In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 08-477V
January 18, 2012
To be Published

GARY BRAGG, Executor of the Estate of EDGAR BRAGG, deceased, Petitioner, v. SECRETARY OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES, Respondent.	*	Flu vaccine; cytokine storm; death of 82-year-old man six days after vaccination; sepsis/ systemic inflammatory response; Zatuchni; pain and suffering of decedent pre-filing of petition

Robert T. Moxley, Cheyenne, WY, for petitioner.
Darryl R. Wishard, Washington, DC, for respondent.

MILLMAN, Special Master

DECISION[1]

Petitioner filed a petition on June 30, 2008 under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10 et seq., alleging that flu vaccine which his father (hereinafter, "the decedent") received on November 4, 2006 caused his illness and death.

A hearing was held on April 26, 2011. Testifying for petitioner were Tomasita Bragg (decedent's daughter-in-law), Rhonda Lawson (decedent's granddaughter), Dr. James Hardee

[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 clearly be an unwarranted invasion of privacy. When such a decision is filed, petitioner has 14 days to identify and move to redact 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 redact such material from public access.

(decedent's treating doctor), petitioner, and Dr. Alan S. Levin (expert immunologist). Testifying for respondent was Dr. Lawrence D. Frankel (expert immunologist and infectious disease physician).

Petitioner filed his post-hearing brief on August 15, 2011, respondent filed her post-hearing brief on August 26, 2011, and petitioner filed his reply brief on September 28, 2011. Petitioner filed a medical article as Ex. 20 on October 3, 2011. Petitioner filed a supplemental brief on November 9, 2011. Respondent filed a supplemental brief on November 15, 2011. The case is ready for decision.

FACTS

The decedent was born on April 4, 1924.

On October 16, 2006, decedent's dentist, Dr. Richard T. O'Day, removed the root tip of one of decedent's teeth without complication. Med. recs. at Ex. 7, p. 3.

On October 31, 2006, decedent saw his primary care physician, Dr. James T. Hardee, for his annual physical examination. Dr. Hardee diagnosed decedent as prediabetic and having hyperlipidemia. Med. recs. at Ex. 1, p. 31. Decedent's blood pressure was 128/68 and his weight was 171 pounds. Id. at 32. Decedent told Dr. Hardee, "I feel great." Id. He was walking up to nine miles a day and riding an exercise bike. His home blood pressure was measured as 114/60 and 118/80. He was going to get a flu shot that weekend. Id. Dr. Hardee noted that decedent continued to do really well. Id. at 33.

On November 4, 2006, decedent received influenza vaccine. Ex. 4, p. 1.

From November 7, 2006 until November 9, 2006, when decedent died, decedent was in Exempla Good Samaritan Medical Center, having first entered the emergency room with dehydration, fever, and weakness, after which he was admitted to the hospital. Med. recs. at Ex.

10, p. 2. The primary diagnosis was respiratory failure. The secondary diagnoses were sepsis, pneumonia, hypotension, renal failure, and liver failure. Id.

In the emergency room, petitioner stated his father had been weak for about a week and had myalgias. On Friday, November 3, 2006, decedent felt malaise. On Saturday, November 4, 2006, he received a flu vaccination. In the last week, he had lost 11 pounds. In the doctor's office on November 7, 2006, he had a temperature of 103° F. with a history that he had had 104° F. at home. Id. at 6-7. Decedent's white blood cell count in the ER was elevated at 12.2. Id. at 7. His platelet count was low at 40,000. Id. His creatinine was elevated. Id. He was diagnosed with weakness, dyspnea, renal failure, thrombocytopenia, rash, and hyperglycemia. The doctor was concerned about early sepsis. Decedent was admitted to the hospital in fair condition. Id.

Decedent was admitted for hypoxia. Med. recs. at Ex. 10, p. 3. He quickly developed a rash which at first was macular, but then became petechial, associated with circumoral desquamation (peeling around the mouth), very concerning for Stevens-Johnson syndrome.[2] Id. Decedent presented with hypotension, renal failure, and elevated liver function tests. Initially, he improved slightly on fluid boluses, but he quickly decompensated, requiring intubation. Id. He was treated with Azithromycin and Itepenem as well as Vancomycin on admission. About 36 hours after admission, he was in florid respiratory failure with severe metabolic acidosis and worsening multi-system organ failure. His son opted to withdraw support, and decedent died within minutes of extubation. Decedent's son declined an autopsy. Id.

[2] Stevens-Johnson syndrome is "traditionally considered to be a severe form of erythema multiforme." Dorland's Illustrated Medical Dictionary, 31st ed. (2007) (hereinafter, "Dorland's") at 1872. Erythema multiforme is "characterized by sudden eruptions of erythematous papules, some of which evolve into target lesions … [representing] reactions of the skin and mucous membranes to factors such as viral skin infections (especially herpes simplex); agents (including drugs) that are ingested or irritate the skin; malignancy; or pregnancy. . . . [T]he more severe type is called *Stevens-Johnson syndrome*." Id. at 651.

An infectious disease consultation on November 8, 2006 with Dr. Daniel Mogyoros revealed that decedent had been in good health until his hospital admission. Id. Decedent was admitted the night before the consultation with complaints of fever up to 103° or 104° F. over the prior several days. The decedent stated that about one week prior to admission, he had a tooth extraction for tooth abscess, which occurred without any complications. Decedent was not put on any antibiotics afterward. Id. Several days prior to admission, decedent began to develop fevers, myalgias, and a dry cough. He lost about five pounds over the course of the week. Id.

On November 7, 2006, decedent saw his primary care physician with these complaints and he admitted him to the hospital out of concern he might have an infection. Id. at 3-4. Decedent noted a rash which began on the day of admission, initially on his lower abdomen but then extending over the entire torso. Id. at 4. The rash was non-pleuritic and not painful. Decedent denied any sick contacts, and had no recent travel or recent rural exposures. In the ER, decedent had volume resuscitation with saline because he was somewhat hypotensive. Id. Decedent's past medical history included hyperlipidemia and hypoglycemia. Id.

Decedent had fever previously of 104° F. although he was afebrile on physical examination. Id. He had recent weight loss. He did not have sore throat, neck stiffness, irregular heart rate, nausea, vomiting, diarrhea, joint pain, or dysuria. He did have cough but no sputum production. He had myalgias and skin rash. Id. His pulse on examination was in the 130s. His blood pressure was 100/58. He was in moderate respiratory distress. Id. A rapid influenza test was negative. Urinalysis was negative. Chest x-ray at the time of admission showed generalized vascular congestion and bilateral effusions with cardiomegaly consistent with congestive heart failure. A CT scan of the thorax showed significant abnormalities and infiltrates in the right upper lobe and bilateral pleural effusions. Id. The impression was sepsis

syndrome which was community-acquired, but the recent tooth extraction put decedent at risk of a more systemic infection with oral flora including strep, fusobacterium, and anaerobes. There was no sign of a neck abscess. Id. at 4-5. The markedly abnormal chest CT scan could represent a community-acquired pneumonia. Id. at 5. Decedent had a significantly elevated white blood cell count of 16.2 with left shift. Id. at 4, 5.

On November 9, 2006, at 4:46 a.m., Dr. Larry E. Van Vleet, an internist, noted that decedent had no chance of survival and might already have serious brain injury since he was not awake and not on sedatives. On advice of family, the staff removed the ventilator support and intravenous drips. On November 9, 2006, the decedent died. The death certificate listed the cause of death as sepsis and pneumonia. Med. recs. at Ex. 1, p. 2.

On November 9, 2006, Dr. James T. Hardee, decedent's treating physician, received a note that decedent had died and tried to telephone petitioner to express his sympathy, Ex. 1, p. 24. Dr. Hardee wrote that, considering that decedent was "feeling great" during his annual physical examination on October 31, 2006, received a flu vaccination on November 4, 2006, and suddenly became quite ill, dying on November 9, 2006 with a suspicion of Stevens-Johnson syndrome, Dr. Hardee communicated these details to the Prevention Chief, Dr. France. Dr. Hardee states, "I don't know if there is any causal relation between the flu shot and the sudden illness & death, but I wanted Dr. France to be aware." Id.

On November 10, 2006, Pamela A. Knigge, RN, noted that a vaccine adverse event report (VAERs) was sent to the Centers for Disease Control because of the "remote possibility that this is related to flu immunization received 11/4 at mass flu clinic." Id. at 28. Nurse Knigge filled out the VAERs form, stating decedent had been previously healthy, but, after flu

vaccination, developed Stevens-Johnson syndrome, and renal and respiratory failure, and died. Med. recs. at Ex. 3, p. 2.

Other Submitted Material

Petitioner filed as Exhibit 12 an article entitled "Cytokine Storm in a Phase 1 Trial of the Anti-CD28 Monoclonal Antibody TGN1412" by G. Suntharalingam, et al., 355 NEJM 1018-28 (2006). As part of a double-blind, randomized, placebo-controlled phase 1 study of the safety of a novel monoclonal antibody, six healthy male volunteers received the drug while two received placebo. Id. at 1018. The six volunteers who took the drug had multi-organ failure and were hospitalized. Id. The median age of the six volunteers was 29.5 years (ranging from 19 to 34 years of age). Id. at 1019. All were clinically well for two weeks before the study and none had a notable medical history. Id.

From 50 to 90 minutes after infusion of the drug, five of the six patients had severe headache accompanied by lumbar myalgia in all six patients. Id. During this early phase, the patients were restless and had varying degrees of nausea, vomiting, bowel urgency, or diarrhea. Five of them had short amnestic episodes associated with severe fever, restlessness, or both. All six patients had a systemic inflammatory response to the drug, including erythema and peripheral vasodilation, hypotension, and tachycardia. Id.

Five hours after the infusion, one patient had signs of respiratory failure, with tachypnea and a partial pressure of arterial oxygen. Chest x-ray revealed pulmonary infiltrates inconsistent with the expected response of a fit young man. There was no clinical evidence of bronchospasm or laryngeal edema. Id. Another patient became hypotensive and, 12 hours after receipt of the drug, had metabolic acidosis and marked respiratory distress with hypoxemia that was refractory

to treatment with supplemental oxygen. He underwent intubation and mechanical ventilation. Id. at 1020.

The six patients were transferred to critical care 12 to 16 hours after receipt of the drug. Id. Duration of abnormalities noted on chest x-rays lasted from less than five to eight days in all six patients. Id. The six patients received corticosteroids for 21 to 33 days. Id. Between 16 and 20 hours after receipt of the drug, the six patients had further signs of respiratory deterioration: tachypnea, inability to complete spoken sentences, and bilateral pulmonary infiltrates on chest x-ray. Id. at 1022. Two patients had symptoms of dyspnea. Id. There was evidence of substantial renal impairment and disseminated intravascular coagulation. Id.

