

**In the United States Court of Federal Claims**  
**OFFICE OF SPECIAL MASTERS**

No. 06-846V

Filed: November 9, 2010

SHARON E. RAYBUCK and RANDALL L. RAYBUCK, as Parents and Natural Guardians of MALACHI M. RAYBUCK,	)	
	)	TO BE PUBLISHED
	)	
Petitioners,	)	
	)	
v.	)	Entitlement: Causation-in-fact;
	)	Influenza (Flu) Vaccination;
SECRETARY OF HEALTH AND HUMAN SERVICES,	)	Seizures; Status epilepticus;
	)	Encephalopathy
	)	
Respondent.	)	
	)	

Ronald L. Rosenfield, Cleveland, Ohio, for Petitioners.

Glenn A. MacLeod, United States Department of Justice, Washington, D.C., for Respondent.

**DECISION**<sup>1</sup>

**LORD**, Chief Special Master.

**I. INTRODUCTION AND SUMMARY**

On December 12, 2006, Petitioners Sharon E. and Randall L. Raybuck (“Petitioners”) filed a claim alleging that their son, Malachi M. Raybuck (“Malachi”), suffered a vaccine injury under the National Vaccine Injury Compensation Program, 42 U.S.C. § 300aa-1 et seq. Petitioners alleged that Malachi developed status epilepticus and encephalopathy from a trivalent influenza (flu) vaccination he received on

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<sup>1</sup> As provided by Vaccine Rule 18(b), each party has 14 days within which to request the redaction “of any information furnished by that party (1) that is 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.” Rules of the United States Court of Federal Claims (RCFC), Appendix B, Vaccine Rule 18(b). In the absence of a timely objection, the entire document will be made publicly available.

December 12, 2003. Petition (“Pet.”) at ¶¶1a, c.<sup>2</sup> In order to connect these injuries to Malachi’s flu vaccination, Petitioners posit an extended chain of causation: that the vaccine caused a rash, the rash caused doctors to change Malachi’s seizure medicine, the change in seizure medicine caused a worsening of Malachi’s epilepsy, and the epilepsy caused status epilepticus and encephalopathy.

I accept the argument that the Palsgrafian chain of causation alleged by Petitioners could establish, in theory, a link between the flu vaccine and Malachi’s injury.<sup>3</sup> For the reasons stated below, however, Petitioners have not provided sufficient evidence to support their theory of causation.

The parties are in agreement about Malachi’s condition before his flu vaccination. At the time of vaccination Malachi already suffered from a significant seizure disorder, and he had been taking the anti-convulsant medication Dilantin to control his seizures. Dilantin was helpful in controlling the seizures but Malachi still suffered seizures periodically, particularly when he had an infection. See Tr. at 24, 40, 63, 67-68 (seizures were “always triggered by either an ear infection or strep throat”); Tr. 70 (seizures sparked by ear infection). In the weeks before his flu vaccination, Malachi suffered a number of seizures. Joint Stip. at ¶5.

Petitioners alleged that the flu vaccine caused Malachi to break out in a severe rash, which resulted in Malachi’s hospitalization on December 26, 2003.<sup>4</sup> At the time, Malachi’s treating physicians did not know the cause of his rash. They decided to discontinue the use of Dilantin, for fear that the rash might signal a potentially life-threatening drug reaction known as Stevens-Johnson Syndrome.<sup>5</sup> As it turned out, Malachi did not have Stevens-Johnson Syndrome, and the rash apparently was not caused by the Dilantin. The parties agreed that it was reasonable, although ultimately unnecessary, for the doctors to stop Malachi’s treatment with Dilantin in late December 2003. Joint Stip. at ¶11. Following the discontinuance of his treatment with Dilantin, however, Malachi’s seizures worsened. Over the next several weeks, his condition deteriorated and Malachi suffered significant, permanent brain injury.

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<sup>2</sup> Status Epilepticus is defined as “a continuous series of generalized tonic-clonic seizures without return to consciousness, a life-threatening emergency.” Dorland’s Illustrated Medical Dictionary (30<sup>th</sup> ed. 2002) at 1756.

<sup>3</sup> Palsgraf v. Long Island R. Co., 248 N.Y. 339, 162 N.E. 99 (1928).

<sup>4</sup> The rash appeared to be mild at first but progressed in extent and severity. The exact date of the rash’s onset is uncertain, but it seems to have appeared around a week or 10 days after the vaccination. See Tr. 29-30, 45; Resp’t Post-Hr’g Br. at 4, n.5.

<sup>5</sup> Stevens-Johnson Syndrome is defined as “a sometimes fatal form of erythema multiforme having flulike prodrome and systemic as well as more severe mucocutaneous lesions.” Dorland’s at 1833.

Petitioners' expert, an immunopharmacologist, initially opined that Malachi's vaccination caused a temporary alteration in his immune response, which in turn caused Malachi to react adversely to the Dilantin in the form of a rash. After considering Respondent's experts' reports, however, Petitioners' expert abandoned his original theory. At hearing, he opined that an immune reaction to the vaccine itself caused Malachi's rash. As support for this theory, the expert relied on VAERS reports and the vaccine package insert indicating that a rash is a possible adverse reaction to the flu vaccine. In theory, this made it possible for Petitioners to establish the chain of causation linking the vaccine to Malachi's permanent brain injury.

All the experts agreed that it was impossible to identify the exact cause of Malachi's rash based on the limited evidence in the medical record. The experts were forced to rely on differential diagnosis; each of them agreed that the flu vaccination, viral infection, and drug reaction were appropriate to be considered as possible causes of Malachi's rash.<sup>6</sup> Respondent submitted that Malachi's rash was too severe to be a typical rash caused by a vaccine, and that the rash was likely not caused by the flu vaccine but by an unknown agent, probably a virus. Conversely, Petitioners' expert asserted that Malachi's rash was too severe to be a typical rash caused by a virus.

For the reasons explained below, I am persuaded that Respondent's experts have the better side of this debate. Based on careful review of the record as a whole, Petitioners have not made out a prima facie case of vaccine causation under Althen v. Sec'y of Health & Human Servs., 418 F.3d 1274, 1280 (Fed. Cir. 2005). The preponderance of the evidence under each of the Althen prongs does not support the conclusion that Malachi's rash was caused by his flu vaccination. This conclusion severs the chain of causation between the flu vaccine and the brain injury at the first link.<sup>7</sup>

## **II. FACTUAL BACKGROUND**

### **A. Medical Record**

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<sup>6</sup> See discussion of differential diagnosis, infra at 17-18.

<sup>7</sup> Additional permutations in the facts and the expert testimony emerged at hearing. Petitioners' expert conceded that "simply withdrawing phenytoin [Dilantin] and status [epilepticus] would not result in the long-term disabilities Malachi suffered." Tr. 321. Petitioners' expert thus severed an additional link in the chain of causation that Petitioners alleged. On the other hand, Respondent's expert testified that Malachi's condition had been improving during his protracted hospitalization until he acquired what appeared to be a nosocomial (originating in the hospital) infection, and that this later-acquired infection caused his ultimate brain injury and disability. See Tr. 201-02, 208-09, 308. Since, it is alleged, Malachi would not have been hospitalized but for his rash, the testimony of Respondent's expert could re-connect the more remote links in the causal chain between the vaccine and Malachi's brain injury. Given my conclusion that the initial link in the chain of causation has not been established, however, the existence of additional links farther down the chain is irrelevant.

