In The United States Court Of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 08-209V

(to be published)

* *	Special Master Corcoran
BRET KREIZENBECK *and* SANDRA KREIZENBECK *as legal representatives of a minor child,* C.J.K.,	Filed: June 22, 2018
Petitioners,	Dismissal Without Hearing; Immune System Dysfunction; Influenza ("Flu") Vaccine; Hypogammaglobulinemia; Diphtheria Tetanus Acellular Pertussis ("DTaP"); Measles-Mumps- Rubella ("MMR"); Varicella; HiB Vaccine; Pneumococcal Conjugate Vaccine ("PCV"); Significant Aggravation; Mitochondrial Disease.
v.	
SECRETARY OF HEALTH AND HUMAN SERVICES,	
Respondent.	
* *	

Richard Gage, Richard Gage, P.C., Cheyenne, WY, for Petitioners.

Ann Martin, U.S. Dep't of Justice, Washington, DC, for Respondent.

DECISION GRANTING MOTION TO DISMISS CASE[1]

On March 26, 2008, Bret and Sandra Kreizenbeck, on behalf of their son, C.J.K., filed a petition seeking compensation under the National Vaccine Injury Compensation Program ("Vaccine Program").[2] The Kreizenbecks allege that the childhood vaccines (Diphtheria Tetanus acellular Pertussis ("DTaP"), measles-mumps-rubella ("MMR"), Varicella, HiB and pneumococcal conjugate ("PCV")) C.J.K. received on April 1, 2005, and the influenza ("flu") vaccine he received on October 12, 2005, significantly aggravated his underlying, but

[1] This Decision will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet**. As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the published Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire Decision will be available in its current form. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758, codified as amended, 42 U.S.C. §§ 300aa-10 through 34 (2012) [hereinafter "Vaccine Act" or "the Act"]. Individual section references hereafter will be to § 300aa of the Act.

asymptomatic and subclinical, mitochondrial disorder, causing him to suffer from immune system dysfunction, or hypogammaglobulinemia.[3] Amended Petition at 1-2, dated Feb. 22, 2012 (ECF No. 27) ("Amended Pet.").

Having now completed my review of the evidentiary record and the parties' filings, I hereby **GRANT** Respondent's Motion for a Ruling on the Record Dismissing the Case, and **DENY** Petitioners' request for compensation. As discussed below, the record does not support Petitioners' contention that C.J.K. had any kind of mitochondrial disease or secondary dysfunction, or that the vaccines he received injured him in any respect. Moreover, the claim is not saved by Petitioners' eleventh-hour attempt to recast this claim as not asserting autism as a vaccine-caused injury.

I. FACTUAL BACKGROUND

Early Medical History

C.J.K. was born on March 23, 2004, following a normal pregnancy and delivery (although he was treated for jaundice prior to being discharged home). Ex. 3 at 2, 5, 7, and 9. Throughout his early childhood (i.e. through six months of age), C.J.K. had well-child exams with his pediatrician at which no notable or concerning health issues were observed or expressed by Petitioners, and his development was normal through his first year. Ex. 4 (Part 1) at 14, 29; Ex. 4 (Part 5) at 9.

The first notable health problem reflected in the medical records is from November 1, 2004, when C.J.K. (almost eight months old at the time) presented with a one-day history of fever, congestion, and runny nose, and was subsequently diagnosed with a viral syndrome. Ex. 4 (Part 1) at 22. Esotropia[4] was also noted. *Id.* Three days later, C.J.K. received a flu vaccine. *Id.* at 23. The medical records set forth no reaction to that vaccination. Then, on December 23, 2004, at nine months of age, C.J.K. returned to his pediatrician for a well-child visit. *Id.* at 24. Again, there were no major health concerns recorded from this visit, beyond the fact that C.J.K.'s "[left] eye turns in." *Id.* C.J.K. returned to his doctor two months later, on February 24, 2005, with a two-week history of congestion and he was diagnosed with nasopharyngitis and treated with an antibiotic. *Id.*

[3] Hypogammaglobulinemia, also sometimes referred to as immunodeficiency, is classified as a condition where a patient has abnormally low levels of all classes of immunoglobulins in the blood. *Dorland's Illustrated Medical Dictionary* 901 (32nd ed. 2012) (hereinafter *Dorland's*). It is also characterized by a deficient immune response. *Id.* at 918.