Four patients continued to have intermittent fever, myalgia, and diffuse erythematous flushing for 48 hours, at which point they improved. Id. at 1024. The other two patients had a more complex course in that, although their erythema and fever diminished 48 hours after receipt of the drug, they subsequently had recurrent fever, increased peripheral vascular permeability, and episodes of diffuse erythematous flushing lasting several days. Id. at 1025. Both patients required intubation and mechanical ventilation. Id.

In their discussion, the authors state the drug produced in these healthy persons "a sudden and rapid release of proinflammatory cytokines." Id. at 1026. This course provided insight into the natural course of the cytokine storm and the systemic inflammatory response syndrome (SIRS). Id. The infused drug was not contaminated with endotoxin, pyrogen, or microbiologic or other agents. Id. All six patients fit the criteria for SIRS in the absence of contaminating organic factors. Id. The most prominent clinical feature was the early appearance of respiratory distress and pulmonary infiltrates, accompanied by renal impairment and profound disseminated intravascular coagulation. Id. at 1026-27. The authors considered this kind of organ impairment

to be consistent with a generalized multi-organ response to inflammation or critical illness. Id. at 1027. However, they noted that the rapid onset and concordance of the lung injury among their six patients seemed unusual and, in the presence of high cytokine levels, these features might be consistent with immune-mediated injury specific to the lung. Id. They surmised that high levels of proinflammatory cytokines is a requirement for pulmonary compromise. Id. They posited that the more rapid onset of lung injury in their six patients may have been due to a combination of the direct effects of the antibody and cytokines on lung tissue. Id.

The authors found equally striking the consistent pattern of immunologic effects and recovery in the six patients. Id. Their severe lymphopenia[3] was unexpected. The authors commented that sepsis may also induce lymphopenia. Id. The authors suggest that the onset of lymphopenia may have been a response to the infused T-cell agonist drug rather than to the cytokine storm alone. Id. The two factors setting apart these six trial subjects' reaction to TGN1412 from a typical cytokine storm were notably early acute lung injury and marked lymphopenia. Id. at 28.

Respondent filed as Exhibit C an article entitled "Death and serious illness following influenza vaccination: a multidisciplinary investigation" by A. Rue-Cover, et al., 18 Pharmacoepidemiology & Drug Safety 504-11 (2009). The authors investigated four deaths and four serious illnesses among 114 recent influenza vaccinees in a long-term care facility and two deaths among vaccinees from a nearby physician's office, all of whom received flu vaccine from the same lot number. Id. at 504. Among cases reported to VAERS who died (four cases) or experienced rapid deterioration in health (four cases) after vaccination with the suspect lot, the time of onset of symptoms varied from the day of vaccination to 11 days, with a median onset of

[3] Lymphopenia is also known as lymphocytopenia which means a reduction in the number of lymphocytes in the blood. Dorland's at 1101, 1103.

4 days. Id. at 506. All eight of the affected patients had multiple underlying chronic medical conditions. Id. The causes of death for patients were listed as cardiac (two cases) and end stage dementia (two cases). Id. One patient reported to VAERS as a serious illness subsequently died from respiratory and cardiac causes during the study period, resulting in a total of five deaths. Id.

During the two-week follow-up period after vaccination in the long-term care facility, 13 vaccinated residents and one unvaccinated resident had a medically attended event. Id. The incidence rate for medically attended events was about twice as high among vaccinated residents compared to unvaccinated residents, but this difference was not statistically significant. Id. at 506-07.

Of the two patients who died from the outpatient clinic, one who was 65 years old had a history of myocardial infarction and onset of chest pain the week before vaccination and the other who was 74 years old had chronic obstructive pulmonary disease and was being treated for a urinary tract infection before vaccination. Id. at 507-08.

From July 1 to December 3, 2004, there were 11 serious adverse events, including seven deaths, reported for the suspect lot compared to no serious adverse events for two other lots of vaccine. Id. at 508. Ten of the 11 serious adverse events occurred in conjunction with the authors' investigation. Id. at 509. The 11th serious adverse event was an apparent hypersensitivity reaction. Id. The authors note that the cluster of serious adverse events associated with the one lot of flu vaccine was not a significantly increased risk and state, "This paper demonstrates the difficulty of thorough assessment of possible vaccine-related SAE [serious adverse event] clusters where the vaccinated population is, at baseline, at increased risk of hospitalization and death due to age and underlying conditions." Id. They noted no similar

symptoms, signs, or consistent pattern of onset in persons with medically attended events. Id. They thought this failure of consistency indicated lack of causal relationship to the vaccine. Id.

Respondent filed as Exhibit D an article entitled "American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis" by Members of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference Committee, 20 Critical Care Medicine 6:864-74 (1992). The goal was to provide a conceptual and "practical framework to define the systemic inflammatory response to infection, a progressive, injurious process that falls under the generalized term 'sepsis' and includes sepsis-associated organ dysfunctions as well." Id. at 864. They state, "Sepsis is an increasingly common cause of morbidity and mortality, particularly in elderly, immunocompromised, and critically ill patients." Id. at 865 (footnotes omitted). One source of confusion in clinical trials to evaluate therapies in the treatment of sepsis has been the application of the terms "sepsis" and "septic syndrome" to noninfectious inflammatory states. Id. The authors note, "The term 'sepsis,' in popular usage, implies a clinical response arising from infection. It is apparent that a similar, even identical, response can arise in the absence of infection. We therefore propose the phrase 'systemic inflammatory response syndrome' to describe this inflammatory process, independent of its cause." Id. (reference to pictorial figure omitted).

The authors state that sepsis has been recognized as a systemic inflammatory response to an active infectious process in the host. Id. at 866. "The use of a broad-based clinical definition of the septic process may facilitate studies of the pathogenetic mechanisms involved in the production of the systemic inflammatory response to infection, as well as the noninfectious causes of systemic inflammatory response syndrome." Id. "A frequent complication of systemic

inflammatory response syndrome is the development of organ system dysfunction, including such well-defined clinical conditions as acute lung injury, shock, renal failure, and multiple organ dysfunction syndrome." Id.

The authors identify two multiple organ dysfunction syndromes. The first, called primary multiple organ dysfunction syndrome, relates to a well-defined insult, such as trauma. Id. at 868. As for the second, "Secondary multiple organ dysfunction syndrome develops, not in direct response to the insult itself, but *as the consequence of a host response,* and is identified within the context of systemic inflammatory response syndrome. The systemic inflammatory response syndrome is also a continuous process, and describes an abnormal host response that is characterized by a generalized activation of the inflammatory reaction in organs remote from the initial insult." Id. (emphasis in original).

Respondent filed as Exhibit E an article entitled "Sepsis-Induced Apoptosis Causes Progressive Profound Depletion of B and $CD4^+$ T Lymphocytes in Humans" by R.S. Hotchkiss, et al., 166 J Immunology 6952-63 (2001). The authors found loss of B and CD4 T cells in those with sepsis which may contribute to the immunosuppression in sepsis by decreasing the number of immune effector cells. Id. at 6952. The authors state that sepsis "represents a state of uncontrolled activation of the inflammatory cascade resulting in cell and organ injury." Id. (citations omitted). But they note that anti-inflammatory therapies have failed. Id. Recent studies in animal models of sepsis as well as in patients who died of sepsis and multiple organ failure have shown that sepsis induces extensive loss of lymphocytes through apoptosis or cell death. Id. The authors note that although they speculate that loss of lymphocytes is detrimental to survival in septic patients because of the resultant immunosuppression, it is possible that lymphocyte apoptosis was actually beneficial to the patient because it "may lead to decreased

production of proinflammatory cytokines, which induce or contribute to the systemic inflammatory response syndrome and organ injury in sepsis." Id. at 6963.

TESTIMONY

Tomasita Bragg, daughter-in-law of decedent, testified first for petitioner. Tr. at 8. Decedent lived with her and her husband for the last 13 years of his life. His typical day would be rising early, walking four miles, eating oatmeal, working out in the basement, and going rollerblading with his granddaughters or engaging in other activities with them. Tr. at 9. Decedent was a big, tall man. Tr. at 10. He was proud to say he was a Marine. Id. If decedent were not taking a walk, he was bicycling. Tr. at 11. He was physically strong. Id. Decedent was a workout freak. Tr. at 13. However, a year before the flu vaccination, when a neighbor gave him a large pumpkin over a fence, decedent's knees buckled and he could not pick the pumpkin up. Tr. at 31, 32.

Ms. Bragg said it was her and decedent's ritual on Saturdays to go to the flea market to eat. Tr. at 14. They went together to Kaiser to get the flu vaccination. Id. This was a drive-through flu vaccination. Tr. at 15. This was early in the morning. Id. They then drove to the flea market eight miles away to meet petitioner for breakfast. Tr. at 17. Decedent told her before they got to the flea market that his whole body hurt as if he had the flu. Tr. at 24. Decedent's color looked odd when they got there, a grayish yellow. Tr. at 17, 26. At breakfast, decedent did not eat all his food. Tr. at 17. Decedent said he was not feeling too good. Tr. at 18. He took the car and drove himself home. Id.

For two days, Saturday and Sunday, both Ms. Bragg and decedent were ill. Id. Decedent had nausea, fever, and chills. Tr. at 35. Decedent was just lying down, which he never did. Id. He did not want to eat anything. Tr. at 20. On Tuesday, petitioner took decedent to see Dr.

Hardee, and petitioner called her to come over because decedent was not feeling good. Id. Dr. Hardee said to take decedent to the emergency room, which they did. Tr. at 21. Decedent went downhill by the hour. Id. The only time she saw decedent's rash is when decedent was in the hospital emergency room. Tr. at 26, 27.

Dr. James T. Hardee, decedent's personal care physician, testified next. Tr. at 37. His specialty is internal medicine. Id. Decedent became Dr. Hardee's patient in 1999, one of Dr. Hardee's first patients after joining Kaiser in Denver. Tr. at 38. Decedent would come in for a physical but rarely for illness. Id. Decedent was notable to Dr. Hardee for being healthy. Tr. at 39. Dr. Hardee sees people who are chronically ill, elderly, or demented, with lots of problems, who come in quite often. Id. He sees a smaller subset of patients who come in infrequently and, when they do, they are healthy and doing great. They tend to come in just to get a pat on the back and encouragement to keep doing what they are doing, and hearing how well they are doing. Id. Decedent was in this latter category. Tr. at 40.

