *Id*. Virtually all those born with holoprosencephaly die by the time there are in their twenties or so. *Id*. They do not progress beyond an infantile state of essentially reflex behaviors. *Id*. They may have difficulty feeding and sucking as Marqiano did. *Id*. A cerebral cortex is necessary to develop beyond an infantile state, but people with holoprosencephaly are born without that part of their brain and are severely developmentally impaired as a consequence. Tr. at 100-01. Not all people with holoprosencephaly die in infancy. Tr. at 101. An English study of decades of people with holoprosencephaly states that 29 percent of infants with holoprosencephaly in the southern part of England survived past their first year. *Id*. Marqiano was enrolled in a hospice program which is aimed at providing comfort to those in a severe state of impairment. *Id*.

Marqiano had two other brain abnormalities: (1) aqueductal stenosis which caused his hydrocephalus, and (2) a kink in the cervical medullary junction of an anatomic type. Tr. at 101-02. In aqueductal stenosis, the conduit between the third and fourth ventricles did not develop normally and the spinal fluid could not flow through it. Tr. at 102. The kink in the cervical medullary junction indicates there was a bend in the lower part of the brainstem where it merges with the other part of the spinal cord. *Id*.

In addition, Marqiano had microphthalmia which is small eyes. Tr. at 103. This is a part of holoprosencephaly. He never had any useful vision. *Id*. He also had an abnormality in the collection system of his kidneys on one side which blocked the ureter that conveys urine to the bladder, causing hydronephrosis, a swelling of the kidney. *Id*. Marqiano also had micropenis and either absent or very small testes, reflecting in utero abnormalities of hormonal control over secondary sexual characteristics. *Id*. It also indicates underlying abnormalities of his

hypothalamus and his pituitary gland function, also a common part of holoprosencephaly because the hypothalamus is in the forebrain. Tr. at 104.

Marqiano developed spasticity, described as increased tone, and he had cortical thumbs, i.e., having his thumbs fisted. This just reflects that the signals coming from his brain affecting muscle tone were abnormal. *Id*. Because of lack of cerebral hemisphere development, he had no head control and a poor suck. Tr. at 105. He had very limited, if any, responsiveness other than tactile and sometimes auditory. *Id*. He was essentially a newborn infant and remained that way. Newborns run on automatic pilot. The difference from a newborn is that Marqiano did not have a good suck. *Id*. He was never able to roll over. *Id*. Dr. Guggenheim did not see any evidence that Marqiano made any progress. *Id*.

Marqiano had a poor suck and inability to swallow and could not adequately take in nutrition. Tr. at 106. He had a feeding tube at two or three weeks of age, but the gastrostomy tube was not working well. *Id*. After six weeks of age, Marqiano did not grow any more and had failure to thrive. Tr. at 107. Two weeks prior to his death, Marqiano was stable although there was trouble with the feeding tube. Tr. at 107-08. Basically, he lay in his crib with his eyes closed although he could open his lids sometimes. Tr. at 108. He had a weak cry and could suck weakly on a pacifier. *Id*. He was rolled from side to side so he would not develop pressure sores. *Id*. He did react to either touch or noise but not to visual stimuli. *Id*. He had difficulty maintaining his temperature, probably due to hypothalamic dysfunction, and was wrapped up and sometimes had a cap on. *Id*.

Dr. Guggenheim does not agree that Marqiano was improving at the time of his second vaccinations and his death. *Id*. The reason he was vaccinated is that the American Academy of

Pediatrics recommends it to all infants, even the very premature, to keep the child healthy and to reduce the likelihood of epidemics. Tr. at 109-10.

Dr. Guggenheim does not see any evidence that Marqiano had an acute encephalopathy which would be seizures, obtundation, and marked changes in tone. Tr. at 110-11. She thinks the reason no autopsy was done on Marqiano was that people thought his underlying holoprosencephaly and brain malformation were the underlying causes of his death and, because he was in an institution, no one was concerned about abuse or injury. Tr. at 111. There is nothing in the record to indicate that the treating doctors thought that Marqiano died because of his vaccinations. Tr. at 111-12.