[4] Esotropia (described colloquially as being "cross-eyed") involves a manifest deviation of an eye's visual axis toward the other, resulting in diplopia/double vision. *Dorland's* at 648.

2005 Vaccinations

C.J.K. received the first set of vaccines alleged as injury-causing in this case (DTaP, Hib, PCV, MMR, and varicella) at his one-year well-child visit on April 1, 2005. Ex. 4 at 27-28; Ex. 5 at 1. At this time, there was again no evidence of developmental problems, as all of the categories on the pre-printed developmental screen were checked as normal. *Id.* The records from this visit set forth no immediate reaction to any of these vaccines – nor do subsequent records contain histories recording after-the-fact that a reaction was observed. As discussed below, however, the Petitioners contend that in fact C.J.K. *did* experience a reaction and a decline in health beginning at this time.

Almost two weeks later, on April 12, 2005, C.J.K. returned to the pediatrician with rhinorrhea. Ex. 4 (Part 1) at 28. Again, no mention is made in the relevant records of any reaction. There is subsequently a gap in the records, with no evidence of medical treatment until four and one-half months later, on August 19, 2005, when C.J.K. presented to his pediatrician with a three-day history of vomiting and decreased appetite, and was diagnosed with acute gastroenteritis. *Id.* at 26. This record does not contain any statement of symptoms stretching into the prior months. The very next month, on September 14, 2005, C.J.K. was treated for croup,[5] following a visit to the emergency room the night before. *Id.* at 30. No treater in any of these records links any vaccine to C.J.K.'s illness, nor did Petitioners report anything of that sort to any medical providers, or complain of observed developmental issues.

On October 12, 2005, at eighteen months of age, C.J.K. was seen by a nurse to administer the inactivated flu vaccine. Ex. 4 (Part 2) at 1; Ex. 5 at 1. Although the record from this date states that he registered a normal temperature, it does not appear that any broader physical examination took place, and there are no other immediately-subsequent records identifying any additional reactions, observed or alleged, to receipt of this vaccine. Again, however, the Petitioners have contended that in the aftermath of the receipt of the flu vaccine, C.J.K.'s behavior changed, and that his health declined even more precipitously.

Evidence of Developmental Problems and Purported Evidence of Immune Dysfunction

Throughout the remainder of 2005 and into 2006, it appears that C.J.K. suffered from many additional incidents of congestion and respiratory issues – although there is no record support in

[5] Croup is defined as a "condition resulting from acute partial obstruction of the upper airway." *Dorland's* at 435. It is more often seen in children and infants. *Id.* Symptoms can include barking cough, hoarseness, and persistent stridor. *Id.*

this period for the contention that the vaccines he had received were in any way associated with his health problems, or that treaters deemed them out of the ordinary for an infant. *See generally* Ex. 4 (Parts 2 & 3). He also began in late 2005 to display developmental difficulties.

C.J.K.'s next medical visit after receipt of the flu vaccine was November 8, 2005 (27 days after the vaccine's administration). He presented with "congestion/fever, fussy/poss[ible] ear infection." Ex. 4 (Part 3) at 12. The doctor's notes specifically state: "congestion x few months, clear runny nose, Ø fever, + teething, just came back from Reno, emesis x 24°, mama-nonspecific, doesn't follow commands, sister [with otitis media]." *Id.* The doctor's diagnoses were "(1) URI, early [otitis media]; (2) Speech Delay." *Id.* This record is accordingly the first directly referencing anything related to C.J.K.'s development problems.

Not long after, Petitioners started expressing additional concerns for C.J.K.'s developmental health. On November 29, 2005, and after his visit to the pediatrician earlier that month at which time hearing problems were identified, C.J.K. had a hearing evaluation at Hanford Speech and Hearing Center in Hanford, California. The notes from this evaluation state that there was "a reported history of unintelligible speech and speech delay with few single words and phrases," while also acknowledging his recent ear infection. Ex. 8 at 1. The impression was "normal hearing for the better ear" and middle ear stiffness on the right, and the treating doctor recommended an evaluation of the "middle ear status." *Id.* at 1-3. The next day, C.J.K.'s pediatrician diagnosed right otitis media and an upper respiratory infection and referred him to an ear, nose, and throat specialist, Daniel J. Schlund, M.D. Ex. 4 (Part 3) at 13.