Decedent brought Dr. Hardee spreadsheets about his health: blood pressure, weight, etc. Id. Few patients do that. Id. Decedent did not have any chronic health problems except for very mild hyperlipidemia (elevated cholesterol), but not severe enough to warrant taking drugs for it. Id. Decedent also had pre-diabetes with very minimally elevated blood sugar, which also did not warrant treatment. Id. Other than some ear wax and some skin spots, that was it. Tr. at 41.

Decedent came to Dr. Hardee on October 31, 2006 for his annual physical. Id. The spreadsheet decedent brought with him showed he weighed himself as 163 pounds, but Dr. Hardee's office scale weighed decedent at 171 pounds. Tr. at 42. A discrepancy in home weight versus office weight is pretty common, and Dr. Hardee always takes a patient's home weight with a grain of salt. Id. Most people weigh themselves at home in their underwear. But in the

office, they are wearing clothes. Tr. at 43. His office does not ask them to empty out their pockets or take off their glasses or shoes when they get weighed. Id. Dr. Hardee noted a great deal of variability in the two weights for decedent on October 31, 2006, but he did not make anything of it. Id.

Dr. Hardee's notes for decedent's October 31, 2006 visit are clear that he was doing well, and quoted him as saying he felt great. Tr. at 44. Most patients, especially in their late 70s and early 80s, are not doing great. It was notable enough for him to write what decedent said into the record. Id. Dr. Hardee also wrote in the record that decedent was walking up to nine miles a day and riding his exercise bike, which was notable for an 82-year-old person. Id. Most people that age are not healthy, so the ones who are "are a blessing in our practice." Dr. Hardee said seeing someone like that "encourages and energizes myself." Tr. at 45.

After checking the patient's vital signs, Dr. Hardee does a head to toe examination. Tr. at 46. Decedent was in no apparent distress on October 31, 2006. He was alert and oriented. He had a lot of ear wax. His nose, carotid arteries, thyroid, and jugular veins were fine. His lungs were clear and his heart sounded fine. Id. His abdomen was soft and he did not have flank pain or chest wall pain, or swelling in his feet or ankles. Id. His only other notable finding beside the ear wax was toenail fungus (onchomycosis). Dr. Hardee checked him for a hernia and did a prostate examination, both of which were unremarkable. Id. Dr. Hardee said that it is unlikely he could have missed decedent's being sick at that visit if he had been sick. Tr. at 47.

Decedent did not exhibit to Dr. Hardee chronic cardiopulmonary disease. Id. Riding an exercise bicycle and walking nine miles a day would be inconsistent with cardiopulmonary disease. Id. Decedent's blood pressure was good and his pulse oximetry in the altitude of

Denver, being 94 percent, was normal for the area, although maybe a little low for sea level. Tr. at 48. Decedent did not show signs of emphysema. His lungs were clear. Id.

Dr. Hardee had no indication that decedent had vascular disease. Id. Dr. Hardee listened for carotid bruits in decedent's neck and did not find any. This means that he did not have blockage there due to atherosclerosis. Tr. at 49. Dr. Hardee mentioned the drive-through flu shot clinic to decedent during the October 31, 2006 visit. Id.

The next time Dr. Hardee saw decedent was a week later, on November 7, 2006. Tr. at 50. Decedent was surprisingly worse than he had been a week before. He was feverish, dehydrated, and weak, and in a wheelchair. Id. He put decedent in his clinic and had a nurse place an IV to give him fluids. He had blood drawn to do some lab work. Tr. at 51. Decedent's creatinine level (which is a kidney blood test) was higher than it had been a week earlier. It had jumped from 1.1 (normal) to 1.7, indicating some degree of kidney trouble, e.g., kidney failure, acute renal insufficiency, dehydration. Id. In addition, decedent's sodium level dropped. Sodium is an electrolyte. Tr. at 53. Decedent had an elevated white blood cell count of 13,000 which is consistent with an infection. Id. There was a left shift which means a predominance of neutrophils which are the acute infection fighting cells. That suggested a more acute infection. Tr. at 91. Dr. Hardee sent decedent to the emergency room. Tr. at 56. Decedent's fevers, malaise, dehydration, and elevated white blood cell count were all very consistent with an infection. Tr. at 59. Once elderly people become septic or have overwhelming infections, the kidneys can shut down and begin to fail. Tr. at 60.

When Dr. Hardee saw decedent on October 31, 2006, there was no indication that he was retaining fluid. Tr. at 61. His jugular veins were not distended. Id. There was no fluid in his ankles or feet. Tr. at 62. Someone could retain fluid due to ingesting too much salt, or due to

congestive heart failure, kidney failure, or cirrhosis of the liver. Id. Dr. Hardee never tested decedent for chronic obstructive pulmonary disorder (COPD) because he was riding an exercise bike and walking nine miles a day. Tr. at 63.

The hospital physicians diagnosed decedent with sepsis, pneumonia, and respiratory distress. Tr. at 64. Dr. Eric France oversees flu vaccinations, and Dr. Hardee noted on November 9, 2006 that he did not know if the flu vaccination caused decedent's sudden illness and death, but he wanted Dr. France to be aware. Tr. at 66. Decedent had also received flu vaccinations in 1999, 2003, 2004, and 2005. Tr. at 66-67. Decedent did not have an adverse reaction to any of those prior vaccinations. Tr. at 67.

When decedent saw Dr. Hardee on October 31, 2006, Dr. Hardee's nurse weighed decedent at 171 pounds. When decedent saw Dr. Hardee on November 7, 2006, his weight was listed as 156 pounds. Tr. at 67-68. The diagnosis was an abnormal loss of weight. Tr. at 68. There is more than one scale in Dr. Hardee's office. Id. Petitioner called Dr. Hardee's office on November 7, 2006 and said that decedent had been weak and tired for the prior 10 days. Tr. at 69. He reported that decedent's weight that morning had been 158 pounds. Id.

When decedent saw Dr. Hardee on November 7, 2006, Dr. Hardee states in his notes that decedent was alert, oriented, and answered questions appropriately. Tr. at 70-71. Dr. Hardee documented fever, achiness, weakness, and shakiness. Tr. at 71. Dr. McAninch, who is one of Dr. Hardee's partners, signed the death certificate, stating that decedent died from sepsis, resulting from pneumonia and renal failure. Tr. at 74.

Pneumonia can be bacterial or viral and means someone might have an infection in the lungs or have a pneumonitis. Tr. at 76. Pneumonia is a clinical diagnosis. Tr. at 77. Sepsis means an infection has overwhelmed the body and bacteria have entered the blood stream, with

the bacteremia causing multi-system organ failure and shutdown. Tr. at 78. Dr. France told Dr. Hardee about the VAERS reporting system. Tr. at 80.

As for petitioner's telling Dr. Hardee's nurse on November 7, 2006 that decedent had been ill for the prior 10 days, Dr. Hardee thinks the nurse got it wrong or wrote it wrong because seven days previously, when Dr. Hardee saw decedent on October 31, 2006, decedent was doing great. Tr. at 81. Decedent was placed on strong antibiotics in the hospital. Tr. at 82. On November 7, 2006, decedent's white blood cell count was 12.2 and the differential showed 79 percent polys, 10 percent bands, which is high, and eight percent lymphocytes. Bands are more acute type cells. Tr. at 92. The result is nonspecific in terms of a specific etiology. Tr. at 93.

Rhonda Lawson testified next for petitioner. Tr. at 99. Decedent was her grandfather. Tr. at 100. She saw him almost daily. Id. Decedent was an outdoorsman, always out for walks, bicycling, roller blading, and focused on staying healthy. Tr. at 101. He was healthy and muscular. Tr. at 102. The last day she saw him was the Friday before the flu vaccination and there was nothing out of the ordinary. Id. He ate like a horse and had to take a flight of stairs up from the basement where he lived in order to get to the bathroom and another set of stairs to the living room and dining room. Tr. at 103.

Ms. Lawson saw decedent the Monday after his flu vaccination and he was not feeling well. Tr. at 106. Before this illness, she would give decedent a 10 out of 10 for physical robustness. Tr. at 107. Because she saw him on Friday, November 3, 2006, the notation that he had been ill for the prior 10 days written on November 7, 2006 had to be wrong. Id. She saw him on Monday, November 6, 2006, when he was weak and lethargic. On Thursday morning, November 9, 2006, he was in the hospital, intubated and in a coma. He died that day. Tr. at 109. She recollects that the week of October 30, 2006, decedent went out biking each day. Tr. at 110.

Petitioner testified next. Tr. at 111. Decedent was the healthiest older person he has ever known. Tr. at 114. Decedent did not take one prescription drug. Id. Up to November 4, 2006, the date of the flu vaccination, decedent did not indicate to petitioner that he was not feeling great. Tr. at 115. On November 4, 2006, petitioner's wife and decedent met petitioner for breakfast at 9:00 or 9:30 a.m. after they had received flu vaccine. Normally, decedent would walk around the flea market after breakfast, but that day, he said he was not feeling well and drove himself home. Tr. at 116. On Sunday, November 5, 2006, decedent still was not feeling well. Id. Petitioner became concerned on Monday, November 6, 2006 when decedent would not eat soup and was very tired. He just wanted to go back to sleep. Petitioner asked him if he wanted petitioner to call a doctor, and he said to wait a week. Tr. at 117.

On Tuesday, November 7, 2006, petitioner noticed that decedent was extremely tired but also shaky and weak. Petitioner decided to call Dr. Hardee's office. He spoke to Nurse Pam Kangge and gave her decedent's symptoms, and they agreed he could bring decedent into the office in the afternoon. Tr. at 118. He asked decedent how long he had been tired and weak, and he replied maybe a week to 10 days, and he thinks Nurse Kangge wrote down 10 days. Id. At that time, decedent was in pretty bad shape and not thinking too well. All he wanted to do was sleep. Id. When he went to get decedent to go to the doctor, decedent was sound asleep. He helped him to dress and helped him up the stairs. When they got to the doctor's office, he had to get a wheelchair to get decedent to the office because he was extremely weak and almost incoherent. Tr. at 119.

When Dr. Hardee saw decedent, he asked him what happened to him because he had just seen him a week earlier and he was fine. Id. He gave decedent an IV and some Tylenol, after which decedent perked up a bit. Id. The time decedent started to track his weight and other vital

statistics was after Dr. Hardee told him he was pre-diabetic. Tr. at 120. On October 31, 2006, he weighed 163 pounds. He would weigh himself in the morning in his underwear before he ate or drank anything. Tr. at 121. On November 7, 2006, petitioner weighed decedent at home and he weighed 156 pounds and he was dressed. At Dr. Hardee's office, they weighed him at 160 pounds. Id. Decedent had not been eating and was very dehydrated. Tr. at 121-22. Before his flu vaccination, decedent appeared to be fine and was eating and drinking normally. Tr. at 123.