Marqiano received acellular DTP, not whole-cell DPT. Tr. at 112. In acellular DTP, the pertussis toxin is nullified although there are still small fragments that can induce immunogenicity. *Id*. Children who receive acellular pertussis have much less incidence of fever and other inflammatory responses. Tr. at 113. Marqiano had no change clinically from the time he was immunized in the early afternoon until about 12 hours later when he was found dead. Tr. at 114. No one found a local reaction or swelling or inflammation. *Id*. Marqiano went from being a stable child with a very infantile state due to his underlying brain malformation, to being dead. Dr. Guggenheim calls this an "abrupt jump, not an evolutionary sequence." Tr. at 115. There are no stepwise changes. He went from stable to dead. *Id*.

Dr. Guggenheim knows of no mechanism by which vaccinations can cause apnea in premature infants. Tr. at 116. Holoprosencephaly is a malformation due to genetic instructions. Tr. at 118. Dr. Guggenheim disagrees with Dr. Pike that Marqiano's brain was immature. It was malformed. Tr. at 119. Those parts not affected by the malformation are otherwise normal. Tr.

at 120. The magic line for neonatologists looking at premature babies is usually 31 to 32 weeks. Tr. at 121. These babies are vulnerable to a whole variety of both somatic and neurologic problems. *Id*.

Marqiano had a weak suck and weak ability to swallow because his brain did not work right. *Id*. The outflow for sucking comes from the medulla of the brainstem through the lower cranial nerves, but the cerebral hemispheres can clearly affect it. *Id*. She does not think it possible to know whether his weak suck and weak ability to swallow were primarily due to a brainstem abnormality or to the lack of cortical feedback and information to brainstem centers. Tr. at 122.

The studies to which Dr. Pike referred were retrospective except for one paper. *Id*. Marqiano was not as premature as the children in those studies. Although giving pertussis vaccine to premature infants might result in some apnea and some cardiac abnormalities, a randomized, prospective study showed no difference in the rate of apnea among premature infants who received DTaP and those not immunized. Tr. at 123-24. Dr. Guggenheim does not believe that the vaccinations contributed to or hastened Marqiano's death. Tr. at 128.

In Dr. Guggenheim's expert report, she wrote that a perturbation of brain function caused Marqiano's death. Tr. at 129. She meant that Marqiano appeared to have central apnea, as opposed to an obstructive type of apnea. *Id*. She agrees with Dr. Pike that there is no evidence that Marqiano had aspiration of a lung or airway problem. *Id*. She stated that something went wrong with Marqiano's brain control of his breathing. Tr. at 130. She does not know whether Marqiano had a primary cardiac malfunction or primary apnea. *Id*. The primary centers for control of breathing and heart rate are in the brainstem, but that connects to the cortex. *Id*.

There is no way to know whether the initial event was that Marqiano had trouble breathing, stopped breathing, had apnea, and then, as a consequence, his heart failed because it was no longer being oxygenated or the converse, i.e., his heart stopped beating, resulting in the lack of oxygenation which caused him secondarily to stop breathing. Tr. at 130-31. He had a cardiorespiratory event. Tr. at 131.

When the undersigned asked Dr. Guggenheim what caused Marqiano's cardiac asystole and apnea, she answered, "Well, it went wrong." Tr. at 132. She stated something went wrong in his brain and added it is not uncommon to see children with complex brain malformations and severe developmental problems requiring total care to be stable and then die. Tr. at 133. No one knows the internal mechanism for that. All we know is that their brains are abnormal and, at an unpredictable time, their brains do not function normally in a crucial respect of cardiorespiratory function. "So these kids are stable until they die." *Id.*

There were times when Marqiano had alterations in his vital signs for no apparent external reason, which is consistent with the abnormal internal stability of his brain function. Tr. at 137. Dr. Guggenheim cannot give a mechanism of why, one minute, Marqiano was breathing and, the next minute, he was not. Tr. at 138. Dr. Guggenheim is not a board-certified toxicologist. *Id.*