Dr. Schlund saw C.J.K. on December 7, 2005 and recorded the following history:

> [C.J.K.] is approximately a 21-month-old male who, by mom's report, has had problems with ear infections and hearing loss. He apparently had a flat tympanogram on the right recently. He does not seem to hear well and does not seem to follow commands, by mom's report. *She has noted more difficulty in the last six months*. She has tried him on soy, but he continues to have these problems. Mom is concerned about delayed speech. He is not exposed to tobacco smoke and he is not in daycare. He does have some occasional nasal drainage and ear pain, but no ear drainage. His remaining history and complete review of systems are otherwise negative or noncontributory.

Ex. 4 (Part 1) at 20 (emphasis added). Tellingly, the above-cited section from the history taken at this evaluation not only does *not* record the dramatic decline in health that Petitioners now allege, but also suggests that the behavior changes complained of at this time may have begun well before the flu vaccine was administered that October.

Following examination, Dr. Schlund's impression was resolved otitis media with effusion and "[p]ossible autistic tendencies based on behavioral observations today." Ex. 4 (Part 1) at 20. One week later, on December 14, 2005, C.J.K, had a speech and language evaluation at Hanford Speech and Hearing Center because of the noted concern by his mother about his delayed speech and language development. Ex. 9 at 2-4. The evaluating treater stated that "Mrs. Kreizenbeck reported that first words emerged between *15 and 18 months of age*. [C.J.K.] has always babbled and produced jargon," but that speech had not continued as Mrs. Kreizenbeck expected. *Id.* at 1 (emphasis added). The speech pathologist's biggest concerns were that C.J.K.'s development in certain areas was not progressing as it should. *Id.* at 1-3. This timeframe, if accurate, would suggest that C.J.K. was still developmentally normal in June and July 2005 (two to three months after the date of the first vaccines at issue in this case), but that sometime in the next few months his developmental progress slowed or changed.

C.J.K. saw hearing and speech specialists throughout the winter of 2005-06. *See generally* Ex. 8 at 1, Ex. 4 (Parts 1 & 3), Ex. 9. On March 28, 2006, C.J.K. was officially diagnosed with autism by Byrna Siegel, Ph.D., Director of University of California's San Francisco's Autism Clinic. Ex. 11 at 1-19. While C.J.K today suffers from Attention Deficit Hyperactivity Disorder ("ADHD"), there is record evidence suggesting that as of 2013, certain treaters had proposed that his autism symptoms had "resolved," and therefore that he no longer appropriately bears the diagnosis. *See* Ex. 36 at 14 (notes from November 11, 2013 visit to Medical Genetics Clinic at Lucile Packard Children's Hospital). Petitioners have thus formally alleged that an autism diagnosis for C.J.K. is now inaccurate.[6]

Alleged Evidence of Immunodeficiency or Mitochondrial Disease/Disorder

Although this case was filed ten years ago, Petitioners' efforts to ascertain the cause of C.J.K.'s purported health problems have continued apace. In particular, the Kreizenbecks have attempted not only to obtain treatment for C.J.K.'s developmental problems, but also for what they perceived to be an immunodeficiency or metabolic disorder in C.J.K. that could be the source of his alleged susceptibility to illness. Records of such treatment and consultation – many of which post-date the petition's filing – bear heavily on the version of the claim that Petitioners currently maintain is the "correct" one.

C.J.K. received his first evaluation for a possible immune deficiency in October 2006 (one year after receiving the flu vaccination), with Dowain Wright, M.D., a pediatric immunologist and rheumatologist at the immunology clinic at Valley Children's Hospital in Madera, California. *See*

[6] As of November 2013, C.J.K. is reported to have had significant developmental improvement, and currently attends normal classes at school, with the assistance of Ritalin. Ex. 22 at 7. Although there were many medical records filed regarding C.J.K.'s early treatment and diagnosis for his developmental delay (and those records have been reviewed), they are largely inapplicable to the amended injury of hypogammaglobulinemia, and will not be discussed herein.

generally Ex. 6.[7] The medical history from these records (likely provided to Dr. Wright by Petitioners) asserted that C.J.K.'s propensity to be ill began at 12 months of age (or March 2005) and was coupled with "a change in social skills," with frequent infections beginning in his "second year of life." *Id.* at 5. Because of this history "an immune evaluation was recommended." *Id.* at 5-6. Dr. Wright's write-up also noted that "some suggestion" was made at the time of the evaluation that C.J.K.'s autism could be connected to immune dysregulation, but discounted the possibility of such an association based upon his own experience ("of all my patients with immune deficiency, only [one] is autistic"). *Id.* at 6-7.