Malachi was born on September 27, 2001. Joint Stip. at ¶1. He suffered his first seizure on February 17, 2002, and was hospitalized twice in 2002 for continued seizures. Id. at ¶¶ 2-3. At 13 months of age, Malachi was able to walk around furniture and pull to a stand, but he had some language delay. His seizures persisted despite Phenobarbital followed by Trileptal and Dilantin, and he was diagnosed with a generalized seizure disorder. Id. at ¶3.

During 2003, Malachi continued to have seizures particularly when he had an infection. Joint Stip. at ¶4; see Tr. at 24, 40, 63, 67-68. He was seizure-free, however, from June 20, 2003 until November 11, 2003. Malachi continued to manifest speech delay and a mildly unsteady gait. Id.

On November 12, 2003, Malachi was seen at the children's clinic for three seizures the previous evening and three that morning, as well as for diarrhea and a decreased appetite. Id. He was treated with an antibiotic and prescribed an increased dose of Dilantin. Id.; Pet'r Ex. 10 at 15.

On December 12, 2003, Malachi received his first trivalent influenza vaccination. Joint Stip. at ¶6. Ten days later, on December 22, 2003, Petitioners brought Malachi to his physician with the complaint of a generalized rash, swollen face and imbalance. The physician described the rash as scarlatiniform, and the physician's impression was that Malachi was experiencing a hypersensitivity reaction to Dilantin.<sup>8</sup> The plan was to change Malachi's anti-convulsant medication from Dilantin to Klonopin. Pet'r Ex. 10 at 16; Joint Stip. at ¶7.

On December 24, 2003, Malachi was seen at the emergency room at University Hospitals of Cleveland for a severe rash. Joint Stip. at ¶8. He was still taking Dilantin. Id. Malachi had a rash described as red all over, and his hands were swollen. Id. The onset of the rash was noted as the previous Friday, December 19, 2003. Id. Physical examination revealed a red rash without itching, including the palms, sparing skin creases, and with peeling on the face. Id. The emergency department records noted a "fixed drug eruption, unlikely to respond to antihistamine, no mucus membrane involvement." Doctors advised the family to discontinue Dilantin and start Klonopin. Pet'r Ex. Vol. II, Ex. 1. Malachi had no fever upon discharge. Joint Stip. at ¶8. His Dilantin was discontinued and he was started on Klonopin. Id.

Two days later, on December 26, 2003, Malachi was admitted to the Rainbow Babies & Children's Hospital because of worsening seizures. Joint Stip. at ¶9. He suffered clusters of generalized seizures requiring transfer to the intensive care unit. Id. A chest x-ray taken on December 26, 2003, the date of Malachi's admission, revealed that there were "[f]indings which may relate to viral and/or reactive airways disease. Question infiltrate in the left lower lobe." Pet'r Ex. 12 at 32. Malachi was discharged on February 17, 2004. Pet'r Ex. 12 at 2-3. During this prolonged hospitalization, Malachi

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<sup>8</sup> Scarlatiniform is defined as "resembling scarlet fever, especially in the skin eruption of scarlet fever." Dorland's at 1662.

suffered encephalopathy leading to developmental regression, with intermittent episodes of fever and another rash.

Malachi was re-started on Dilantin in March 2005, and he tolerated the drug well. Joint Stip. at ¶10. The parties have stipulated that the decision of the physicians on December 22, 2003, to switch Malachi's anti-convulsant medication from Dilantin to Klonopin was not unreasonable under the circumstances. Id. at ¶11.

## **B. Petitioners' Theory of the Case**

Petitioners' theory is predicated on the assertion that Malachi's flu vaccination caused the rash he suffered in December 2003, some two or three days after his flu shot. Pet'r Post-Hr'g Br., June 22, 2010, at 2. Based on that assertion, Petitioners sought to establish that Malachi's rash led to the decision to change his anti-convulsant medication, which led to the worsening of his seizure disorder and consequent brain injury. Id. at 8-9. Petitioners also asserted that Malachi required repeated hospitalization because of his increased seizures and that, in the course of his second hospital stay, it was possible that Malachi contracted a nosocomial viral infection that resulted in his encephalopathy. Id. at 9.

### **1. Dr. Michael Rieder's Testimony**

Petitioners relied principally on Dr. Michael Rieder's report and his testimony as evidence to substantiate their claim.<sup>9</sup> Dr. Rieder is a professor at the University of Western Ontario in Canada and a medical doctor, with a Ph.D. in pharmacology. He holds an endowed chair in pediatric pharmacology at the University, where he conducts research. Dr. Rieder is a consultant and attending physician of the Children's Hospital of Western Ontario and Director of the regional Adverse Drug Reactions Clinic, which covers drugs, vaccines and biologics. He testified as an expert in pharmacology, pharmacoimmunology (the interaction between drugs and the immune system) and pediatrics. Tr. 76-77, 97. Dr. Rieder sees patients with adverse reactions to vaccines. Tr. 77-78.

Dr. Rieder did not testify that he knew the exact cause of Malachi's rash. Instead, he offered an opinion based on differential diagnosis, balancing the probabilities among three possibilities: (1) viral rash; (2) drug-related rash; and (3) rash related to immunization. Tr. 80-82.

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<sup>9</sup> Dr. Amy S. Paller also submitted a report on behalf of Petitioners, but did not testify. Dr. Paller's report stated, "there is precedent in the literature to suggest that the influenza immunization can increase the circulating levels of Dilantin thus leading to increased potential toxicity [citations omitted]. Given that the likelihood that the reaction, if related to the Dilantin, occurred because of administration of the influenza vaccine, it is unlikely that the reaction would have occurred without the vaccination." Pet'r Ex. A at 001 (Report of Dr. Amy S. Paller, M.D). At hearing, Petitioners abandoned the theory of causation outlined in Dr. Paller's report. See Tr. 129-30.

### **a. Viral rash**

Dr. Rieder discounted the possibility of a viral rash because Malachi's medical records showed no evidence of "prodromal symptoms" indicating a viral infection, and because the physical characteristics of the rash, in particular, the extension of the rash to Malachi's palms, were not typical of viral rashes. Tr. 81, 101-02, 306-07. He testified that a viral cause was the least likely possibility because "the majority of viral rash[es] occurring in association with a viral infection are fairly minor." Tr. 86-87, 101-02. In addition, according to Dr. Rieder, viral rashes "tend to occur" in association with other symptoms, such as fever, runny nose, vomiting, and diarrhea, none of which were present in Malachi's case in December 2003. Id.

Dr. Rieder stated that Malachi's abnormal chest X-ray was a "non-specific finding" and "a lot of things" other than an infection can cause the "[f]uzziness in the chest" noted by the radiologist. Tr. 87-88. In sum, Dr. Rieder noted no sign of a viral syndrome in Malachi's medical records. Tr. 88-89; see also Tr. 112-13.