Dr. Pike on Rebuttal

Dr. Pike testified on rebuttal that, in his opinion, the apnea occurred first. Tr. at 143. The respiratory center is primarily responsible in the brainstem for stimulating the spinal nerves that allow the periodic expansion of the lungs. *Id.* The heart is controlled primarily from the brainstem through the vagus nerve. *Id.* Dr. Pike thinks the respiratory apnea had to have

occurred first because the cardiac myocytes, i.e., the heart muscle cells themselves, have inherent automaticity. The heart will beat even when completely denervated from the brain. Tr. at 144. Even if the cardiac center of the brainstem had been damaged, the automaticity of the heart cells themselves would have continued to beat. Tr. at 145-46. That is why the apnea had to be the inciting event leading to Marqiano's death. Tr. at 146.

As for pertussis toxin being present in acellular DTP, Dr. Pike stated that the idea is that pertussis toxin is inactivated either through the use of glutaraldehyde or formaldehyde or other chemicals to produce a toxoid. *Id*. Even though there is pertussis toxoid in the vaccine, there are also pertussis proteins there. *Id*. We assume that the chemicals are 100 percent effective in destroying pertussis toxin, but assays used to determine whether the toxin is completely inactivated are very crude and rely on whether a mouse injected intraperitoneally with the vaccine died. Tr. at 147. We do not have a very good means of knowing in any particular lot or sample how much of the pertussis toxoid is totally inactive. We also do not know that the toxoid is completely void of any effects that are toxic to neurons. *Id*.

Dr. Pike agrees with Dr. Guggenheim that the acellular form of the vaccine is much less toxic than the whole-cell form. Tr. at 149. However, the acellular pertussis concentrates the most active component of the pertussis toxin, presumably inactivated, to deliver the immunogenicity intended against Bordetella pertussis bacterium. Tr. at 149-50. In the FDA's clinical trials, adverse effects were seen with both DTaP and DPT. Tr. at 150. The toxicity is less, but not absent, in the acellular form. *Id*. We know this because there are still adverse effects reported from acellular vaccine, e.g., fevers, sores, pain, malaise, seizures, anorexia, fussiness, diarrhea, restlessness, insomnia, unusual crying, encephalopathy, but they occur less

often than with whole-cell. *Id*.; tr. at 151. He explained the failure to find apnea among premature recipients of pertussis vaccine as due to it being a rare event. Tr. at 152. Prospective studies are not sufficiently powerful to be able to detect an extremely rare event. Tr. at 154. Retrospective studies, however, have looked at infants who had apnea after vaccination, and noted that the premature infants were more likely to have apnea than those that were not premature. *Id*.

Dr. Pike reiterated Dr. Guggenheim's description of holoprosencephaly in which the full brain does not develop, although the part of the brain that controls ventilation, i.e., the midbrain, is not the forebrain and was not affected except for some type of anatomical kinking reported on MRI. Tr. at 155. Marqiano's brain development was arrested at a critical point in time in gestation, probably six months forward. Tr. at 156. His brain was more like a premature brain because it had not developed compared to a normal brain. *Id*. The studies Dr. Pike cited dealt with premature infants with normal brains and normal brain maturation after birth, but that was not Marqiano's brain. *Id*.

Dr. Pike said that Marqiano's brain was arrested at a very premature stage in utero during fetal development and never progressed past what he had. Tr. at 157. His premature infant brain made Marqiano more susceptible to the pertussis toxin in the DTaP. Tr. at 158. Even children with congenital malformations often have inciting events, for example urinary tract infection or pneumonia, that cause a perturbation leading to death. Tr. at 159. Death just does not happen to them. There has to be a reason. Marqiano's physicians were not expecting him to die that night. *Id*. "This was a death that was totally unexpected, shocked everybody, needed an explanation and should have been a medical examiner's case, but for some reason that didn't happen," said

Dr. Pike. Tr. at 160. Marqiano's brainstem was functioning perfectly well and something, as Dr. Guggenheim wrote, perturbed that function. Dr. Pike believes it was the pertussis vaccine that perturbed that function and led to his apnea and death. *Id.*

Dr. Pike testified that it is the actual absorption of the pertussis toxoid/toxin into the bloodstream crossing the blood-brain barrier and interacting with neurons or glial cells at a biomolecular cellular level that causes the damage. Tr. at 161. It does not take a lot of toxin to cause substantial damage in the nervous system when we talk about Bordetella pertussis because the toxin is extremely potent in very small quantities. Tr. at 162.