Dr. Wright performed a comprehensive evaluation, with a physical examination and extensive lab work (including tests for a variety of antibodies). Ex. 6 at 6. No abnormalities were noted; in particular, total immunoglobulin levels were deemed normal, as well as his IgG and IgM levels.[8] *Id.* During the initial evaluation, Dr. Wright was unable to reach a clear conclusion as to the source of C.J.K.'s recurrent infections, although he did express the view that C.J.K.'s repeated sore throats alone were not evidence of immune deficiency. *Id.* at 7. Dr. Wright proposed that he follow up with C.J.K. the next month, in November. By this time, however, he opined that C.J.K. more likely suffered from allergic rhinitis than chronic viral infections (as had been related to him by Petitioners at the first visit). *Id.* at 2. After an additional physical examination, and based on the total picture he had obtained from exams plus testing, Dr. Wright affirmatively stated that he found no evidence of an immune deficiency, and therefore scheduled no additional follow-up visits. *Id.* at 3-4.

A year and one-half later, C.J.K. was evaluated in April 2008 by Sudhir Gupta, M.D., Ph.D., at the University of California Immunology Clinic in Irvine, California. Exs. 18, 32. (Notably, the present lawsuit had been initiated by that date). The records from this evaluation are limited, including no disclosure of test results, and are scrawled in an undecipherable hand. *See, e.g.*, Ex. 32 at 1-5. It does appear, however, that Dr. Gupta found significant that (as the Petitioners likely informed Dr. Gupta) C.J.K. had been a healthy child until 12 months of age when he "started having rec[urring] U[pper] R[espiratory] I[nfections]." *Id.* at 1. Dr. Gupta's impression was that C.J.K. suffered from hypogammaglobulinemia/immune deficiency. *Id.* at 2.

[7] Petitioners' prehearing brief assiduously avoided mention of C.J.K.'s evaluation by Dr. Wright. *See* Prehearing Memorandum, dated May 9, 2017, at 5 (jumping from 2006 treatments to 2013).

[8] Immunoglobulin G (IgG) and Immunoglobulin M (IgM) are antibodies produced in response to infection, and their titer levels can help monitor or detect immune deficiencies. IgM is an indicator of current infection, while IgG reflects exposure to a past infection. Increased levels of IgG or IgM are indicia of hepatic diseases (including connective tissue diseases and acute/chronic infections), while decreased levels are found in patients with primary/secondary immune deficiencies. *See Immunoglobulins (IgG, IgA, and IgM), Serum*, Mayo Clinic Med. Laboratories, https://www.mayomedicallaboratories.com/test-catalog/Clinical+and+Interpretive/8156 (last accessed May 30, 2018).

A letter, dated April 9, 2008, from Dr. Gupta to the Kreizenbecks' health insurance company provides a more legible, if succinct, explanation for Dr. Gupta's findings. *See generally* Ex. 18. The letter notes that "[i]mmunological analysis revealed low levels of IgG," which "confirms [the] diagnosis" of immune deficiency. *Id*. These testing results, however, do not appear to have been filed in this case, and it is not apparent from this set of records whether the analysis referred to was performed by Dr. Gupta or some different treater. Dr. Gupta noted the appropriateness of IVIG treatments[9] for an immune deficiency every four weeks, and asked Petitioners' insurance company to approve such treatments for the next six months until a re-evaluation could be performed (although no such reevaluation evidence appears to have been filed). *Id.*

In the ensuing several years, C.J.K. received a variety of treatments (some of which would be charitably deemed "alternative medicine") to assist him with his immunodeficiency and autism, including hyperbaric oxygen treatments and nutritional guidance. *See, e.g.*, Ex. 21 at 33-71, 87-90, 464; Ex. 21 at 334, 453. Then, in November 2012, C.J.K. (now eight years old) came under the care of immunologist Sean A. McGhee, M.D., at the Lucile Packard Children's Hospital in Palo Alto, California, for "[r]ecurrent infection." Ex. 25 at 3. The history of present illness section in the record from the first visit with Dr. McGhee reported the numerous infections C.J.K. had experienced and their insidious nature. *Id*. at 3. The history also claimed C.J.K. had experienced adverse reactions to the MMR, chickenpox, and influenza vaccines – although as noted above the contemporaneous record does not corroborate such assertions. *Id.* He noted at the time of C.J.K.'s initial presentation as well that C.J.K. received nine different medications, including carnitine,[10]