Between the time decedent received flu vaccine on Saturday, November 4, 2006, and Tuesday, November 7, 2006, when petitioner brought decedent to Dr. Hardee's office, petitioner noticed that decedent would occasionally come from his bedroom in the basement up the stairs to use the bathroom on the next level and then go down again to his bedroom in the basement. Tr. at 140. Petitioner would see decedent walking up the stairs pretty slowly and heading for the bathroom, and asked decedent how he was doing. He replied not too good and that was it. Id.

It took 30 minutes to get to the emergency room. Tr. at 124. They took decedent's vital signs and put him on oxygen. Id. When decedent took his clothes off, they saw the rash on his chest. His eyes were pink around the eyelids. Tr. at 125. Dr. Paik took a history and wrote down that decedent had been ill a week. Id. Petitioner disagreed with his wife about when decedent dropped the pumpkin that a neighbor passed over a fence. Petitioner said it occurred in 1993 or 1994. Tr. at 127.

In the hospital, decedent started shivering. Tr. at 128. He had a temperature of 103 or 104 degrees. Id. Petitioner and his wife returned on Wednesday, November 8, 2006, and asked decedent how he had slept. He replied not well because he had trouble breathing. Id. The hospitalist said the hospital staff thought decedent had either bacterial or viral pneumonia and they were going to take some cultures which would take 48 hours to develop and, in the

meanwhile, put him on antibiotics. Id. Later, the hospital put decedent on a ventilator. Tr. at 120. In the evening, a nurse said to be prepared for the worst. Id. The nurse called him at 4:30 a.m. and told him to come back to the hospital. Tr. at 130. All of decedent's organs had failed. They decided to take decedent off the ventilator and he survived for five to 10 minutes and then died. Tr. at 131. Afterwards, Dr. Brown said that all the cultures and tests on decedent were negative. Tr. at 136.

Dr. Alan S. Levin testified next for petitioner. Tr. at 147. He is board-certified in allergy and immunology, and clinical pathology. Tr. at 149. He is also a founding member of the American College of Emergency Physicians but is no longer active in the group. Id. He went to law school and became an attorney. He is licensed to practice law in California, Nevada, and Texas. Id. He mostly practices law and is also involved in patent law. Tr. at 149-50. He also serves as an expert witness in tort and vaccine cases, but 90 percent of his income comes from being a lawyer. Tr. at 150.

Respondent's counsel conducted a voir dire of Dr. Levin. Tr. at 153. The last time Dr. Levin worked more as a physician than as an attorney was in 1993. Id. He sees patients only on referrals. Id. He does medical testing and lab testing and is current on immunology. Id. He sees patients in a colleague's office because he does not have his own office. Id. He is involved in a biotech company in China. Tr. at 155. He is exploring the therapeutic use of cytokines to treat cancer, infectious diseases, and obesity. Tr. at 156. He has been described in the past as a junk scientist and has stated that some drug companies are corrupt. Id. In a non-vaccine case, a court excluded his testimony as speculative and unreliable. Tr. at 158. Respondent's counsel, after an extensive voir dire, had no objection to Dr. Levin's being admitted as an expert in immunology and pathology. Id.

Dr. Levin's opinion is that flu vaccination was a substantial contributor to decedent's death and, but for the flu vaccination, decedent would not have died when he did. Tr. at 159. Decedent had all the findings consistent with aging: atherosclerosis, and some pulmonary and cardiac issues. Tr. at 160. But decedent was apparently compensating very well until he received flu vaccine. A vaccine requires cytokine production to be able to create an immune response, but in decedent's case, this cytokine production also dysregulated his cardiovascular, renal, and vascular systems, leading to a cytokine-induced death. Id. This is a fairly common occurrence and not an unusual phenomenon. Id.

Cytokines are generally proteins that work as second messengers. They interact with certain receptors causing cells to react, either to produce more or less protein, and to move in one or another direction, to release certain mediators of inflammation. Id. Cytokines are hormones that cause inflammation. Tr. at 161. Under normal circumstances, inflammation is good. Id. Inflammation is the means by which we rid ourselves of damaged cells and protect ourselves from pathogens. It is even the way we regulate the size and shape of our organs. Id. But when cytokines become dysregulated in people such as decedent who are very fragile, they can cause a cascade, i.e., the type of chain reaction that decedent developed. Id.

Sepsis is a cytokine reaction. Id. It is the body's reaction to toxins being secreted by bacterium. Id. The clinical symptoms recognized as sepsis, e.g., low blood pressure, fast heart rate, fever, and rashes, are cytokine-induced disorders provoked by bacteria initially and/or viruses. Tr. at 161-62. Damaged cells can also provoke the same kind of phenomenon. Tr. at 162. A crush syndrome, whereby someone gets hit by a car and survives but the crushed tissues cause the immune system to become hyperactive, produces the type of clinical syndrome which decedent in this case had. Id.

Petitioner's Exhibit 12, the article from the New England Journal of Medicine about cytokine storm after a phase one trial of an anti-CD28 monocolonal antibody, is relevant. Id. Before this phase one trial, doctors had never seen pure cytokine-induced disease in people. Id. In this phase one trial, this particular disease process was provoked by directly activating the cells that secrete cytokines, and it shows what cytokines do when they are dysregulated. They cause the syndrome which is quite similar to the illness which decedent had. Tr. at 163. We now know that what we used to think was caused by bacteria, fungi, or viruses is really the body's response to the etiologic agent. In other words, this article shows dysregulation of this particular system and its side effects, some of which look like pneumonia but obviously are not because there were no organisms involved. Id.

In this process, the heart, kidneys, lungs, brain, and muscles are involved, which is multi-organ system failure. Tr. at 164. The undersigned asked Dr. Levin why he called decedent fragile since his family and personal physician had described him as having exceptional good health. Tr. at 164-65. Dr. Levin said he called decedent fragile because of the x-ray findings and his having atherosclerosis. He was 82 years old. Tr. at 165. He was very well compensated and doing well, but he could not handle vaccination as well as someone in his 50s. Tr. at 167. Decedent had an adverse reaction which progressed to his death. Tr. at 167-68.

The undersigned inquired if Dr. Levin meant by "well compensated" that, although decedent had these chronic illnesses which are common in the elderly, in some way, his body was able to hold these illnesses at bay until the cytokine elevation. Tr. at 168. Dr. Levin agreed. Id. Dr. Levin believes that the hospital diagnosis of decedent having an infection was appropriate based on the available evidence that his white count was elevated with a left shift. Id. However, Dr. Levin said decedent did not have bacterial sepsis. Tr. at 169. The hospital's

blood cultures were negative for bacterial infection. Id. Dr. Levin has run a clinical laboratory and done a lot of cultures. It is uncommon to have a negative blood culture and have sepsis. Id. Decedent was not started on antibiotics until the hospital drew blood for the cultures. More than likely, decedent did not have sepsis. Id.

Dr. Levin testified that even if decedent did have sepsis, the sepsis was probably the end product of shock because nearly everyone dies when our gastrointestinal tract is no longer being perfused and the bacteria in the gastrointestinal tract releases E. coli causing septic shock. Id. At the time decedent was sick, he was not septic or at least he did not have bacteria circulating. Id. All the viral cultures the hospital did were also negative. Tr. at 169-70. More likely than not, Dr. Levin said, when decedent suffered from his terminal illness, he was not yet septic. Tr. at 170. Normally, our immune systems protect us from the bacteria that are in our gastrointestinal tract. Tr. at 170. Our immune systems function because we can perfuse the ducts with oxygen and carry away carbon dioxide. When the heart stops functioning and the gastrointestinal tract ceases to be perfused, the organisms from the gastrointestinal tract get into the peripheral circulation and secrete endotoxins, causing death. Id.

Dr. Levin explained decedent's 13,000 white blood count elevation with a left shift and 10 percent bands was caused by the dysregulated cytokines, not bacteria. Tr. at 170-71. Dr. Levin does not know why decedent's 2006 flu vaccination resulted in a cytokine storm, but his 1999, 2003, 2004, and 2005 flu vaccinations did not. Tr. at 171-72. It depends on the nature of the vaccine. Tr. at 172. Every year, the flu vaccine is different. Id.

Decedent's cytokine storm was a result of the flu vaccine and his age. Id. Most people who receive flu vaccine get flu-like symptoms, indicating cytokine release. But most of them

can control it because most people are not fragile. But decedent apparently was quite fragile and could not control the cytokine release which began to cascade leading to his death. Id.

Dr. Levin testified that the onset of decedent's illness was consisted with the flu vaccine causing the cytokine cascade especially since he had been vaccinated before. Tr. at 173. His prior vaccinations meant he was going to have a vigorous response to the flu virus as well as a vigorous cytokine response. Healthy people can have the onset of those symptoms 90 minutes after vaccination. Id. Dr. Levin stated that if decedent had not received flu vaccine, this cytokine storm, resulting in multi-organ system failure and death, would not have occurred at the time it did. Id.

Dr. Levin stated that sepsis is a generalized inflammatory response. Tr. at 175. In bacterial sepsis, the bacteria create toxins which evoke cytokines. The cytokine storm, not bacteria, caused the symptoms decedent had. Id. In the end, unless someone is in a plane crash, everyone dies from bacterial sepsis because, when the heart stops, the gastrointestinal tract is no longer perfused, and the bacteria emerge and cause sepsis. Tr. at 176-77. Decedent's heart stopped not because of bacteria. Tr. at 177. Decedent's pneumonia was also not bacterial or viral but a result of the cytokine storm. Id. All his cultures for bacteria and viruses were negative. Id. The standard of care for good medical practice is to take the cultures before administering antibiotics. Tr. at 178. This is the same type of pneumonia that the test subjects in the monoclonal antibodies clinical trial experienced, except for one subject who had bacterial pneumonia. Tr. at 179.

The hospital did not find any positive culture, but even if it had, decedent was well compensated and, if he did have a minor upper respiratory infection, the vaccination made it worse, which is also well-documented. Tr. at 180. It is possible that decedent had a subclinical

infection at the time he was vaccinated. Tr. at 195. An acute infection would be a new onset phenomenon. Tr. at 197. A shift to the left in the white blood cell count means that the neutrophils and bands, which are the cells that are very active in antibacterial infections, were elevated. Id. But this can also happen with an increased production of certain cytokines. Id. Chemotactic factors were being secreted by certain cells to recruit these neutrophils into the area. Id. Cytokines can cause the massive production of neutrophils and the release of these cells from the spleen and the lymph nodes. Tr. at 198.