Other Submitted Material

Dr. David Hirsch, medical director of Hacienda HealthCare (where Marqiano died) and a board-certified pediatrician specializing in developmental disabilities, wrote a report dated May 21, 2008 in which he said that the vaccines Marqiano received together with his underlying medical condition caused his death. This opinion differs from his statement in the record that the vaccines were unlikely to have caused his death. He stated he did additional research and consideration of the timing and circumstances which explains his change of opinion. Ex. 8, pp. 1, 2.

Dr. Hirsch provided a supplemental report, dated August 8, 2009 and filed August 21, 2009, after reviewing material he did not previously have, stating that Marqiano had an unstable, likely progressive neurological condition related to an underlying congenital brain malformation. Page 1. After his second series of vaccinations, there was "no reason to believe that he was going to get worse that evening or the next day, let alone dying. The only variable was the vaccinations he received at his four month check-up." Page 2. The physical examination

performed by Dr. Herr prior to administering the four-month vaccinations did not indicate any signs of clinical distress. Page 3.

Respondent's expert Dr. Guggenheim stated in her report, filed January 29, 2010 as Exhibit A, that "it is reasonable to conclude that a perturbation of brain function caused his [Marqiano's] death." Ex. A, p. 3.

Respondent filed as Exhibit D an article entitled "Absence of an Increase in Cardiorespiratory Events After Diphtheria-Tetanus-Acellular Pertussis Immunization in Preterm Infants: A Randomized, Multicenter Study" by T. Carbone, et al., 121 Pediatrics 5:e1085-90 (2008). The authors inoculated 93 preterm children with DTaP and used a control group of 98 preterm children whom they did not inoculate, and found almost the same rate of bradycardia (2.6 in the immunized group and 2.7 in the control group). The degree of apnea was the same in both groups: 0.5 episodes. *Id*. at e1085. The authors conclude that preterm infants who received DTaP at two months were no more likely to experience prolonged apnea and bradycardia than preterm infants who were not vaccinated. *Id*. The study was done because of case reports describing severe apnea requiring resuscitation after immunization of preterm infants, and numerous studies subsequently reporting an increased incidence in apnea and bradycardia in preterm infants even when acellular pertussis vaccine was used instead of whole-cell pertussis. *Id*. at e1086. The mean postconceptional age for the DTaP group in Carbone's study was 34.9 weeks and for the control subjects, 35.1 weeks. *Id*. at e1087. The authors state that these extremely preterm infants "were at increased risk for significant cardiorespiratory events." *Id*. at e1088. They continue:

> The study population clearly represented an extremely vulnerable group of infants, as indicated by their gestational age, birth weight,

> and the high incidence of the common complications of marked prematurity.... The vulnerability of the study population is also demonstrated by the high incidence of both prolonged apnea and prolonged bradycardia, as well as the high incidence of severe cardiorespiratory events.

Id. They describe these infants as "medically fragile." *Id*. The authors were concerned that pediatricians were not vaccinating the extremely preterm infants even though the American Academy of Pediatrics (AAP) recommended that they do so. *Id*. The results of the study were supportive of the AAP recommendations. *Id*. at e1089. The authors acknowledge that the high dropout rate of infants from the study due to technical difficulties with monitoring equipment is a limitation on the study. *Id*.

DISCUSSION

Petitioners have not alleged a Table case, but a causation in fact case. To satisfy their burden of proving causation in fact, petitioners must prove by preponderant evidence "(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." Althen v. Sec'y of HHS, 418 F.3d 1274, 1278 (Fed. Cir. 2005). In Althen, the Federal Circuit quoted its opinion in Grant v. Sec'y of HHS, 956 F.2d 1144, 1148 (Fed. Cir. 1992):

> A persuasive medical theory is demonstrated by "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury[,]" the logical sequence being supported by "reputable medical or scientific explanation[,]" *i.e.*, "evidence in the form of scientific studies or expert medical testimony[.]"