[9] Intravenous Immunoglobulin ("IVIG") therapy is used to treat immune system disorders. During an IVIG treatment, immunoglobulin (a combination of antibody proteins) is injected into the body to help the immune system fight off infections. *See Primary Immunodeficiency*: *Treatment*, Mayo Clinic, https://www.mayoclinic.org/diseases-conditions/primary-immunodeficiency/diagnosis-treatment/drc-20376910 (last accessed on May 31, 2018).

[10] Carnitine is a betaine derivative found in the skeletal muscle and liver, and is typically acquired naturally through diet. *Dorland's* at 297. It is required for mitochondrial beta oxidation of fatty acid. *Id.* A deficiency in carnitine can prevent the body from using fat for energy, and can result in brain dysfunction, heart failure, liver problems, and weakness in severe cases. *See Primary Carnitine Deficiency*, NIH, https://ghr nlm nih.gov/condition/primary-carnitine-deficiency (last accessed on May 31, 2018). However, some patients with a carnitine deficiency are asymptomatic. *Id.*

creon,[11] leucovorin,[12] and fish oil.[13] *Id.*

Dr. McGhee's physical examination of C.J.K. was negative for any problems or concerns. Ex. 25 at 4. Lab work revealed no concerns either, and found IgG levels (given the IVIG replacement treatments he was receiving) normal. *Id.* Dr. McGhee recommended continued IVIG treatment, and included in the differential the possibility as well that C.J.K. had a "possible mitochondrial disorder," although complete disposition of that diagnosis would require additional treatment records that had not yet been provided to Dr. McGhee. *Id.* The Kreizenbecks had a follow-up visit with Dr. McGhee in December 2012. *Id.* at 1-2. Dr. McGhee again noted a "presumed" mitochondrial disorder, but identified no new treatment record evidence that would support this diagnosis, and otherwise encouraged the Kreizenbecks to maintain IVIG treatments for C.J.K. *Id.* at 1.[14]

Around the same time as the visits to Dr. McGhee, C.J.K. also received an evaluation in November 2012 from a gastroenterologist, Nasha Khavari, M.D., MPH, also at Lucile Packard Children's Hospital. *See generally* Ex. 25 at 6-28. Petitioners were referred to Dr. Khavari to obtain her views as to whether C.J.K. suffered from some kind of inflammatory bowel condition, given his history of such symptoms (which the Kreizenbecks reported had begun at the age of three – two years after the first round of vaccinations in question in this case). *Id.* at 6. Dr. Khavari's history also noted C.J.K.'s immune deficiencies and IVIG treatments. *Id.* At the time of the initial consultation, C.J.K. had no notable abdominal symptoms, however, and the medical records provided to Dr. Khavari from more recent years also showed no gastrointestinal

[11] Creon is a trademark for preparation of pancrelipase. *Dorland's* at 429. Pancrelipase is used to help improve food digestion in certain patients with diagnoses relating to a pancreas disorder. *Pancrelipase (Oral Route)*, Mayo Clinic, https://www.mayoclinic.org/drugs-supplements/pancrelipase-oral-route/description/drg-20065293 (last accessed on May 31, 2018).

[12] Leucovorin is a calcium salt found in folinic acid. *Dorland's* at 1026. Leucovorin supplements are used to treat deficiencies in folic acid, for example. *Leucovorin (Oral Route, Intravenous Route, Injection Route)*, Mayo Clinic, https://www.mayoclinic.org/drugs-supplements/leucovorin-oral-route-intravenous-route-injection-route/description/drg-20064503 (last accessed on May 31, 2018).

[13] Fish oil is a dietary supplement used to treat a deficiency in omega-3 fatty acids (a substance needed for muscle activity and cell growth). *Fish Oil*, Mayo Clinic, https://www.mayoclinic.org/drugs-supplements-fish-oil/art-20364810 (last accessed on May 31, 2018).