Dr. Levin stated that cytokines caused decedent's rash. Decedent had a generalized vasculitis. Dysregulated cytokines cause an inflammatory process which affects the endothelial cells in the blood vessels, causing them to die, leak, and swell, and causing rashes and pulmonary infiltrates. Tr. at 181. Cytokines are hormones because they are regulatory molecules. They regulate growth and differentiation, and the status of blood vessels. Tr. at 182. Dysregulation resulting in a cytokine storm occurred in this case because of decedent's reaction to flu vaccine. Id. Besides the vasculitis and pulmonary infiltrate, the cytokine storm caused brain and kidney problems, resulting in a cessation of kidney function. Tr. at 184. The cytokine storm is a dysregulation of the cytokine cascade. Id. One molecule will turn on the production of another molecule which continues the process. Each of these segments is heavily regulated by other molecules so that the cascade is well controlled. Id. When this control becomes dysregulated, we see damage. Tr. at 184-85. The cascade is the biochemical sequence of events. When the cascade goes out of control and too fast, it produces the storm. Tr. at 185.

Dr. Levin testified that the symptoms of cytokine storm are generally the same: weakness, fever, lethargy, disorientation, rash, and difficulty breathing. Tr. at 188. The hospital's use of broad spectrum antibiotics in this case before getting the results of the blood

cultures done on decedent was absolutely correct. Tr. at 190. Decedent's genetic make-up also had something to do with his response to the vaccine and his death. Id. "But given the nature of cytokine storm, probably by the time it got to be uncontrollable, virtually anybody would have had the same clinical outcome that he did." Id. Dr. Levin attributes decedent's weight loss to his dehydration and not eating. Tr. at 191. He was also febrile and burning up a lot of tissue. Id.

Dr. Levin stated that decedent had two long-term morbid processes that preceded his vaccination, atherosclerosis and chronic changes in his lungs, which made him fragile. Tr. at 201. Being fragile, however, does not mean decedent was ill because, in decedent's visit to Dr. Hardee, he described himself as walking miles, his respiratory system was functioning normally, and his pulse oximetry was normal. Tr. at 203.

Exhibit 12 deals with a clinical phase one trial of a monoclonal antibody that caused cytokine storm without the presence of a virus or bacterium. Dr. Levin testified this is relevant to flu vaccine initiating a cytokine storm since this article is the first report of a pure cytokine storm without bacterial or viral causality. He said this article helps explain how flu vaccine can cause the same type of reaction. Tr. at 204. The answer is that flu vaccine causes cytokines, and cytokines can cause these symptoms. Id. The aim of the drug trial was to use cytokines to enhance treatment for cancer patients. Id.

Dr. Levin's opinion is that decedent had a cytokine response immediately upon receiving flu vaccine. Tr. at 205. Cytokine response was the goal of administering flu vaccine. Id. At some time when decedent sequestered himself in the basement where he lived and stopped eating and drinking, his cytokine response turned into a cytokine storm and went from curable to incurable. Id. His condition became irreversible some time around Monday, November 6, 2006. Tr. at 205-06. Decedent was not terminally ill at that point. He was able to walk and get up and

eat. He could communicate on November 4th and 5th. On the 6th, he had a funny color, and was taken to the hospital on the 7th. Tr. at 206. How fast a cytokine storm occurs depends on the individual and what is provoking the storm. Tr. at 206-07. It can happen within hours and within days. Tr. at 207.

Dr. Levin said there are multiple entries in decedent's medical records about the flu vaccine, which resulted in the issuance of a VAERs report. Id. Obviously, some medical personnel considered the vaccine involved in decedent's death. Tr. at 207-08. Dr. Levin stated the history of decedent's having received flu vaccine was important enough to be in the medical records. Tr. at 209. It was Dr. Hardee's nurse who filled out the VAERS report after Dr. France spoke to Dr. Hardee about it (subsequent to Dr. Hardee's communicating what happened to decedent to Dr. France). Id. Dr. Levin does not disagree that decedent's cause of death was sepsis with lung and respiratory distress because that is precisely how he died. Tr. at 210. The vaccine was the cause of these conditions because of the cytokines provoked from the vaccination, and the cause was not bacteria or viruses. Tr. at 210-11. Sepsis can occur in the absence of positive lab tests and cultures, but it is rare. Tr. at 211.

Decedent was aging and he was not able to handle the adverse effects of the cytokines invoked by the vaccine. Tr. at 214. The vaccination is the only thing that could have caused what happened to decedent. Tr. at 215. There is no difference between the cytokine storm evoked in the monoclonal antibody phase one trial and the cytokine storm evoked in decedent after vaccination. Tr. at 217.

Dr. Lawrence D. Frankel testified for respondent. Tr. at 221. He is retired from the practice of pediatrics, allergy and immunology, and pediatric infectious disease. Tr. at 223. He last took care of patients five years ago. Id. When he did practice, he treated patients with sepsis

and pneumonia. Id. This was Dr. Frankel's first time testifying in a Vaccine Act case. Tr. at 224. He spends 30 to 40 percent of his time teaching, 10 percent of his time on research, 15 percent of his time in various administrative duties, and the rest of his time on personal matters. Id. He was offered as an expert in immunology and infectious diseases. Id.

Dr. Frankel's opinion is that decedent's flu vaccination had nothing to do with his illness and death. Tr. at 226. He stated that, just as Dr. Levin testified, cytokines are extremely common and are really the worker bees of the immune system. Id. They transmit signals between immune cells and between cells and target cells of the human host. Tr. at 226-27. Cytokines are both regulatory and stimulatory, and are necessary for the natural and effective functioning of the immune system. Occasionally, they become dysregulated as Dr. Levin testified and can cause harm. Tr. at 227. When cytokines become dysregulated, hundreds if not thousands are released and do appreciable harm to the human host, as manifested by hypotension, vascular collapse, organ failure, erythematous rash, subterfused lungs, brain edema, diarrhea, abdominal pain, renal failure, etc. Id.

Dr. Frankel stated that every immune reaction is mediated by a cytokine response or multiple cytokine responses. Tr. at 227-28. The immune system relies on cytokines to combat foreign invaders such as bacteria, viruses, or cancer. Tr. at 228. To the best of Dr. Frankel's knowledge and the best of his analysis of the medical literature, there is no description of a flu vaccination causing cytokine storm. Id. Dr. Frankel thought it illogical for a killed virus flu vaccine with limited antigenicity, and which was specifically developed to produce B-cell immune responses, to cause a cytokine storm. Id. His fellow immunologists do not discuss cytokine storm as a type of mechanism of injury arising from flu vaccination. Id.

Petitioner's Exhibit 12, the article about monoclonal antibody provoking a cytokine storm in a phase one trial, describes hyperactivity manifestations occurring within about two hours of injection and persisting for two days. Tr. at 229-30. The antibody that provoked this cytokine storm is known to hyperstimulate certain cells that participate in controlling and elaborating cytokines. Tr. at 230. After two days, the disease process either quiets down or kills the patient with disastrous end organ damage. Id. The article describes the trial subjects having lymphocytosis (an increase in white blood cells). Decedent in the instant action, however, had lymphopenia (a decrease in white blood cells). Tr. at 233. One tends to see more lymphopenia in bacterial or viral infections. Lymphocytosis is a phenomenon of cytokine storm because of the stimulatory activity of cytokines. Id.

Dr. Frankel stated that millions of people receive flu vaccination without a pattern of adverse reaction suggestive of cytokine storm occurring. Tr. at 231. He did not believe that decedent died due to cytokine storm and stated his death was not due to flu vaccination. Decedent was elderly with co-morbid conditions. Id. If decedent had cytokine storm, it should have occurred more quickly after the vaccination, and he should have had other symptoms earlier. Tr. at 232. A fragile individual would not be able to sustain a cytokine storm for three days before going to the doctor. Id. Dr. Frankel does not believe decedent's sepsis was related to the vaccination. Tr. at 234.

Dr. Frankel stated that, in the past five or 10 years, doctors have realized they should not be diagnosing sepsis because the term implies a bacterial etiology, but rather should diagnose an individual as having a systemic immune response syndrome. Tr. at 236. That syndrome can include damage, cytokine release, and end organ failure caused not only by bacteria, but also by viruses, trauma, burns, and certain immunologically mediated diseases. Id. Many of the older

doctors talk about sepsis as if it were the same as systemic immune response syndrome, and they know it can be caused by viruses, trauma, burns, and other things. Id. The community-acquired sepsis with which decedent was diagnosed in the hospital means he acquired pneumonia outside, not inside, the hospital and it progressed to sepsis. Tr. at 236-37.

Dr. Frankel thinks that flu vaccine decreases a person's risk of acquiring sepsis because it prevents influenza disease, which can be followed by a number of severe bacterial infections from streptococcus, staphylococcus, and haemophilus influenzae, which are bacteria associated with influenza virus disease. Tr. at 237. Influenza vaccine decreases not just the incidence of influenza disease but also sepsis and other complicated conditions. Id.

Decedent's course is consistent with sepsis, which is end organ failure that came from cytokine release. Tr. at 238. He had hypotension, dehydration, neutrophils, respiratory distress, pulmonary involvement, renal involvement, renal shutdown, and renal compromise, all consistent with sepsis. Id. He had a positive chest x-ray, low oxygenation, increased respiratory rate, and fever, all consistent with pneumonia. Id. In people with pneumonia, viral and bacterial cultures yield a diagnosis only 25 percent of the time. Id. Thus, in 75 percent of cases, one will fail to diagnose a specific etiology. Id.

As for the weight discrepancies, Dr. Frankel said that it may well be that scale variability explains the six pounds of weight decedent seemed to have gained plus being undressed at home and dressed in Dr. Hardee's office while being weighed. Tr. at 239. That decedent lost weight between his visits to Dr. Hardee's office on October 31, 2006 and November 7, 2006 indicates decedent was ill. Tr. at 240. Decedent was becoming dehydrated. He was not taking fluids and was not eating. He was resting and staying in his basement apartment, slowly going downhill. Id.

Dr. Frankel agreed with petitioner's expert Dr. Levin that decedent was fragile and that an 82-year-old can be subtly fragile. Id. There can be asymptomatic, unrecognized, and perhaps even unrecognizable co-morbid conditions occurring that can manifest themselves when the host is stressed in a drastic fashion. Tr. at 240-41. He can see where decedent's family could regard decedent as strong and vigorous and not be aware, and even decedent not be aware, that subtle things are occurring that manifest adverse unhealthy processes. Tr. at 241.