In Capizzano v. Sec'y of HHS, 440 F.3d 1317, 1325 (Fed. Cir. 2006), the Federal Circuit said "we conclude that requiring either epidemiologic studies, rechallenge, the presence of

pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect is contrary to what we said in Althen ...." Such an approach is inconsistent with the use of circumstantial evidence. *Id*. The Federal Circuit stated in Althen, 418 F.3d at 1280, that "the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body."

Close calls are to be resolved in favor of petitioners. Capizzano, 1440 F.3d at 1327; Althen, 418 F.3d at 1280.

Without more, "evidence showing an absence of other causes does not meet petitioners' affirmative duty to show actual or legal causation." Grant, 956 F.2d at 1149. Mere temporal association is not sufficient to prove causation in fact. *Id*. at 1148.

Petitioners must show not only that but for the vaccine, Marqiano would not have had the apnea, cardiac arrest, and death, but also that the vaccine was a substantial factor in bringing about his apnea, cardiac arrest, and death. Shyface v. Sec'y of HHS, 165 F.3d 1344, 1352 (Fed. Cir. 1999).

In essence, the special master is looking for a medical explanation of a logical sequence of cause and effect (Althen, 418 F.3d at 1278; Grant, 956 F.2d at 1148), and medical probability rather than certainty (Knudsen v. Sec'y of HHS, 35 F.3d 543, 548-49 (Fed. Cir. 1994)). To the undersigned, medical probability means biologic credibility rather than specification of an exact biologic mechanism. As the Federal Circuit stated in Knudsen:

> Furthermore, to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program. The Vaccine Act does not contemplate full blown tort litigation in the Court of Federal Claims. The Vaccine Act established a federal "compensation

> program" under which awards are to be "made to vaccine-injured persons quickly, easily, and with certainty and generosity." House Report 99-908, *supra*, at 3, 1986 U.S.C.C.A.N. at 6344.
>
> The Court of Federal Claims is therefore not to be seen as a vehicle for ascertaining precisely how and why DTP and other vaccines sometimes destroy the health and lives of certain children while safely immunizing most others.

35 F.3d at 549.

As the Federal Circuit stated in Knudsen, 35 F.3d at 548, "Causation in fact under the Vaccine Act is thus based on the circumstances of the particular case, having no hard and fast *per se* scientific or medical rules." The undersigned's task is to determine medical probability based on the evidence before the undersigned in this particular case. Althen, 418 F.3d at1281 ("judging the merits of individual claims on a case-by-case basis").

Basically, the dispute in the instant action is whether because of Marqiano's brain abnormalities, Marqiano was more vulnerable to the effects of acellular pertussis vaccine and suffered a reaction and died or he was going to die at any moment regardless of vaccination.

Both sides agree Marqiano was vulnerable. Dr. Guggenheim wrote in her initial report that Marqiano died from a brain perturbation. But she does not think the perturbation was due to acellular pertussis vaccine. She did think he had cardiac arrest first and then apnea. Dr. Pike noted that acellular pertussis vaccine, although toxoided to remove its toxicity, is incompletely toxoided and can cause adverse reactions. For someone as medically fragile as Marqiano, this toxicity tipped the scales for him. Dr. Pike testified that Marqiano developed apnea first and then cardiac arrest. He stated that someone's heart can keep beating even if the brainstem is not functioning properly due to automaticity of the heart cells, but someone whose brainstem is not functioning properly will get apnea and stop breathing. Dr. Pike's explanation of the course of

events (first apnea; then cardiac arrest) in Marqiano's death is persuasive and takes into consideration the lack of proper functioning of Marqiano's brain.