[14] Petitioners also filed a more recent record from their visits with Dr. McGhee in 2017. *See generally* Ex. 55 (February 13, 2017 progress notes). In this record, Dr. McGhee summarizes C.J.K.'s status, noting his awareness of Dr. Natowicz's 2013 diagnosis of mitochondrial dysfunction based on certain testing (as discussed below). After consulting with Mrs. Kreizenbeck and learning that C.J.K. was generally doing well, Dr. McGhee proposed continued IVIG treatments and a follow-up visit in a year, but made no novel diagnoses based on any additional evidence.

issues of significance. *Id.* at 6-7.[15]

After review of the results of prior endoscopies and colonoscopies performed on C.J.K. as well as some additional testing, Dr. Khavari was unable to provide a diagnosis to explain C.J.K.'s alleged illness or condition. Ex. 25 at 24-25. All prior biopsies had produced normal results, and testing requested by Dr. Khavari was not consistent with inflammatory bowel disease. *Id.* at 24. At best, Dr. Khavari was able to propose that C.J.K. had "some kind of autoimmune inflammatory illness," but could not precisely name it. *Id.* Dr. Khavari also noted that C.J.K. could probably stop taking medication for colitis – and indeed that it might not be called for, given the lack of evidence of active inflammation and its possible side effects. *Id.* at 25.

Testing for Possible Mitochondrial Disorder

In early 2013, Petitioners obtained formal testing for C.J.K. to evaluate whether he suffered from some form of mitochondrial disease or dysfunction. Significantly, this testing was performed (a) five years into this case's life, and (b) almost *eight* years after the first round of vaccines in question had been administered to C.J.K. in April 2005.

On February 6, 2013, C.J.K. saw Dr. Marvin Natowicz at the Cleveland Clinic's Medical Genetics Clinic in Cleveland, Ohio, to obtain a genetic and metabolic diagnostic evaluation. *See generally* Ex. 26. The Cleveland Clinic is recognized as having special competence in research and treatment of metabolic disorders such as mitochondrial disease. *See, e.g.*, *Pope v. Sec'y of Health & Human Servs.*, No. 14-078V, 2017 WL 2460503, at *9 (Fed. Cl. Spec. Mstr. May 1, 2017). Dr. Natowicz's history for C.J.K. identified his developmental problems as manifesting with attention issues, and having begun at 16 months, or the midsummer of 2005 (and thus several months after the April 2005 vaccinations at issue). Ex. 26 at 1. Based upon the history provided to him, Dr. Natowicz noted that although "we do not establish an etiological basis for a person's autism in the majority of persons with forms of autism," nevertheless "the family history forces one to consider various metabolic and genetic processes and much of [C.J.K.'s] clinical story is potentially explainable on the basis of mitochondrial energy production disorder." *Id.* at 6. Dr. Natowicz therefore proposed that blood testing be immediately performed, with possible genetic testing later. *Id.* at 7.

[15] The only possible findings of concern to Dr. Khavari contained in the medical records related to an endoscopy performed in 2007 by Dr. Arthur Krigsman. Ex. 25 at 6. Notably, Dr. Krigsman is a gastroenterologist who has testified or been referenced in other Program cases claiming autism as a vaccine injury, and has proposed in the past that there is a plausible relationship between gastrointestinal conditions and autism. *R.K. v. Sec'y of Health & Human Servs.,* No. 03-632V, 2015 WL 10936124, at *115 n.265 (Fed. Cl. Spec. Mstr. May 23, 2016), *mot. for review den'd*, 125 Fed. Cl. 57 (2016), *aff'd*, 671 F. App'x 792 (Fed. Cir. 2016). This concept, however, has never been accepted by any special master in any entitlement decision.

On March 4, 2013, Dr. Natowicz commented on the results of the testing he had just ordered. Ex. 26 at 7. Most results were normal or unworthy of concern, except for a finding of mildly increased serum 3-methylglutaconate ("serum 3") at 314 (with normal as in the range of 126 - 298). Dr. Natowicz noted that this compound was observed in increased levels in "only a relatively small number of conditions, including disorder of mitochondrial energy metabolism." *Id*. He therefore proposed some follow-up tests – in particular, skin fibroblast cell[16] culture tests designed to measure the energy-producing functionality/efficiency of the mitochondria in such cells.[17] *Id.* Dr. Natowicz did not, however, propose conducting a muscle biopsy – a test that has often been used to confirm the presence of a mitochondrial disorder[18] – given his sense that there was not a "compelling enough clinical history or lab data" to justify it, and he also did not propose genetic testing given the expense. *Id.*