Dr. Frankel believes that if epidemiology does not support causation, there is no statistically valid causal relationship. No epidemiologic study has causally connected flu vaccine with sepsis. Tr. at 242. Influenza vaccine is composed of neuraminidase and hemagglutinin which are isolated and genetically modified to elicit antibodies. Tr. at 243. They turn on B cells so they will make antibodies and prevent subsequent infection with live viruses. Id. The nature of this vaccine is not a hyperstimulating agent that could or should be associated with cytokine storm. Id.

Dr. Frankel agrees that decedent had multi-organ system failure. Tr. at 247. He does not think decedent's case manifests a classic cytokine storm. Tr. at 248. Dr. Frankel believes that decedent had what used to be caused sepsis but is now called systemic inflammatory response syndrome. Id. It can be a response to bacteria, viruses, or trauma. Tr. at 248-49. In decedent's case, we do not know to what it was a response because the hospital could not culture out a virus or a bacterium. Tr. at 249. Decedent's co-morbid conditions made him vulnerable. Id. To Dr. Frankel, decedent's systemic inflammatory response was a response to an unknown. Tr. at 251.

Dr. Frankel said that science, epidemiology, and an appreciation of human biology suggest that the cause was not the vaccine but something else. Tr. at 252. Decedent's manifestations of disease were not indicative of a cytokine storm. Id. The time frame and

characteristics of the manifestations were different from a cytokine storm. Id. A cytokine storm starts immediately or almost immediately after the antigenic challenge. Tr. at 253. Decedent did not feel well 30 minutes after his vaccination, but there is a difference between not feeling well and getting sick in both the quantity and quality of response. Id.

Dr. Frankel stated that what happened to decedent did not start like a cytokine storm, but was slower in onset. A cytokine storm is precipitous, rapid, and dramatic in onset. Tr. at 255. His opinion is based upon reading because he has seen very few patients having cytokine storm. Tr. at 256. Dr. Frankel disagrees with Dr. Levin that decedent had Stevens-Johnson syndrome because its pattern and causation are different. Tr. at 257.

Dr. Frankel interprets petitioner's Exhibit 12 to be saying that cytokine storm progresses to a systemic inflammatory response and, by looking at cytokine storm, we can understand systemic inflammatory response better, but they are not identical. Tr. at 261. The difference between the clinical trial participants and decedent was the notably early acute lung injury and marked lymphopenia in the drug trial participants. Tr. at 262. A cytokine storm has as its end point systemic inflammatory response, which used to be called sepsis. Tr. at 263.

The undersigned asked Dr. Levin if he agreed with Dr. Frankel that a cytokine storm would have to occur earlier than it did in decedent. Tr. at 263. Dr. Levin said that petitioner's Exhibit 12 showed that although the test subjects began to complain about feeling bad within 90 minutes of receiving the monoclonal antibody, they began to have really serious critical problems 12 to 16 hours later, which is quite consistent with decedent's course. Tr. at 264. In addition, cytokine storm is a variant of systemic inflammatory response. Id. He said decedent's course is absolutely consistent with cytokine storm. Id.

Dr. Levin testified on rebuttal for petitioner. Tr. at 268. He stated there is a spectrum of cytokine cascade and cytokine storm. The magnitude of the storm and the frailty of the patient are factors determining the outcome. Tr. at 270. In most cases, a cascade is a normal phenomenon, just a chemical process. But when the cascade becomes dysregulated, it becomes a storm. Tr. at 271.

Dr. Frankel was recalled for respondent. Tr. at 273. The epidemiological paper upon which Dr. Frankel relied which failed to show a cytokine reaction to flu vaccine had a sample size of 114 people. Tr. at 275. He agreed that a cytokine storm is a very, very rare event. Tr. at 276. A cytokine storm is even rarer than being struck by lightning. Tr. at 278.

DISCUSSION

To satisfy his burden of proving causation in fact, petitioner 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:

> While this case involves the possible link between [tetanus toxoid] vaccination and central nervous system injury, a sequence hitherto unproven in medicine, 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.

418 F.3d at 1280. The Federal Circuit in Althen affirmed the finding of the judge that the special master erred in dismissing the case, and the judge's holding that petitioner's tetanus toxoid "vaccination caused her central nervous system demyelinating disorder." 418 F.3d at 1282.

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.

"Petitioner need not show that the vaccine was the sole or predominant cause of her injury," just that the vaccine was a substantial factor in causing her injury. De Bazan v. Sec'y of HHS, 539 F.3d 1347, 1351 (Fed. Cir. 2008).

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.

The Federal Circuit in Capizzano emphasized that the special masters are to evaluate seriously the opinions of the vaccinee'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).

The Federal Circuit stated in Knudsen that "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." 35 F.3d at 548. The undersigned's task is to determine medical probability based on the evidence before the undersigned in this particular case. Althen, 418 F.3d at 1281 ("judging the merits of individual claims on a case-by-case basis").

The Federal Circuit in Knudsen also stated: "The special masters are not 'diagnosing' vaccine-related injuries." 35 F.3d at 549.

As for epidemiological support for causation, the Federal Circuit in Knudsen ruled for petitioners even when epidemiological evidence directly opposed causation from DPT vaccine. 35 F.3d at 551. The case concerned the cause of a baby's encephalopathy after a vaccination.

Respondent provided evidence that more encephalopathies are caused by viruses than by vaccines, convincing the special master to rule against petitioners. Id. at 546. Even though epidemiological evidence supported respondent's view that viruses are more likely to cause encephalopathy than vaccines, the Federal Circuit held that that fact alone was not an impediment to recovery of damages. The Federal Circuit stated:

> 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.

Id. at 550.

The special masters "are entitled–indeed, expected–to make determinations as to the reliability of the evidence presented to them and, if appropriate, as to the credibility of the persons presenting that evidence." Moberly v. Sec'y of HHS, 592 F.3d 1315, 1325 (Fed. Cir. 2010).

Under the three Althen prongs, petitioner needs to prove a medical theory connecting flu vaccine and illness and death (the "can it?" question), a logical sequence of cause and effect that flu vaccine caused decedent's illness and death (the "did it?" question), and a medically appropriate temporal relationship between vaccination and onset. Knudsen, Althen, Capizzano.

Here, respondent's expert Dr. Frankel agreed with petitioner's expert Dr. Levin that an immunologic challenge can lead a fragile, elderly person to experience systemic inflammatory response syndrome causing multi-organ failure leading to death. The only difference between Dr. Levin's opinion and Dr. Frankel's opinion is that Dr. Levin identifies that immunologic challenge as decedent's flu vaccination and Dr. Frankel says he does not know what the immunologic challenge was, but it was not the flu vaccination.

Althen Prong One

The first prong of Althen is can influenza vaccine cause illness and death. Petitioner's expert Dr. Levin relied heavily on the striking results of an experiment in a phase one trial of a monoclonal antibody administered to six volunteers, resulting in acute lung injury and multi-organ failure in the absence of any infection, i.e., bacterium, fungus, or virus, as described in the article petitioner filed as Exhibit 12. Dr. Levin's point was that flu vaccine, being an immunologic challenge, can in susceptible recipients, create cytokine dysregulation. All vaccines are supposed to produce an immunologic response which takes the form of cytokines. But if a cytokine stimulus becomes dysregulated, the consequence is a cascade and then a storm of cytokines, leading to multi-organ failure and death.

Dr. Frankel stated that flu vaccine, being a killed virus vaccine, could not produce cytokine dysregulation, cascade, and storm. The components of the virus in the vaccine cannot be equated with the monoclonal antibody used in the phase one trial that is described in Exhibit 12.

The undersigned has heard respondent's experts in other cases testify that influenza vaccine cannot cause various reactions because it is a killed virus vaccine. The undersigned has not found this testimony persuasive. In Brown v. Sec'y of HHS, No. 09-426V, 2011 WL 5029865 (Fed. Cl. Spec. Mstr. Sept. 30, 2011) (flu vaccine and upper respiratory infection caused acute disseminated encephalomyelitis), and Mouille v. Sec'y of HHS, No. 05-1204V, 2009 WL 4456207 (Fed. Cl. Spec. Mstr. Nov. 17, 2009) (flu vaccine and upper respiratory infection caused encephalitis), the undersigned ruled that flu vaccine can and did cause neurological disease in the context of upper respiratory infection.

In Brown, one of respondent's experts, Dr. Thomas P. Leist, testified that there is no evidence that flu vaccine, which is an inactivated vaccine and not a live-virus vaccine, can cause encephalitis or inflammation of the brain. 2011 WL 5029865, at *25. However, on cross-examination, Dr. Leist said he accepted that a vaccine could potentially cause a demyelinating injury. Id. at *27. Respondent's other expert in Brown, Dr. Raoul L. Wientzen, testified he does not believe it is biologically plausible for influenza vaccine to cause acute disseminated encephalomyelitis (ADEM). Id. at *33. He did admit that vaccines can occasionally cause neurologic problems, and that it is proven that flu vaccine can cause peripheral neurologic disorders. Id. He thought there was insufficient evidence to confirm or deny that flu vaccine can cause central nervous system disorders, although it could potentially happen very rarely. Id. He routinely asks his patients if they have had any recent vaccinations before seeing him. Id.

The undersigned mentioned that there had been lengthy discussion at the hearing of the increased incidence of Guillain-Barré syndrome (GBS) after swine flu vaccination, which was confirmed epidemiologically. Swine flu vaccine was a killed-virus (or inactivated) vaccine which caused a demyelinating illness. Id. at *41. Respondent's experts' opinion that flu vaccine cannot cause neurologic illness was contrary to the conclusions of two epidemiological studies filed into evidence showing that swine flu vaccine caused a greater incidence of GBS among vaccinees than among the unvaccinated. Id. at *42. In addition, other medical literature petitioner filed supported the opinion that flu vaccine can cause ADEM. Id. An excerpt petitioner filed from the Institute of Medicine's 1994 book on vaccine causality states it is biologically plausible for inactivated viral vaccine to induce an autoimmune response in a susceptible host. Id. The undersigned held in Brown that flu vaccine can cause ADEM based on

petitioner's expert's testimony, various articles, case reports, and epidemiological studies. Id. at *43.

In Mouille, one of respondent's experts, Dr. Max Wiznitzer, testified that an inactivated vaccine, such as flu vaccine, cannot cause encephalitis because it is not an infectious organism. 2009 WL 4456207, at *9. He admitted that flu vaccine can cause a low-grade fever as well as aching during the evening of the vaccination. Id. He agreed that swine flu vaccine can cause GBS. Id. Respondent's other expert in Mouille, Dr. Neal A. Halsey, testified that it is not biologically plausible for flu vaccine to cause encephalitis or meningoencephalitis. Id. at *10. He denied that administering flu vaccine to a child with a mild upper respiratory infection can make the infection worse. Id. The undersigned held in Mouille that the child vaccinee was vulnerable to an immunologic assault, and that both the upper respiratory infection and the flu vaccine caused his meningoencephalitis. Id. at *14.