Dr. Guggenheim emphasized the Carbone study in which preterm infants were divided into two groups: one receiving DTaP and the other group not being immunized. As Dr. Pike testified, these children were premature, but were not identified as having a missing cortex or other brain difficulties such as hydrocephalus. Nevertheless, both groups in the Carbone study had the same incidence of apnea and bradycardia regardless of vaccination status. Those events were very infrequent among both groups. Of the 93 immunized preterm children, only 2.6 had bradycardia (slowed heart beat). Only 0.5 of the 93 had apnea. Of the 98 unimmunized preterm children, only 2.7 had bradycardia. Only 0.5 of the 98 had apnea. Beyond the question of how a fraction of a child has either bradycardia or apnea, the undersigned can agree that these are very small numbers. Dr. Pike pointed out that the Carbone study describes only a small number of infants, too small to detect a very rare event as occurred in the instant action. Dr. Pike's concern about the failure of epidemiology to detect very rare events echoes the Federal Circuit's concern in Knudsen.

The Federal Circuit in Knudsen ruled for petitioners even when epidemiological evidence directly opposed causation from DPT vaccine. The case concerned the cause of a baby's encephalopathy after vaccination. Respondent filed epidemiologic evidence showing that more encephalopathies are caused by viruses than by vaccines, resulting in dismissal of the petition based on those epidemiologic studies. But the Federal Circuit held that epidemiologic evidence should not bar petitioners from prevailing, stating:

> The bare statistical fact that there are more reported cases of viral encephalopathies than there are reported cases of DTP

> encephalopathies is not evidence that in a particular case an encephalopathy following a DTP vaccination was in fact caused by a viral infection present in the child and not caused by the DTP vaccine.

35 F.3d at 550.

Dr. Hirsch, the medical director of Hacienda where Marqiano died, submitted two reports stating that the vaccines caused Marqiano's death. He stated that no one at the facility expected Marqiano to die. The Federal Circuit in Capizzano emphasized that the special masters are to evaluate seriously the opinions of petitioner's treating doctors since "treating physicians are likely to be in the best position to determine whether a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury." 440 F.3d at 1326. See also Andreu v. Sec'y of HHS, 569 F.3d 1367, 1375 (Fed. Cir. 2009). Although Dr. Hirsch was the head of the facility where Marqiano died and not necessarily a treater, he was associated with those who did treat Marqiano and has familiarity with the expectations of those treaters. Dr. Hirsch explained that his initial opinion in the medical records that the vaccines did not cause Marqiano's death was a consequence of his being uninformed of the particulars of the case and his focus on the Synagis vaccine that Marqiano received with DTaP and other vaccines. In his two reports, Dr. Hirsch states that the only variable leading to Marqiano's death was the vaccinations.

In concert with Dr. Hirsch's opinion that no one at Hacienda expected Marqiano to die, Dr. Pike testified that if Marqiano's pediatrician Dr. Herr expected Marqiano to die, why would he give him his second series of vaccinations. The natural conclusion is that Marqiano's treaters expected him to benefit from the vaccinations which were to protect him from illness. Being protected from illness would be important for an individual as medically fragile as Marqiano.

Moreover, respondent's expert Dr. Guggenheim stated that children born with holoprosencephaly can live until their twenties or beyond and that almost one-third can live beyond one year. There is nothing persuasive then in the record to show that Marqiano was going to die exactly when he did die irrespective of vaccination.

Dr. Pike's thesis is that because Marqiano was grievously brain-damaged, he was more vulnerable to the effect of the numerous vaccines he received, particularly pertussis. His opinion makes sense. The Carbone study authors call children born at 35 weeks medically fragile. This is about the age of gestation when Marqiano was born, but he was born not just prematurely; he was missing his neocortex.

The fact that someone has a known factor unrelated to the vaccine that is a substantial factor in causing illness and death does not prevent petitioners prevailing under the Vaccine Program. In Shyface, Cheyenne Shyface received whole-cell pertussis vaccine at the same time he harbored the beginning of an E-coli infection. Both the vaccine and the infection can produce fever. After the vaccination, Cheyenne had a fever of 109 degrees and, when it reached 110 degrees, he died. 165 F.3d at 1345. Testimony from his treating doctor was that both the whole-cell DPT and the E-coli infection caused Cheyenne's fever and death. *Id*. at 1347. The Federal Circuit held that both the DPT and the infection were equal substantial factors in causing Cheyenne's vaccine reaction and death, and that without his receiving the vaccination, he would not have gotten such a high fever and died. The Federal Circuit awarded compensation to petitioners. *Id*. at 1353.