The following year, the Kreizenbecks returned to Dr. Natowicz in March 2014 for a follow-up visit. *See generally* Ex. 33. Dr. Natowicz's write-up from this visit reviewed C.J.K.'s status, but also discussed some of the additional testing results that were obtained since the time of his 2013 visit. Thus, Dr. Natowicz considered whole exome sequencing genetic testing that C.J.K. had separately undergone in 2013, noting that it was largely inconclusive in aiding a mitochondrial disease or disorder diagnosis (although certain variants shared with a tested sibling were deemed worthy of future evaluation). Ex. 33 at 5-6; *see also* Ex. 39. He also considered the results of three fibroblast cell tests that he had requested in the prior year. *See generally* Ex. 37. Two of the tests yielded normal results, although the third – a fibroblast oxidative phosphorylation test ("Ox Phos") – found a defect in two electron transport chain complexes, a finding that (in conjunction with the serum 3 mild elevation previously observed) suggested to Dr. Natowicz that any mitochondrial dysfunction present was "more likely a secondary phenomenon." (Ex. 33 at 6, 7).

As a result of the above, Dr. Natowicz proposed another action item list to the Kreizenbecks featuring some additional testing, although he indicated that further follow-up

[16] Fibroblasts are connective tissue cells. *Dorland's* at 701.

[17] As noted in *R.K.*, 2015 WL 10936124, at *39, "[m]itochondria use oxygen and food to produce adenosine triphosphate ("ATP"), the primary source of energy for all bodily functions, through a process labeled "the respiratory chain" or "electron transport chain." Fibroblast cell culture tests measure ATP synthesis rates, and specifically whether they appear impaired (thereby suggesting the presence of a mitochondrial disorder). *Id.* at *43.

[18] In the past, muscle biopsies were deemed the "gold standard" for assessing the presence of a mitochondrial disease or disorder, although technological advancements (in particular, the ability to conduct genetic testing) has reduced reliance on such testing. *R.V. v. Sec'y of Health & Human Servs.,* No. 08-504V, 2016 WL 3882519, at *11, 20 (Fed. Cl. Spec. Mstr. Feb. 19, 2016), *mot. for review den'd*, 127 Fed. Cl. 136 (Fed. Cl. July 1, 2016), *appeal dismissed*, No. 16-2400 (Fed. Cir. Oct. 26, 2016).

would be dependent on the results of that testing. Ex. 33 at 7. The filed medical records reveal that some additional testing was performed (Ex. 33 at 9-17) but largely deemed either normal or not diagnostic of a specific disorder – although serum-3 levels were again observed to be slightly increased, and therefore to suggest "the possibility" of disturbance of mitochondrial function. *Id.* at 11.

Dr. Natowicz had another follow-up visit with C.J.K. in May 2017. *See generally* Ex. 54. The notes from this visit recount the above-referenced test results and reveal no additional testing or factors that would corroborate or rebut Dr. Natowicz's earlier proposals about the possibility of C.J.K. having some form of mitochondrial disorder. *Id.* at 1-7. An addendum to this record, from May 29, 2017, however, does indicate that additional follow-up blood and urine tests were "negative or unremarkable," and that overall findings did not constitute in Dr. Natowicz's view any basis for altering the existing metabolic treatment plan, which Mrs. Kreizenbeck had reported had been effective in increasing C.J.K.'s energy levels. *Id.* at 1, 7, and 8.

C.J.K. is currently enrolled in public school in an age appropriate class (receiving some tutoring in speech and handwriting), but continues to have weekly IVIG injections and is on a special diet (with dietary supplements) for his gastrointestinal issues.

II. EXPERT REPORTS

A. Petitioners' Experts

1. *Dr. Alan Levin*

Dr. Levin offered the first of Petitioners' expert opinions. *See* Expert Report, dated July 27, 2013, and filed as Ex. 28 (ECF No. 52-3) ("Levin Rep."). Although a curriculum vitae ("CV") was never filed for Dr. Levin, his expert report indicates that he is a pathologist and board-certified immunologist, and currently works at Immunology, Incorporated. *Id.* at 1.[19]