### **b. Drug reaction**

Dr. Rieder discounted the possibility that Malachi's fever was caused by a hypersensitivity reaction to Dilantin (trade name for phenytoin), because there was "no evidence that there was an alteration in the phenytoin concentration in his blood." Id. at 82, 85-86. But Dr. Rieder stated that an infection, in particular influenza, could "significantly alter [ ] drug handling." Id. He noted the possibility that Malachi's vaccination may have caused him to react to Dilantin in a way that he had not previously. Id. Dr. Rieder stated in his expert report that the vaccination may have altered the metabolism of the phenytoin, causing a "transient elevation in serum phenytoin concentrations associated with immunization." Pet'r Ex. C at 6 (First Supplemental Expert Report of Dr. Rieder, M.D., Ph.D.). Dr. Rieder stated that this effect "may have produced a transient rash which resolved after the serum phenytoin concentration declined." He noted that while this situation was possible, it was "less likely than alternate explanation[s]." Id. at 7. At hearing, Dr. Rieder abandoned this theory as a likely cause of Malachi's rash as there was no evidence of such a reaction in this case. See Tr. 129-30 (testifying there was no evidence of a reaction between Dilantin and the vaccine in this case).

### **c. Vaccine reaction**

With the caveat that: "I'm no immunologist. . . . I'm an immuno-pharmacologist, but I'm no immunologist," Dr. Rieder proposed that the persistence of Malachi's rash could be explained by the fact that, although the vaccine itself remains in the body only briefly, "the immune response does linger." Tr. 309.<sup>10</sup> He stated that the presumptive

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<sup>10</sup> Immunopharmacology is defined as a branch of pharmacology concerned with the application of immunological techniques and theory to the study of the effects of drugs especially on the immune system. Merriam Webster's Online Dictionary, <http://mw3.merriam-webster.com/medical/immunopharmacology>.

mechanism underlying his theory was that the vaccine created an “aberrant [] or misdirected immune response” and therefore the rash persisted after the antigen itself had been cleared. Tr. 108. Dr. Rieder appeared, however, to cast doubt on his own hypothesis of immune misdirection. See Tr. 115, 125, 130.

Dr. Rieder noted that, in the VAERS reports, a rash is a “very common event” in reaction to a flu vaccination. Tr. 82-83. He remarked that seizures “occur commonly, too.” “I would say in the balance of best probabilities, it would be that the rash related to influenza vaccine is the likeliest explanation.” Tr. 83. “[T]he bottom line is, you know, at the bottom line something happened. . . .I’m drawn to that influenza [vaccine] . . . because of considering the other possibilities.” Tr. 84-85.

Dr. Rieder also stated that the fact that the influenza virus can cause a rash made it “reasonable to presume that some people” who are immunized would get a rash, but “there’s not much work suggesting that it’s likely a problem with immunization.” Tr. 123. He testified that a vaccine containing killed viruses, such as that contained in the influenza vaccine, still could cause a rash, albeit less frequently than a live virus. Tr. 135. He stressed throughout his testimony that, rather than asserting a causal relationship between the vaccine and the rash in this case, he was only weighing various factors to determine the likeliest one, recognizing that he could not ascertain the actual cause. Tr. 119, 122, 132.

As to the timing of the onset of Malachi’s rash, Dr. Rieder testified that “the majority of rashes and adverse events occurring with immunization . . . take a day or so to evolve. . . . So a rash occurring [within] two or three days [of immunization] would be consistent with both VAERS and my clinical experience . . . .” Tr. 90.

Dr. Rieder agreed that none of the physicians who treated Malachi for his rash ascribed its cause to the influenza vaccine. Tr. 103. He also agreed that a wild influenza infection can cause a rash that “tends to be fairly mild” and of short duration. Tr. 107. “It doesn’t look like the rash Malachi had,” he added. Tr. 118. Dr. Rieder conceded that a “wide variety” of rashes can be caused by viruses, and testified that most rashes caused by viruses are not specific. Tr. 100-01, 105-06. He also agreed that Malachi’s rash “could be consistent” with a viral rash. Tr. 101.

Dr. Rieder testified that most cases of viral or flu vaccine-induced rashes are self-limited, whereas Malachi’s rash worsened over a period of several days. Tr. 108-09. He agreed that a rash lasting as long as Malachi’s did, i.e., in excess of about two weeks, was longer than would be expected for a viral rash or a vaccine-caused rash. Tr. 110. Dr. Rieder also acknowledged that a person can have a viral infection without symptoms. Id.

Dr. Rieder testified that there are no well-characterized descriptions of a vaccine-induced rash, and that rashes, even in reaction to viruses, are not well-understood. Tr. 128-29.

Dr. Rieder's conclusion rested in large measure on what he termed the law of Occam's Razor, an age-old dictum advancing the proposition that the simplest explanation is usually the best. Tr. 113.<sup>11</sup> He asserted that there were problems fitting the facts of Malachi's case into any of the diagnostic possibilities he outlined, including vaccine causation. Dr. Rieder testified, "I would agree that this seems to me more so you wouldn't expect from a vaccination rash." Id. Rather than a simple matter of "black and white . . . this is a case where there's a lot of gray." Id.<sup>12</sup>

## **2. Petitioners' Medical Literature**

Dr. Rieder attached 11 articles to his initial report. Most were submitted to support the theory that Malachi's rash was caused by a change in how his body reacted to his antiepileptic medication as a result of being administered the flu vaccination. Some of the articles indicated that a rash can be a common side effect of antiepileptic drugs in children. Petitioners at hearing did not pursue any theory based on an interaction between the flu vaccine and Dilantin.

In one article (Levin), a study involving 15 individuals was conducted to determine whether the influenza vaccine affected the phenytoin levels in the participants. See Pet'r Ex. C-3, M Levine et al., Increased Serum Phenytoin Concentration Following Influenza Vaccination, 3 Clinical Pharmacy 505-09 (1984). The mean age of this group was 76.7 years and the group had been receiving "long term phenytoin therapy for seizure disorders." Id. In four individuals, the serum phenytoin concentrations temporarily increased 14 days after influenza vaccination. Id. The authors concluded that serum phenytoin concentrations may be temporarily increased in some individuals and that patients should be monitored, but that the increased levels eventually returned to normal. Id.

In another article (Smith/Bledsoe) studying the effect of the influenza vaccination on individuals with seizure disorders taking phenytoin, the authors found that while phenytoin concentrations in certain individuals changed after flu vaccination, no changes in seizure frequency were seen. See Pet'r Ex. C-4 (CD Smith, et al., Effect of Influenza Vaccine on Serum Concentrations of Total and Free Phenytoin, 7 Clinical Pharmacy 626-32 (1988).

Dr. Rieder cited an article authored by Hadjiloizou and Bourgeois indicating that phenytoin can cause encephalopathy. See Pet'r Ex. C-1 (SM Hadjiloizou et al., Antiepileptic Drug Treatment in Children, 7(2) Expert Review Neurother 179-93 (2007).

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<sup>11</sup> Occam's Razor (also Ockham's razor) is "[t]he principle of parsimony. William of Occam (14<sup>th</sup> century) stated it thus: 'The assumptions introduced to explain a thing must not be multiplied beyond necessity.'" Stedman's Medical Dictionary 27<sup>th</sup> ed. (2000) at 1250.