The undersigned regards respondent's Exhibit C in the instant action to be instructive on the question of whether flu vaccine can lead to severe illness and even death among the elderly who have co-morbid conditions. (Decedent in the instant action had co-morbid conditions, hence both parties' experts testified he was fragile.) The article is entitled "Death and serious illness following influenza vaccination: a multidisciplinary investigation." This investigation was prompted by the occurrence of four deaths and four serious illnesses among 114 residents of a long-term care facility who had recently received flu vaccine, in addition to two other deaths arising from the same flu vaccine lot administered at a nearby physician's office. All eight of the long-term care facility residents had chronic medical conditions. One patient initially reported as seriously ill after flu vaccination subsequently died, making a total of five deaths under investigation.

During a two-week follow-up period after vaccination in the long-term care facility, 13 vaccinated residents and one unvaccinated resident had a medically attended event. The incidence rate for medically attended events was about twice as high among the vaccinated residents as among unvaccinated residents. This difference between the rates of illness among vaccinees compared to the unvaccinated was not statistically significant, leading the authors of the article to conclude that there was no causation from flu vaccine involved. However, they admitted that it was difficult for them to assess thoroughly the possibility of vaccine causation of serious adverse event clusters when the vaccinated population had an increased risk of hospitalization and death due to age and co-morbid conditions. They thought that the fact that the ill, elderly vaccinees had inconsistent patterns of symptoms, signs, or onset meant there was no causal relationship to the vaccine. To the undersigned, however, the difference in onset, symptoms, or signs can be due to the underlying co-morbidities of these elderly residents.

The undersigned is not constrained by a lack of statistical significance as the Federal Circuit in Knudsen, Althen, and Capizzano has stated that petitioner does not have the burden of supporting his allegations with epidemiological studies in order to prevail. The fact that flu vaccination resulted in almost twice as many illnesses and death among the elderly compared to the unvaccinated elderly indicates to the undersigned that flu vaccination put the elderly at increased risk of developing adverse reactions, not only because of their advanced age, but also due to their co-morbid conditions.

In addition to respondent's Exhibit C, petitioner's other two submissions, Exhibits D and E, are informative because, although they do not refer to flu vaccines, they do address systemic inflammatory response syndrome, what used to be called sepsis, which can occur in circumstances not involving bacteria or viruses. The issue in the instant action was whether flu

vaccine (which is not a bacterium or a live virus) can cause sepsis, or systemic inflammatory response syndrome. The purpose of the authors writing what is filed as Exhibit D was to change the medical community's use of the term "sepsis" in order to encompass other causes of multi-organ failure besides bacterial infection. Using the term "systemic inflammatory response syndrome," the members of the American College of Chest Physicians stated that this process can occur from the response of the host to an indirect insult to the system. Exhibit E provides the information that immunosuppression occurs in sepsis, a process representing a state of uncontrolled activation of the inflammatory cascade resulting in cell and organ injury.

Based on the testimony of Dr. Levin, and the three articles respondent filed, particularly Exhibits C and D, the first of which deals with the excess occurrence of serious adverse events among elderly vaccinees, and the second of which redefines sepsis as systemic inflammatory response syndrome which can be caused from noninfectious agents, as well as the undersigned's previous experience with inactive viral vaccines causing neurologic as well as non-neurologic adverse reactions, the undersigned rules that flu vaccine can cause systemic inflammatory response syndrome, previously known as sepsis, in the elderly who, not only because of their age but also their co-morbid conditions, may die from their reaction.

Althen Prong Two

Having held that flu vaccine can provoke systemic inflammatory response syndrome, previously known as sepsis, in the elderly who, because of age and co-morbid conditions, may die from their reaction, the next question is did flu vaccine cause decedent's illness and death in this case? Dr. Levin described a medical theory involving cytokines that go out of control, i.e., become dysregulated, forming a cascade that leads to a storm with multi-organ damage and death. That description does not differ markedly from the description in respondent's Exhibit D

describing the second modality of multi-organ failure due to noninfectious reasons. Dr. Levin's exemplar is Exhibit 12, the cytokine storm elicited in a phase one trial of anti-CD28 monoclonal antibody THB1412 which caused in healthy young men multi-organ dysfunction in a brief period of time, sending the six subjects to the hospital which saved their lives. The similarities between their conditions and that of decedent in this case are close except for the presence of lymphopenia (fewer white blood cells) in the test subjects, whereas decedent had lymphocytosis or an excessive number of white blood cells when first examined. The undersigned notes that decedent's lymphocytosis was detected early in his six-day final illness and not when he was perilously ill a few days later. Moreover, the authors of Exhibit 12 comment on the unique aspect of these test subjects because of their early acute lung injury and lymphopenia. Apparently, the authors expected greater, not fewer, white blood cells to be evoked.

Dr. Levin explained decedent's excess white blood cells with a left shift as caused by cytokines. Another possible explanation is that decedent was harboring a subclinical upper respiratory infection. There is a notation in the emergency room records of his having malaise the day before vaccination. On the other hand, malaise is non-specific and no expert commented upon it at trial. Decedent's granddaughter saw decedent the day before his vaccination and said he was athletic as usual. His daughter-in-law took him for the vaccination and did not remark that he was ill in any way before the vaccination. Dr. Levin stated at the hearing that if decedent had been harboring a subclinical infection, the vaccination made it worse. There is not enough evidence in the record to state the decedent had an infection before vaccination, but if he had, both the infection and the vaccination were substantial factors in causing decedent's systemic inflammatory response syndrome, based on Dr. Levin's testimony.

Dr. Frankel never offered an opinion as to whether cytokines could have caused decedent's elevated white blood cell count with the left shift when decedent saw Dr. Hardee on Tuesday, November 7, 2006, and went to the emergency room later that evening. The only evidence therefore that the undersigned has on this issue comes from Dr. Levin. The undersigned notes that the authors of Exhibit 12 noted how unusual their test subjects' lymphopenia was, as if they had expected the opposite, i.e., an elevation of white blood cells. To explain their test subjects' lymphopenia or low white blood count, the authors suggest this may have been a response to the monoclonal antibody rather than to the cytokine storm. If it were the monoclonal antibody, rather than the cytokine storm, that caused the test subjects' lymphopenia, that would explain why decedent's white blood count in the instant action was high, not low, because he did not receive this monoclonal antibody but instead flu vaccine which is far less potent.

The point Dr. Levin stressed throughout his testimony is that Exhibit 12 is a template for what happened to decedent with some differences, notably the decrease in white blood cells among the test subjects. Of note, Dr. Levin testified that one of the test subjects had bacterial pneumonia after reacting to the monoclonal antibody, showing that a cytokine storm can worsen a subclinical disease. In light of the subjects being healthy for two weeks before the trial, this is confirmation that this one person's infectious process was subclinical. This event supports Dr. Levin's testimony that, if decedent herein were harboring a subclinical infection, the vaccination worsened it.

The subjects in the phase one trial became ill 50 to 90 minutes after infusion of the monoclonal antibody. Decedent herein became ill 30 minutes after his flu vaccination. The subjects had severe fever. Decedent herein had 103° or 104° F. temperature. Unlike the subjects

(who had diarrhea and vomiting), decedent herein did not have either. The test subjects had erythema (redness of the skin). Decedent herein had a rash. One subject had respiratory failure with pulmonary infiltrates while another had marked respiratory distress and underwent intubation. Decedent herein had pneumonia and underwent intubation. Between 16 and 20 hours after receipt of the monoclonal antibody, the six subjects had further signs of respiratory deterioration, including bilateral pulmonary infiltrates on chest x-ray. Decedent herein had pulmonary infiltrates on chest x-ray. The test subjects had substantial renal impairment. Decedent herein had kidney failure. Four test subjects continued to have intermittent fever, myalgia, and diffuse erythematous flushing for 48 hours. Decedent herein had intermittent fever, achiness, and rashes. The test subjects had hypotension and metabolic acidosis. Decedent herein had hypotension and metabolic acidosis.

The authors of Exhibit 12 attribute the cause of the six test subjects' downhill course to a sudden and rapid release of proinflammatory cytokines, which they said provided insight into the natural course of cytokine storm and systemic inflammatory response syndrome. There was no contamination of the monoclonal antibody with endotoxin, pyrogen, or microbiologic or other agents. All six patients fit the criteria for systemic inflammatory response syndrome. Decedent herein fits the criteria for systemic inflammatory response syndrome. The authors considered the course of illness consistent with a generalized multi-organ response to inflammation or critical illness.

The difference between the test subjects and decedent also involves the fact that the test subjects were young men in general good health whereas decedent herein was 82 years old and had co-morbid conditions involving atherosclerosis, pre-diabetes, and hyperlipidemia.

Dr. Frankel agreed that decedent had systemic inflammatory response syndrome, but did not know in response to what. Decedent's cultures were negative. Dr. Frankel said that in 75 percent of cases, the cultures are negative. That means decedent either had an unidentified virus or bacterium or he had no virus or bacterium, and there is no way to choose between them. Both experts agreed that decedent's systemic inflammatory response syndrome together with his co-morbid conditions led to his death. What caused his systemic inflammatory response syndrome? Flu vaccine is an immunologic agent because that is its purpose. Based on the testimony of Dr. Levin, the example of the same type of disease process in Exhibit 12, and the Brown and Mouille cases in which the undersigned held flu vaccine with infectious co-factors caused injury, the undersigned holds that flu vaccine not only can cause systemic inflammatory response syndrome but did so in this case, leading to decedent's death.

Althen Prong Three

The timing is compelling in this case. Decedent felt ill 30 minutes after receiving the flu vaccination. He never felt any better but continued to get worse until he died. There is no question that decedent was exposed to cytokines from the effect of the vaccine because the purpose of the vaccine is to evoke an immune response. But the quality of this response, i.e., dysregulation of the cytokines, was not part of the purpose of vaccination. It unfortunately happened. When someone becomes ill with a vaccine injury and worsens day by day until he dies, a reasonable conclusion is that the immunologic challenge caused the illness. Dr. Levin thought the timing in this case appropriate. Dr. Frankel did not. He thought a cytokine storm (which he denied decedent ever had) would occur quicker. Dr. Levin said it depends on the source of the cytokine storm and the health of the individual.