In Zatuchni v. Sec'y of HHS, 69 Fed. Cl. 612 (2006), Barbara Snyder's estate's representative appealed a denial of compensation for Ms. Snyder's prior allegation that the

rubella component of MMR vaccine caused her fibromyalgia. The appeal was successful and her fibromyalgia was deemed a vaccine injury. 69 Fed. Cl. at 624. The case was remanded to determine if her death were caused by her vaccine injury. Her treating doctor testified that Ms. Snyder died from smoking-induced chronic obstructive pulmonary disease (COPD). 2006 WL 1499982 (Fed. Cl. Spec. Mstr. 2006), *adopted in part, vacated in part on other grounds*, 73 Fed. Cl. 451 (2006), *aff'd on other grounds*, 516 F.3d 1312 (Fed. Cir. 2008). Ms. Snyder would have died in any event from her primary illness COPD. But her fibromyalgia made it impossible for her to exercise for 13 years. Had she been able to exercise, she would have not died at the time she did from COPD, but later on. 2006 WL 1499982, at *4. Ms. Snyder's representative prevailed even though the known factor unrelated to the vaccine, i.e., the COPD, was the predominant substantial factor in causing her death because the vaccine injury fibromyalgia was also a substantial factor. Similarly, Marqiano's grievous birth condition would have led to an early death which could have happened after the age of one or even in his twenties. But he died sooner than that because of his vaccine reaction.

The Federal Circuit in Shyface stated that the vaccine does not have to be a predominant substantial factor in causing the injury and death, merely a substantial factor. 165 F.3d at 1353. In Shyface, the vaccination and the infection were equal substantial factors.

In Zatuchni, the COPD was the predominant substantial factor and the fibromyalgia from the rubella vaccine was merely a substantial factor in causing Ms. Snyder's death. 2006 WL 1499982, at *5.

In the instant action, the combination of the absent neocortex and medical fragility of Marqiano's brain and the effects of the pertussis toxin were both substantial factors in causing

his apnea and cardiac arrest, leading to his death. Without his having received acellular pertussis vaccine, he would not have died at that time, although he would have died at some time in the future, just as Ms. Snyder in Zatuchni would have died from COPD eventually if not for her fibromyalgia. Whether the severe prematurity of Marqiano's brain was a predominant substantial factor or merely substantial is irrelevant since, as long as the vaccine is a substantial factor, without which the injury and death would not have occurred, petitioners prevail.

The undersigned accepts that, in light of the reports of vaccine adverse reactions following DTaP, there are still rare difficulties with the toxoidal processing of pertussis toxin. The undersigned accepts that a medically fragile premature infant is more susceptible to the challenge of receiving pertussis vaccine even in its acellular form. The undersigned further accepts that had Marqiano not received his second DTaP, his life would probably have been shortened because of his grievous physical condition, but there is no indication medically, from the opinion of Dr. Hirsch, or the testimony of Dr. Pike, that he would have died on the night he did die. Dr. Guggenheim admitted in her initial report that Marqiano died from a perturbation in his brain. The undersigned holds that that perturbation came from the acellular pertussis vaccine which can, in rare cases, cause apnea and cardiac arrest in a medically fragile vaccinee (Althen prong one), and did cause apnea and cardiac arrest in this case (Althen prong two) within a medically appropriate time interval (14 hours) to signify causation (Althen prong three), and that without having received acellular pertussis vaccine, Marqiano would not have died when he did.

Petitioners have proven causation in fact.

CONCLUSION

Petitioners are entitled to $250,000.00, the award for a vaccine-related death under § 300aa-15(a)(2) of the Vaccine Act. A check shall be made payable to petitioners in the amount of $250,000.00. In the absence of a motion for review filed pursuant to RCFC, Appendix B, the clerk of the court is directed to enter judgment herewith.[7]

IT IS SO ORDERED.

September 30, 2010
DATE

s/ Laura D. Millman
Laura D. Millman
Special Master

[7] Pursuant to Vaccine Rule 11(a), entry of judgment can be expedited by each party's filing a notice renouncing the right to seek review.