<sup>12</sup> Dr. Rieder was in every respect a reliable witness. His testimony was clear, candid, and informed. Although in this decision I do not ultimately adopt the conclusions he espoused at hearing, this does not diminish my very favorable impression of Dr. Rieder, or my appreciation of his participation in the Vaccine Program.

Dr. Rieder submitted additional articles to support his theory that Malachi suffered from a misdirected immune response as a result of the flu vaccine. These articles described adverse drug events associated with such drugs as anticonvulsants in individuals with a compromised immune system. See Pet'r Ex. C-6 (D Lin et al., Increased Adverse Drug Reactions to Antimicrobials and Anticonvulsants in Patients with HIV Infection, 40 *Annals of Pharmacotherapy* 1594-1601 (2006)); Pet'r Ex. C-7 (G Venezia et al., Acute Polymyositis During Treatment of Acute Hepatitis C with Pegylated Interferon Alpha-2b, 37 *Digestive and Liver Disease* 882-85 (2005)); see Pet'r Ex. C-8 (HH Lee et al., Cutaneous Side-Effects in Patients with Rheumatic Diseases During Application of Tumour Necrosis Factor-x Antagonists, 156 *British Journal of Dermatology* 486-91 (2007)).<sup>13</sup>

In the article by Sing and Perfect, HIV-infected individuals were given anti-retroviral therapy. The authors concluded that adverse drug reactions, including increased morbidity and mortality, were markedly increased in HIV-positive patients. See Pet'r Ex. C-9 (N Singh et al., Immune Reconstitution Syndrome Associated with Opportunistic Mycoses, 7 *Lancet Infectious Diseases* 395-401(2007)).

Another article discussed an episode of erythema multiforme temporally associated with a diphtheria-pertussis-tetanus (DPT) vaccination. See Pet'r Ex. C-10 (Y Karıncaoglu et al., Erythema Multiforme Due to Diphtheria-Pertussis-Tetanus Vaccine, 24(3) *Pediatric Dermatology* 334-35 (2007)). Malachi did not have erythema multiforme and he did not receive the DPT vaccination in December 2003.

During the hearing, Petitioners submitted two additional medical articles relied upon by Dr. Rieder that were marked as Petitioners' Exhibits 1000 and 1001. The article marked as Exhibit 1000 used VAERS data to examine the causality of adverse events in children who received the trivalent influenza vaccine. Pet'r Ex. 1000 (M Rosenberg et al., Serious Adverse Events Rarely Reported After Trivalent Inactivated Influenza Vaccine (TIV) in Children 6-23 Months of Age, 27 *Vaccine* 4278-83 (2009)). Rash is listed as an adverse event reported after flu vaccination. In Exhibit 1001, the authors listed and grouped the adverse events, including rashes, reported in children who received the flu vaccine. Pet'r Ex. 1001 (AW McMahon et al., Adverse Events After Inactivated Influenza Vaccination Among Children Less Than 2 Years of Age: Analysis of Reports From the Vaccine Adverse Event Reporting System, 1990-2003, 115(2) *Pediatrics* 453-60 (2005)).

### **C. Respondent's Theory of the Case**

Respondent asserted that Malachi's rash in December 2003 was most likely caused by a viral infection unrelated to vaccination. Resp't Post-Hr'g Br. at 11-12. Respondent opined that Dr. Rieder's testimony was "not substantiated by the record."

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<sup>13</sup> Respondent also submitted studies performed on immunocompromised patients. See infra at 13-14. There is no evidence that Malachi suffered from any immune deficiency.

Id. at 11-13. Respondent asserted that Dr. Rieder had conceded that Malachi's rash was not typical of a vaccine-related rash. Id. at 13-14.

### **1. Dr. Christine McCusker's Testimony**

Respondent relied on the testimony of Dr. Christine McCusker, a pediatric immunologist at Montreal Children's Hospital and McGill University Health Center. She sees children in the emergency room at Montreal Children's and also in a private practice Urgent Care for Children Center. Tr. 143-44.

Dr. McCusker agreed with Dr. Rieder that the three possible causes in the differential diagnosis for Malachi's injuries are viral syndrome, drug reaction, and vaccine reaction. Tr. 146. She identified Malachi's symptoms as "an acute viral rash" for several reasons. First, Malachi had a history of rash associated with viral illnesses. Tr. 146-48, 222. Second, the most common cause of rashes in children is an acute viral illness. Tr. 149-50. Third, Dr. McCusker stated that at the time of his initial hospitalization on December 26, 2003, Malachi's chest x-ray was read as indicating either an acute viral infection or reactive airways disease. "As Malachi at that time and subsequently has not been diagnosed with asthma or reactive airways disease, you would postulate that the radiologist was seeing evidence of a virus," Dr. McCusker reasoned. Tr. 150-51.

Dr. McCusker did not identify any particular virus as causative. Tr. 155. She explained that identifying Malachi's rash as "viral" was not based on specific evidence of a viral agent, but as "sort of a generic term [indicating] something active as opposed to something passive," meaning "there was ongoing inflammation." Tr. 227-28. Dr. McCusker confirmed that she used the term "virus" in this case loosely, to indicate a "common external thing that triggers the immune system . . . sort of a generic term . . . ." Tr. 227.

Dr. McCusker characterized rashes caused by reaction to flu vaccine as typically localized, occurring soon after vaccination, and lasting one to two days. Resp't Post-Hr'g Br. at 15-16; Tr. 167. According to Dr. McCusker, a viral rash, on the contrary, "can actually last . . . anywhere from a few days to three to six weeks." Tr. 167. Dr. McCusker testified that Malachi's rash "'peaked somewhere around the 26<sup>th</sup> [of December] and was gone or at least mostly gone . . . by the 29<sup>th</sup>.'" Resp't Post-Hr'g Br. at 16-17, n.14; Tr. 225. Dr. McCusker explained the lack of other viral symptoms by testifying that most viral infections are asymptomatic, and some infections manifest only as a rash. Resp't Post-Hr'g Br. at 17; Tr. 179.

Dr. McCusker explained the biological process resulting in "these sort of generalized rashes" known as viral exanthems. Tr. 160.<sup>14</sup> She also testified generally about the immune process in response to a viral infection as opposed to vaccination. Id. at 162-165. With respect to vaccines containing killed viruses (such as the flu shot Malachi received), she opined that the effect is limited because there is no live vaccine

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<sup>14</sup> "Exanthem" is a "skin eruption or rash." Dorland's at 651.

to replicate and increase reactive symptoms. Tr. 165-66. The immune response therefore tends to be localized or, if generalized, to arise and clear quickly. Tr. 166-67. Dr. McCusker stated that she was unaware of any medical literature reporting a flu vaccine-caused rash lasting 14 days. Resp't Post-Hr'g Br. at 17-18; Tr. 173.