In understanding the import of a continuous process of illness to death, a discussion of Allen v. Sec'y of HHS, 24 Cl. Ct. 295 (1991), is appropriate. The Honorable Eric G. Bruggink affirmed the award of damages in a case where parents alleged that their child died from hypotonic-hyporesponsive (HHE) shock collapse within 72 hours of receipt of DPT vaccine. There had been a prior remand for the special master to determine that there was causation between the HHE (a Table injury at the time) and the death (which is not a Table injury). After receipt of DPT, the baby started crying, had fever and unusual sleep patterns, fed poorly, and was not responsive to stimuli. She had some pallor and no apparent muscle tone. Fifteen minutes after the last time she was observed, she was found dead. Id. at 296. Judge Bruggink stated, "The result in any given case then must depend on whether there is an observable, and relatively uninterrupted progression from vaccination, through HHE, to death. In this case that conclusion can legitimately be drawn." Id.

The instant case does not deal with a Table injury in which there is a presumption of causation. But the same compelling logic that led the special master and Judge Bruggink in Allen to accept that the baby's HHE led to her death was both the continuous nature of the symptoms until death and the onset of HHE occurring quite closely to the vaccination.

In the instant action, the timing of decedent's onset of his mortal illness is consistent with systemic inflammation response syndrome, the response being to flu vaccination. The response proceeded in a continuous, deteriorative fashion until decedent died, a pattern of events reminiscent of the baby's pattern of symptoms leading to death in Allen.

The timing in the instant action is also reminiscent of the pattern of timing in the monoclonal antibody phase one clinical trial discussed in petitioner's Exhibit 12 in which the test

participants became ill 50-90 minutes after the infusion of the drug. Decedent herein became ill about 30 minutes after receiving flu vaccine.

Petitioner has satisfied the three prongs of Althen and proven causation in fact.

Damages

Damages for a wrongful death under the Vaccine Act are $250,000.00. 42 U.S.C. § 300aa-15(a)(2). Under the Federal Circuit decision in Zatuchni v. Sec'y of HHS, 516 F.3d 1312, 1320-21 (Fed. Cir. 2008), the Federal Circuit stated that § 11(b)(1)(A) defining a petitioner inter alia as one who represents a person who died from a vaccine-related injury "plainly does not dictate that a properly filed petition by the estate of a person who suffered both vaccine-related injuries and a vaccine-related death . . . may not contain a request for any and all of the types of compensation listed in § 300aa-15(a)." That means petitioner herein may recover more than the $250,000.00 death award.[4] See Griglock v. Sec'y of HHS, 99 Fed. Cl. 373 (2011), aff'g No. 09-275V, 2011 WL 839738 (Fed. Cl. Spec. Mstr. Feb. 11, 2011) (petitioner could have received decedent's survival damages if petitioner had filed petition within 36 months of onset of vaccine injury; time-barred except for receipt of death award), appeal docketed, No. 2011-5134 (Fed. Cir. Sept. 29, 2011) (petitioner asserts legal error that he needed to satisfy the 36-month statute of limitations to obtain personal injury compensation for decedent as well as satisfy the 24-month statute of limitations to receive the death award).

[4] The instant action is not the case where the decedent had a vaccine injury but died from an unrelated cause, as in Figueroa v. Sec'y of HHS, No. 10-750V, ___Fed. Cl. ___, 2011 WL 6369773, at *1 (2011), aff'g 2011 WL 2784586 (Fed. Cl. Spec. Mstr. June 22, 2011) (petitioner suing for death award when decedent's vaccine injury was unrelated to his death from cancer had no standing to sue under the Act because she did not satisfy the statutory requirement under 42 U.S.C. § 300aa-11(b)(1)(A) that petitioner inter alia represent a person who died from a vaccine-related injury; petition dismissed). In that situation, petitioner recovered nothing.

Decedent in the instant action did not have any wage loss or unreimbursed medical expenses. In petitioner's first post-hearing brief, petitioner asked for one item of damage: "Such pain and suffering as is appropriate." P Br. at 12. Respondent denied in her post-hearing brief that petitioner is entitled to receive an award for decedent's pain and suffering, while admitting that respondent lost this argument in Griglock. R Br. at 19-20 & n. 14. Respondent also stated that petitioner waived the demand for pain and suffering by not raising it before trial, which argument the undersigned regards as inappropriate since the hearing was devoted to entitlement and not damages. R Br. at 19.

On October 27, 2011, the undersigned issued an Order for the parties to file memoranda on the appropriate amount for decedent's pain and suffering if the undersigned were to rule for petitioner.

On November 9, 2011, petitioner filed his supplemental brief, requesting $200,000.00 for decedent's pain and suffering. P Supp. Br. at 5. Petitioner cites first Dullard v. Berkeley Associates Co., 606 F.2d 890 (2d Cir. 1979), affirming a $20,000.00 award for conscious pain and suffering of the decedent, a construction foreman, who was struck on the head by a piece of lumber that fell from at least 10 stories above him. 606 F.2d at 893. Plaintiff's decedent was partly conscious before he died. 606 F.2d at 894-95.

Petitioner also cites Oliveira v. Jacobson, 846 A.2d 822 (R.I. 2004), affirming the award of $100,000.00 for the pain and suffering of a newborn who died from asphyxiation 27 minutes after birth after three attempts at resuscitation. 846 A.2d at 824, 827. The baby was pale and blue as a result of oxygen deprivation, and his heart was barely beating. Id. at 827. He twice attempted to cry and gasped for breath. Id. The reason that the first two attempts to intubate the baby failed was that the tube was inserted in the baby's esophagus instead of his airway. Id. The

doctors repeatedly compressed the baby's chest to facilitate his heartbeat. Id. The Supreme Court of Rhode Island concluded that these 27 minutes were "extremely traumatic and unpleasant." Id. The case for wrongful death arose in the context of medical malpractice. In the instant action, petitioner does not assert that decedent received improper medical care.

The last substantive case that petitioner cites was another medical malpractice case, Bingaman v. Grays Harbor Community Hospital, 103 Wash.2d 831, 699 P.2d 1230 (Wash. 1985), in which a mother died two days after giving birth. Her husband and two sons were representatives of her estate, and her husband, as personal representative, instituted a survival action, obtaining $412,000 for decedent's pain and suffering. 103 Wash.2d at 831-32; 699 P.2d at 1230-31. Decedent died from eclampsia or toxemia of pregnancy. 103 Wash.2d at 832; 699 P.2d at 1231. Defendants failed to treat her condition, resulting in increased blood pressure and seizures. Id. Her condition resulted in uncontrolled hemorrhaging causing bleeding in her brain. Id. Plaintiff introduced uncontradicted evidence of decedent's physical agony and awareness of her impending death. Id. She complained of headache, backache, nausea, and hurt everywhere. She screamed, "Why don't you help me," and complained of pain while banging on the side rails of her bed and moaning. 103 Wash.2d at 833; 699 P.2d at 1231. Decedent complained to her roommate, "I'm dying. I know I'm dying. Why can't they help me? What is the matter with me?" When the roommate offered to ring for the nurses, she replied, "No, it won't do any good. They won't give me anything. They can't help me." 103 Wash.2d at 834; 699 P.2d at 1232. During the early morning hours of the next day, decedent suffered three separate grand mal seizures over three hours. Following each seizure, she regained consciousness and was alert. Id. She had blood in her urine and nausea, as well as vomiting and severe headaches, the latter being symptoms of cerebral edema. Id. Her abdominal pain was evidence of liver problems. Id.

The mortal illness of decedent in the instant action is nowhere near the magnitude of the deplorable dying process of the decedent in Bingaman. For the last day and one-half of his life, decedent in the instant action was mostly unresponsive and uncommunicative. Although he experienced fever and chills early in his illness, and difficulty breathing leading to intubation the day before he died, the medical records and the testimony of decedent's relatives do not reflect that he was in pain. He was weak, sleeping a lot, and not eating or drinking, but he was not hemorrhaging, vomiting, or seizing. There is no evidence either that he knew that he was dying. Two days into his illness, he advised his son upon his son's inquiry whether he wanted to see Dr. Hardee that if he were not better in a week, he would see the doctor. This shows that he was unaware that he was experiencing a mortal illness unlike decedent in Bingaman. The Washington Supreme Court described decedent's mental and physical state in that case as follows: "[D]uring much of that period of time she not only suffered extreme conscious pain, fear and despair at not being helped, but also had the conscious realization her life and everything fine that it encompassed was prematurely ending." 103 Wash.2d at 838-39; 699 P.2d at 1233-34. Based on the record, the 82-year-old decedent in the instant action did not experience the physical pain and mental agony of the dying mother in Bingaman.

On November 15, 2011, respondent filed her supplemental brief, stating that the $200,000.00 petitioner demanded for decedent's pain and suffering was near the maximum amount awardable for pain and suffering under the Vaccine Act, 42 U.S.C. § 300aa-15(a)(4) (the maximum being $250,000.00), and noting that petitioner did not cite one Vaccine Program case in his brief in support of his request. R Supp. Br. at 2 n.2.

Respondent quoted legislative history stating the special master should, in awarding an amount for pain and suffering, consider as well the benefits conferred by other forms of

compensation within the legislation. H.R. Rep. No. 99-908, pt.1 at 21 (1986); R Supp. Br. at 4. But the award for decedent's pain and suffering is conferred on the estate as a survival benefit, whereas the amount awarded as a death benefit is conferred solely on the estate for the estate's loss. The amounts of the two awards are not contingent upon each other. A pain and suffering award depends solely on the quantity and extent of the decedent's pain and suffering, not on the fact that his estate receives the statutory amount of $250,000.00 for his death.

Decedent became ill the morning of Saturday, November 4, 2006, right after his flu vaccination. He stayed in bed for a good portion of the next four days, sleeping, but eating and drinking little, although he did go up and down the staircase to reach the bathroom during the first three days. By the fourth day, November 7, 2006, he was shivering from fever and dehydration. His son brought him to Dr. Hardee the afternoon of November 7, 2006 where decedent was given IV fluids and sodium. He was hospitalized that night. By November 8, 2006, he had difficulty breathing and was intubated. He died in the early morning of November 9, 2006. A fair amount for pain and suffering for these six days, with decedent's worst symptoms on the fifth and sixth days (November 8 and 9, 2006), is $25,000.00. This is not to belittle decedent's sad experience. Monetary awards are insufficient to approximate sorrow, but this is the best that the legal system can do to compensate in this area.

Petitioner is awarded **$275,000.00**, composed of the $250,000.00 death award and $25,000.00 for decedent's pain and suffering.

CONCLUSION

Petitioner has prevailed in this case. 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.[5]

IT IS SO ORDERED.

January 18, 2012
DATE

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

[5] 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.