Dr. McCusker drew exactly the opposite conclusion as Dr. Rieder from the spread of Malachi's rash to his palms. According to Dr. McCusker, the accompanying redness on the palms of Malachi's hands did not indicate a vaccine reaction, but was "a sign that there's an acute immune response going on in this child" more consistent with a virus than a transient vaccine reaction. Tr. 175. Palmar erythema "is a sign that there's an acute immune response going on in this child because that's what gives you the rash." Tr. 176. Such a reaction would not have occurred 10 to 14 days after vaccination if the rash were caused by the flu vaccine. The flu vaccine is "gone from the arm by now. It's been cleared. The immune system has taken care of it." Tr. 176-77. Therefore, "the rash on the palms indicates that there is strong pro-inflammatory stimulus going on that is triggering the rash that's progressing it." Tr. 177. In other words, Dr. McCusker believed that the rash on Malachi's palms indicated an ongoing response to a virus that was still in his body, rather than reaction to a vaccine that would have been cleared from his system by the time the palmar erythema appeared.

Dr. McCusker testified further that many viruses are asymptomatic, and that there are many viruses for which no testing is available. In addition, a viral rash can appear before or after other symptoms. Tr. 179-80. Numerous viruses could cause the scarlatiniform rash described by the doctors in Malachi's case. Tr. 154; see also Tr. 155 (no tests were performed for viral agents in Malachi's case, but a test for streptococcus [strep] was performed).

Dr. McCusker conceded that Malachi's rash was atypical because of its progression and long duration. Id. at 19; Tr. 175-76. Dr. McCusker testified that atypical rashes can occur in many virally mediated illnesses.

Dr. McCusker agreed that 14% of VAERS reports submitted from 1990 to 2003 identified an unspecified rash as temporally associated with trivalent flu vaccination. Tr. 218-19; Pet'r Ex.1 to Pre-Hr'g Br. She described the limitations of the VAERS reports in determining causation. See Tr. 170-171, 219.

On cross-examination, Dr. McCusker testified that Malachi suffered a new rash suspected to be of viral or allergic origin on January 22, 2004, while he was hospitalized at University Hospitals of Cleveland. Tr. 203-08. Dr. McCusker stated that this was not the same rash Malachi had in December 2003 and agreed with the characterization that in January 2004 Malachi contracted a "nosocomial infection," that is, a disease acquired de novo in the hospital. Tr. 209.

In response to Dr. Rieder's assertion that Malachi's rash could have persisted long after his vaccination because of a continuing immune reaction, Dr. McCusker explained in detail the nature of the immune response that is activated by a vaccine. Tr.

335-39. In particular, she explained that the initial inflammatory reaction to vaccination is distinct from the long-term immunity formed by antibodies. Different cell types are involved in these distinct processes. The “memory cells” formed in the long-term response to vaccination are quiescent and become active only in reaction to the antigen they recognize. According to Dr. McCusker, this immune process was distinct from and would not produce the type of reaction seen in Malachi.

## **2. Dr. Gerald Raymond’s Testimony**

Respondent also argued that, even assuming Malachi’s rash was caused by his vaccination, the vaccine was not a substantial factor in causing his status epilepticus and encephalopathy. Resp’t Post-Hr’g Br. at 20. On this point, Respondent relied on the expert testimony of Dr. Gerald Raymond, a neurologist and clinical geneticist with board certifications in neurology and clinical genetics. (Dr. Raymond previously held a board certification in pediatrics, but no longer holds this certification.) Dr. Raymond is director of neurogenetics at the Kennedy Krieger Institute and a professor of neurology at Johns Hopkins Hospital. Tr. 246. He has a background in pediatrics and sees patients, including children, in an emergency room setting. Tr. 248-49.

Dr. Raymond agreed that vaccine causation was appropriately included within the differential for Malachi’s diagnosis, but he differed with Dr. Rieder in the weight he ascribed to the vaccine as a possibly causative factor. Tr. 289. He reiterated that Malachi’s treating physicians came to no conclusion as to the cause of his increased seizures and encephalopathy in late 2003 and 2004. Tr. 269. More likely than not, Dr. Raymond concluded, Malachi “had a viral exanthem . . . that resulted in his encephalopathy . . . an increase in his seizures and an alteration in his mental status.” Tr. 266, 291. He confirmed that no specific virus was identified. Tr. 266.<sup>15</sup>

On cross-examination, Dr. Raymond reiterated that, in his view, the course of Malachi’s illness could be explained only by a viral process. Tr. 272. He identified several factors that he said confirmed his opinion, including the appearance of Malachi’s rash, the chest x-ray, the exacerbation of his seizures, and his encephalopathy. Tr. 273-74, 281. Dr. Raymond agreed that Malachi’s rash was atypical for a viral rash. Tr. 279-80. He testified that he started his analysis with the assumption that, because vaccine rashes are rare as compared to rashes associated with viruses, virus and not vaccine was the likely cause of Malachi’s rash. Tr. 278.

On re-direct examination, Dr. Raymond testified that about 80 percent of cases of viral encephalopathy involve an agent that cannot be identified. Tr. 284. He also testified that it was unlikely Malachi’s deterioration was caused solely by the withdrawal of Dilantin. Tr. 285, 288. Unlike Dr. McCusker, Dr. Raymond did not believe that a second, nosocomial viral infection exacerbated Malachi’s condition. He hypothesized that the response to his first infection (in December 2003) may have continued after the active phase of that infection had passed. Tr. 297.

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<sup>15</sup> Dr. Raymond is a neurologist, not an immunologist. In balancing the probabilities, I gave less weight to his testimony than to Dr. McCusker’s as to the cause of Malachi’s rash.

### **3. Respondent's Medical Literature**

#### **a. Dr. McCusker's Medical Literature**

Dr. McCusker's report attached seven articles. Several of the articles showed that the influenza vaccine could safely be administered to immunocompromised individuals. See Resp't Ex. E-4 (P Mamula, et al., Immune Response to Influenza Vaccine in Pediatric Patients with Inflammatory Bowel Disease, 5 Clin. Gastroenterol Hepatol. 851 (2007)), Resp't Ex. E-5 (B. Holvast et al., Influenza Vaccination in Systemic Lupus Erythematosus; Safe and Protective? 6 Autoimmunity Rev. 300-05 (2007)).

Another article (Lammintausta and Kortekangas-Savolainen), concerned patients who had skin reactions to certain medications, including phenytoin. Of these patients, 60% showed a reaction upon reintroduction of the phenytoin, while 40% did not, suggesting that the 40% developed a tolerance to the medication. See Resp't Ex. E-6 (K Lammintausta et al., Oral Challenge in Patients With Suspected Adverse Drug Reactions: Findings in 784 Patients Over a 25 Year Period, 85 Acta Derm Vereol, 491 (2005)).

An article by Sehgal et al. stated that spontaneous remission was noted in patients who had previously had a fixed drug eruption. See Resp't Ex. E-7 (V. Sehgal, et al., Fixed Drug Eruptions (FDE): Changing Scenario of Incriminating Drugs, 45 Int. J. Derm., 897 (2006)).

#### **b. Dr. Raymond's Medical Literature**

Dr. Raymond submitted 25 articles with his expert report. The articles relevant to this decision are described briefly below.

In the article by Jann and Fidone, a temporary increase in total phenytoin levels was noted following influenza vaccination. The authors recommended that dosage adjustments of the anticonvulsant medications may be necessary based on the patient's clinical status and careful monitoring of the serum concentrations of the anticonvulsant drug. See Resp't Ex. C-7 (M Jann and G Fidone, Effect of Influenza Vaccine on Serum Anticonvulsant Concentrations, 5 Clinical Pharmacy 817-19 (Oct. 1986)). A similar finding was made in the article by Marc Levine et al., that the mean serum phenytoin concentration levels following influenza vaccination were mildly, temporarily, increased in patients taking an anticonvulsant. See Resp't Ex. C-8 (M Levine et al. Increased Serum Phenytoin Concentration Following Influenza Vaccination, 3 Clinical Pharmacy 505-09 (1984)).

In contrast, in the article by Sawchuk et al., several patients were found with lower phenytoin levels following influenza vaccination. See Resp't Ex. C-9 (RJ

Sawchuk et al., Effect of Influenza Vaccination on Plasma Phenytoin Concentrations, 1(2) Therapeutic Drug Monitoring 285-88 (1979)).

In the article by Smith et al., the authors examined the total and free phenytoin levels in patients following influenza vaccination. While there was a rise in the total concentration of phenytoin levels, there was a decrease in the free levels of phenytoin.<sup>16</sup> The authors concluded that the initial transient increase following vaccination was probably not significant. See Resp't Ex. C-10 (CD Smith et al., Effect of Influenza Vaccine on Serum Concentrations of Total and Free Phenytoin, 7(11) Clinical Pharmacy 828-32 (1988)).

Dr. Raymond acknowledged that there have been case reports of rashes following a variety of vaccinations, but stated that causation in each case was questionable. See Resp't Ex.C-14 (Y Karıncaoglu et al., Erythema Multiforme Due to Diphtheria-Pertussis-Tetanus Vaccine, 24(3) Pediatric Dermatology 334-35 (2007); Resp't Ex. C-20 (CP Howson et al., Adverse Events Following Pertussis and Rubella Vaccines: Summary of a Report of the Institute of Medicine, 267(3) JAMA 392-96 (1992)). Dr. Raymond stated that he could find no case reports of rash (erythema multiforme) following influenza vaccination. Resp't Ex. A to Rule 4 Rp't at 8.

Dr. Raymond also cited to an article indicating that a change in anticonvulsant medications typically is not a process that leads to encephalopathy. See Ex. C-24 (E Barry et al., Status Epilepticus and Antiepileptic Medication Levels, 44(1) Neurology 47-50 (1994)). Another article stated that in some individuals, status epilepticus (defined by Dr. Raymond as a prolonged seizure or series of seizures that do not allow full recovery between episodes, see Tr. 262) marks the onset of an encephalopathy. See Ex. C-25 (N Hussain et al., Aetiology, Course and Outcome of Children Admitted to Paediatric Intensive Care with Convulsive Status Epilepticus: A Retrospective 5-year Review, 16(4) Seizure 305-12 (2007)).

### **III. DISCUSSION**

#### **A. Summary of the Law**

Petitioners seeking to establish causation-in-fact must show by a preponderance of the evidence that but for vaccination they would not have been injured, and that vaccination was a substantial factor in bringing about the injury. Cedillo v. Sec'y of Health & Human Servs., 617 F.3d 1328, 1338 (Fed. Cir. 2010); Shyface v. Sec'y of Health & Human Servs., 165 F.3d 1344, 1352 (Fed. Cir.1999).<sup>17</sup> Proof of actual

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<sup>16</sup> In the blood, phenytoin is highly bound to serum proteins. Only the portion of phenytoin that is unbound or "free" is pharmacologically active. The free phenytoin concentration is most indicative of both toxicity and therapeutic activity. See Resp't Ex. C-10 at 29.

<sup>17</sup> Petitioners do not allege a "Table" injury. The Secretary of Health and Human Services maintains a Vaccine Injury Table by regulation. See 42 C.F.R. § 100.3, as adopted and revised pursuant to the authority of 42 U.S.C. § 300aa-14(c). "[T]he Table lists symptoms and injuries

causation must be supported by a sound and reliable “medical or scientific explanation that pertains specifically to the petitioner’s case, although the explanation need only be ‘legally probable, not medically or scientifically certain.’” Moberly v. Sec’y of Health & Human Servs., 592 F.3d 1315, 1322 (Fed. Cir. 2010) (quoting Knudsen v. Sec’y of Health & Human Servs., 35 F.3d 543, 548-49 (Fed. Cir. 1994)); see also, Grant v. Sec’y of Health & Human Servs. 956 F.2d 1144, 1148 (Fed. Cir.1992) (medical theory must support actual cause).

Causation is determined on a case-by-case basis, with “no hard and fast per se scientific or medical rules.” Knudsen, 35 F.3d at 548. A petitioner may use circumstantial evidence to prove the case, and “close calls” regarding causation must be resolved in favor of the petitioner. Althen, 418 F.3d at 1280.

Petitioners’ burden is to show that the vaccination brought about Malachi’s injury by providing (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury. Cedillo, 617 F.3d at 1338 (citing and quoting Althen). If Petitioners succeed in establishing a prima facie case of causation, the burden then shifts to Respondent to prove alternative causation by a preponderance of the evidence. Id. (citing Walther v. Sec’y of Health & Human Servs., 485 F.3d 1146, 1151 (Fed. Cir. 2007); see generally de Bazan v. Sec’y of Health & Human Servs., 539 F.3d 1347, 1352 (Fed. Cir. 2008) (explaining requirements to establish “factor unrelated to the administration of the vaccine”). If petitioners fail to establish a prima facie case of causation, however, the burden does not shift. Doe 11 v. Sec’y of Health & Human Servs., 601 F.3d 1359, 1357-58 (Fed. Cir. 2010); see Cedillo, 617 F.3d at 1335 (citing Walther, 485 F.3d at 1151).

In evaluating whether a petitioner has presented a legally probable medical theory, “the special master is entitled to require some indicia of reliability to support the assertion of the expert witness.” Cedillo, 617 F.3d at 1339, n.3 (collecting cases). Assessing the reliability of an expert opinion in Vaccine Act cases can be challenging, because often there is little supporting evidence for the expert’s opinion. See Althen, 418 F.3d at 1280 (noting that the “field [is] bereft of complete and direct proof of how vaccines affect the human body”). Consequently, most expert opinions extrapolate from existing data and knowledge. The weight to be given to an expert’s opinion is based in part on the size of the gap between the science and the opinion proffered. Cedillo, 617 F.3d at 1339 (Fed. Cir. 2010) quoting Gen. Elec. Co. v. Joiner, 522 U.S. 136, 146 (1997)). A special master is not required to rely on a speculative opinion that “‘is connected to existing data only by the ipse dixit of the expert.’” Snyder v. Sec’y of Health & Human Servs., 88 Fed. Cl. 706, 745, n.66 (2009) (quoting Gen. Elec. Co., 522

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associated with each listed vaccine and a timeframe for each symptom or injury.” de Bazan v. Sec’y of Health & Human Servs., 539 F.3d 1347, 1351 (Fed. Cir. 2008). If a listed symptom occurs after vaccination within the times specified, causation is presumed. Id. Injuries not listed on the Table or injuries suffered outside the specified times following vaccination are deemed off-Table injuries, and causation is not presumed. Id.

U.S. at 146); accord, e.g., Cedillo, 617 F.3d at 1339, n.3 (“[a]n expert opinion is no better than the soundness of the reasons supporting it”) (citing and quoting Perreira v. Sec’y of Health & Human Servs., 33 F.3d 543, 548 (Fed. Cir.1994)).

## **B. Analysis**

### **1. Significant Aggravation**

If a symptom or manifestation of an injury appears before vaccination, a petitioner cannot claim that the vaccination caused the injury, see Shalala v. Whitecotton, 514 U.S. 268, 274 (1995) (interpreting the statutory requirements for proving a Table Injury), but she may claim that the vaccination significantly aggravated a preexisting injury. See id. at 277-78 (O’Connor, J., concurring); see also § 300aa-11(c)(1)(C)(ii)(I). It is undisputed here that Malachi’s seizure disorder preceded his flu vaccination in December 2003. Also undisputed is that Malachi at times suffered rashes in connection with infections.

It is not entirely clear whether to treat this as a claim for direct vaccine causation, or as a claim for significant aggravation of a pre-existing condition due to vaccination. Petitioners did not allege a significant aggravation theory, nor did Respondent raise Malachi’s pre-existing conditions as an obstacle to compensation for vaccine injury. But see Resp’t Post-Hr’g Br. at 6-7 (stating, “This change in therapy, according to petitioners, caused Malachi to suffer a cluster of break-through seizures, and status epilepticus on December 24-25, 2003, which in turn resulted in an acute encephalopathy and further brain injury, and significant aggravation of his seizure disorder”).

To prove a claim for significant aggravation, petitioners must establish the combined causation factors identified in Whitecotton v. Sec’y of Health & Human Servs., 81 F.3d 1099 (Fed. Cir.1996), and the Althen causation factors. Thus, Petitioners must show (1) the person’s condition before administration of the vaccine; (2) the person’s current condition (or condition following vaccination); (3) whether the person’s current condition constitutes “significant aggravation” of the person’s condition before vaccination; (4) a medical theory causally connecting such a significantly worsened condition to the vaccination; (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation; and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation. Loving v. Sec’y of Health & Human Servs., 86 Fed. Cl. 135, 144 (Fed. Cl. 2009). Viewed as a case of significant aggravation, I have no difficulty finding that the first three factors of the Loving test are satisfied here. Malachi’s neurological condition is significantly worse than before his flu vaccination. His condition, however, has not been shown to be the result of his vaccination, for the reasons explained below. The Althen prongs, in other words, have not been established. Thus, the Petitioners’ case fails whether viewed as a direct causation case or one based upon significant aggravation.

## **2. Althen Prong 1 - Could Vaccination Have Caused Malachi's Rash?**

Under Althen Prong 1, a petitioner must set forth a biologically plausible theory explaining how the vaccine received by the petitioner could cause the injury complained of. See, e.g., Andreu v. Sec'y of Health & Human Servs., 569 F.3d 1367, 1375 (Fed. Cir. 2009). This requirement has been interpreted as "can the vaccine(s) at issue cause the type of injury alleged?" Pafford v. Sec'y of Health & Human Servs., 451 F.3d 1352, 1355-56 (Fed. Cir. 2006). Evidence should be viewed by the preponderance of the evidence standard and "not through the lens of the laboratorian." Andreu, 569 F.3d at 1380. Although the theory of causation need not be corroborated by medical literature or epidemiological evidence, the theory must be sound, reliable, and reputable -- in other words, the theory need not be scientifically certain, but it must have a scientific basis. See Andreu, 569 F.3d at 1379-80.

Petitioners attempted to present a medical theory causally connecting the vaccination and the injury through their expert, Dr. Rieder. Dr. Rieder did not actually endorse any biological theory to explain the alleged vaccine injury. One theory that Dr. Rieder initially presented was that he believed the flu vaccination could have caused an immunological response in Malachi that lingered after the vaccine itself was cleared from Malachi's system. Dr. Rieder did not elaborate on this theory to any degree, and he seemed in his testimony to discount its reliability. See Tr. 141-42. In so doing, Dr. Rieder explained that he is not an immunologist and essentially retracted the theory that the vaccine triggered an immune response that caused the rash.<sup>18</sup>

Dr. Rieder relied on "differential diagnosis" to attempt to establish causation between Malachi's rash and the flu vaccine.<sup>19</sup> Dr. Rieder stressed throughout his testimony that, rather than asserting a causal relationship between the vaccine and the rash in this case, he only was weighing various factors to determine the likeliest one, recognizing that he could not ascertain the actual cause. Tr. 119, 122, 132. By process of elimination, Dr. Rieder concluded that the most likely cause of Malachi's rash was a vaccine reaction.

The underlying basis for Dr. Rieder's attribution of causation thus is not a biological theory, but a conclusion that the alternatives on the differential -- drug reaction and viral syndrome -- are less likely than vaccine causation. The process of eliminating other possible causes, i.e., differential diagnosis, does not necessarily mean

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<sup>18</sup> As noted above, Dr. Rieder also changed his opinion about the theory that the vaccine altered the way in which Malachi metabolized Dilantin, such that it caused an allergic-type reaction manifesting in rash. See Tr. 86-87.

<sup>19</sup> Differential diagnosis is a standard scientific technique used to identify the cause of a medical problem by eliminating the potential causes until the most probable cause is identified. Westburry v. Gislaved Gummi AB, 178 F.3d 257 (4th Cir. 1999). Differential diagnosis "generally is accomplished by determining the possible causes for the patient's symptoms and then eliminating each of these potential causes until reaching one that cannot be ruled out or determining which of those that cannot be excluded is most likely." Id.

that a remaining factor (here the flu vaccine) caused the condition. See Moberly, 592 F.3d at 1323. On the other hand, sufficiently rigorous differential diagnosis can support a finding of causation under the Vaccine Act. See Hocraffer v. Sec'y of Health & Human Servs., 63 Fed. Cl. 765, 777, 779 (2005); see also Ruggiero v. Warner-Lambert Co., 424 F.3d 249, 254 (2d Cir. 2005) (stating that the district judge has broad discretion in determining whether in a given case a differential diagnosis is enough by itself to support a causation opinion). In this case, Dr. Rieder's opinion is not sufficient to establish that Malachi's vaccination could likely have caused a rash of this type. As discussed below, the preponderance of the evidence indicates that the vaccination could not have done so.

Dr. Rieder included the flu vaccine in his differential diagnosis primarily based on VAERS reports listing rash as a possible side effect of the flu immunization. In addition, Dr. Rieder relied on (a) the appearance of the rash, (b) the absence of symptoms indicating that it was associated with a viral infection, and (c) the temporal association between the flu vaccination and the occurrence of the rash. Tr. 80-85.

Dr. McCusker's testimony refuted each of the factors relied upon by Dr. Rieder. As a pediatric immunologist, she opined convincingly that the type of immune response generated by the flu vaccine probably could not result in the rash Malachi developed. In addition, she was able to identify other agents that are more likely to have the capacity to produce the kind of rash Malachi had, and she was able to explain why this is so.

According to Dr. McCusker, a rash associated with vaccination typically would only last a few days and would "disappear quickly." Dr. McCusker explained that when a vaccine containing a "killed" virus is injected into the arm "nothing grows. It's fixed." Tr. 165-66. Sometimes there is a localized rash, swelling, and soreness in the arm associated with the vaccination. Id. Rashes that occur after a vaccination are "often on quickly and off quickly. They're acute. They're usually within the first couple of days, usually after 24 hours, and they disappear quickly, two-to-three days maximum." Tr. 167. Malachi's rash, which lasted for nearly two weeks, perhaps longer, did not fit the description of a possible vaccine reaction.

Also, as described by Dr. McCusker, a rash due to a flu vaccination would not likely be as severe as Malachi's rash, which required hospitalization. Dr. McCusker supported her opinion by noting that Malachi's palmar erythema, which developed 10 to 14 days post vaccination, is not characteristic of a transient reaction to a vaccine containing a killed virus. Because she is a specialist in pediatric immunology, Dr. McCusker's view that the nature and severity of Malachi's rash is inconsistent with a vaccine reaction is more persuasive than Dr. Rieder's conclusion. In addition, Dr. Rieder's opinion was predicated in part on the VAERS data, and there were no serious adverse events, such as Malachi experienced, attributed to rashes associated with vaccination in the VAERS reports. See Pet'r Ex. 1000, Table 2 at 428; Tr. 172.

Further, in weighing the evidence, I have noted that VAERS reports are not regarded as strongly probative on the causation issue in vaccine cases. Information

extracted from the VAERS database may not be reliable because information entered into the VAERS database may not be accurate. The United States Court of Federal Claims “uniformly has upheld the . . . concerns about the reliability of VAERS data.” Analla v. Sec’y of Health & Human Servs., 70 Fed. Cl. 552, 558 (2006) (citing cases). To the extent that Dr. Rieder’s opinion was predicated on reports of rashes in the VAERS data, I gave his opinion less weight.

Dr. McCusker integrated information about Malachi’s individual medical condition and history into her conclusion that vaccine causation was unlikely. Dr. McCusker pointed out that there were findings in the chest x-rays conducted on December 26, 2003, consistent with a viral infection. Pet’r Ex. 12 at 32; Resp’t Ex.C at 3 (Dr. McCusker’s report). The duration of Malachi’s rash also was consistent with a rash caused by a viral agent, according to Dr. McCusker. See Tr. 167 (some reported to have lasted in excess of 14 days). Dr. McCusker also noted that Malachi had a history of rash associated with viral illnesses. Tr. 147-48. This testimony reflects the evidence in Malachi’s records and the evidence presented at hearing. See supra at 2; Tr. 24, 40, 63, 67-69.

Petitioners did not provide an effective rebuttal to Dr. McCusker’s testimony. On the contrary, Dr. Rieder seemed to agree in large part with Dr. McCusker’s testimony.<sup>20</sup> He recognized that the duration of Malachi’s rash would be unexpected if its cause were a vaccine reaction. Tr. 110. He also agreed that a person can have a viral infection without symptoms. Id. Dr. Rieder agreed further that the rash Malachi experienced could be consistent with a viral rash. Tr. 101.

Petitioners have not established a biological theory supported by reliable evidence indicating possible vaccine causation in Malachi’s case. Based on the preponderance of the evidence, I conclude that it is unlikely the flu vaccine could have caused a rash of the type Malachi experienced.<sup>21</sup>

### **3. Althen Prong 2 - Is There A Logical Sequence Of Cause And Effect Showing That The Flu Vaccine Was The Reason For Malachi’s Injury?**

The second prong of Althen requires a petitioner to prove “a logical sequence of cause and effect show[ing] that the vaccination was the reason for the injury.” Andreu,

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<sup>20</sup> In fact, there were significant areas of agreement among all the experts. This does not mean that the case was “close,” but rather that the area of disagreement among the experts was narrow. As to the narrow question whether the flu vaccine could have caused this type of a rash, the evidence clearly preponderated in Respondent’s favor.

<sup>21</sup> Because Dr. Rieder used differential diagnosis as the basis for his prong 1 opinion, much of the evidence discussed above also pertains to the question of whether the flu vaccine actually did cause Malachi’s rash. I incorporate the discussion of the evidence under prong 1 into the section below concerning prong 2 of Althen.

569 F.3d at 1374 (quoting Althen). Under prong 2 of Althen, Petitioners are not required to show “epidemiologic studies, rechallenge, the presence of pathologic markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect . . . .” Capizzano v. Sec’y of Health & Human Servs., 440 F.3d 1317, 1325 (Fed. Cir. 2006). Instead, circumstantial evidence and reliable medical opinions may be sufficient to satisfy the second Althen factor. Capizzano, 440 F.3d at 1325-26; Andreu, 569 F.3d at 1357 (treating physician testimony).

As noted above, no treating physician opined that Malachi’s rash was related to his flu vaccination. Malachi did receive a flu vaccination, he did suffer a rash thereafter, and flu vaccine can cause rashes. If nothing more is required to satisfy Althen prong 2, it was satisfied in this case. There is no logical connection between Malachi’s vaccination and his rash, however, because the evidence indicates that it is unlikely the flu vaccine caused a rash with the particular characteristics described in Malachi’s case.

#### **4. Althen Prong 3 – Is There A Temporal Association Between The Flu Vaccine And The Onset Of Malachi’s Injury?**

To show causation, a petitioner must establish that the injury occurred within a time frame that is consistent with the theory of causation set forth. Pafford, 451 F.3d at 1358. What constitutes an appropriate temporal association is a question of fact and will vary with the particular theory of causation advanced. Id.; de Bazan, 539 F.3d at 1352. Evidence showing the injury occurred in a medically acceptable time frame “is even more important in cases involving contemporaneous events other than the vaccination, because the presence of multiple potential causative agents makes it difficult to attribute ‘but-for’ causation to the vaccination.” Pafford, 451 F.3d at 1358.

The time frame for developing a rash in reaction to a flu vaccination is, in this case, appropriate as to onset, but not as to duration. Malachi’s rash emerged approximately two days after he received the flu vaccination. Tr. 42-3,109. The experts appeared to agree that this is within the time frame in which such a rash might manifest if it were caused by the vaccination. Tr. 90 (Dr. Rieder); Tr. 167 (Dr. McCusker); Tr. 289 (Dr. Raymond). If onset is all that matters, prong 3 is satisfied. As noted above, however, the duration of this rash is too long to be consistent with a flu vaccine reaction. See Grant, 956 F.2d at 1148 (temporal relation alone is not sufficient to prove causation).

#### **IV. CONCLUSION**

Based on the entire record, Petitioners have not presented a prima facie case of vaccine causation-in-fact. Petitioners’ Petition for compensation is **DISMISSED**. In the absence of a motion for review, the Clerk shall enter judgment accordingly.

**IT IS SO ORDERED.**

s/ Dee Lord  
Dee Lord  
Chief Special Master