In his two-page report, Dr. Levin opined, in somewhat conclusory fashion, that C.J.K. "was born with asymptomatic inborn errors of metabolism which were triggered to become symptomatic in the form of immunological anomalies by the cytokines released by the vaccinations he received on *April 1, 2005*." Levin Rep. at 2 (emphasis added). For factual support, Dr. Levin briefly summarized C.J.K.'s medical history, noting that he was diagnosed by Dr. Gupta in 2008 (as noted above, three years after the vaccinations at issue) with hypogammaglobulinemia, and asserting that

[19] Dr. Levin has testified on behalf of Vaccine Program petitioners on numerous occasions. *See, e.g.*, *Carter v. Sec'y of Health & Human Servs.*, No. 13-633V, 2015 WL 5445828 (Fed. Cl. Spec. Mstr. Aug. 19, 2015); *Bigbee v. Sec'y of Health & Human Servs.*, No. 06-663V, 2012 WL 1237759 (Fed. Cl. Spec. Mstr. Mar. 22, 2012).

other physicians had characterized C.J.K. as having inborn errors of metabolism (although he offered no record citation for the latter proposition – one the medical records do not support). *Id*. at 1.

To support his theory, Dr. Levin cited only two pieces of medical literature. *See, e.g.*, J. Ming, et al., *Syndromes Associated with Immunodeficiency*, 46 Advanced Pediatrics 271 (1999), filed as Ex. 30 (ECF No. 53-1) ("Ming"); K. Tsumiyama, et al., *Self-Organized Criticality Theory of Autoimmunity*, PLoS ONE, e8382.doi:10.1371/journal.pone.0008382 (2009). Only Ming, however, was filed in the case, and only in abstract form. Ming makes broad assertions about the etiology of immune deficiency disorders and their associated "abnormalities," which include "inborn errors of metabolism." Ming at 1.

2. *Dr. Marcel Kinsbourne*

Dr. Kinsbourne prepared Petitioners' second-filed expert report. *See* Report, dated May 29, 2015, filed as Ex. 43 (ECF No. 80-2) ("Kinsbourne Rep."). His report largely attempts to provide a link between C.J.K's autism/ADHD and his October 2005 receipt of the flu vaccine.

As his CV indicates, Dr. Kinsbourne is board certified in pediatrics. Ex. 44 (ECF No. 81-1) ("Kinsbourne CV"), at 1. He received his medical degree in England, and he has been licensed to practice medicine in North Carolina since 1967. *Id*. From 1967 to 1974, Dr. Kinsbourne served as an associate professor in pediatrics and neurology and a senior research associate at Duke University Medical Center before holding a series of academic positions, including professorships in pediatrics, neurology, and psychology. *Id*. at 2. His clinical experience includes serving as a senior staff physician in Ontario from 1974-1980, and a clinical associate in neurology at Massachusetts General Hospital from 1981-1991, although (as noted in other cases) many years have passed since he regularly saw patients. He has published several articles examining autism (Kinsbourne CV at 15, 21-22, 27), and he is on the editorial board of several journals that deal with the brain, such as *Brain and Cognition* and *Brain Research*. Kinsbourne CV at 3.

Overall, Dr. Kinsbourne opined that vaccines can activate immune system cells, which in turn generate "oxidative stress." Therefore, he believed it to be medically reasonable that mitochondria could be stressed by vaccination (in this case, the flu vaccine) and cause "[C.J.K.'s] current and ongoing disabilities which are sequelae of this significant aggravation." Kinsbourne Rep. at 5.

Dr. Kinsbourne specifically proposed that C.J.K "developed [a]utistic disorder soon after his influenza vaccination," and that his autism (which later evolved into ADHD) was a result of his "genetic susceptibility and the environmental insult offered by the third influenza vaccination."

Kinsbourne Rep. at 3. In particular, he proposes that the October 2005 vaccination interfered with C.J.K.'s subclinical mitochondrial dysfunction (not discovered in C.J.K. until years later) by increasing oxidative stress, which then clinically manifested as autistic regression. *Id.* at 3-4. Dr. Kinsbourne does not propose that these vaccines directly caused C.J.K.'s developmental problems, but that they significantly aggravated his alleged underlying mitochondrial disorder. *Id*. at 4.

As Dr. Kinsbourne explains in his report, mitochondria - the organelles in the body's cells responsible for energy production - are vulnerable to oxidative stress. Vaccines can generate oxidative stress by activating the immune system, producing proinflammatory cytokines[20] which can tip the balance of reactive oxygen species, resulting in cell damage and (later) autistic symptoms once the damage arrives in the brain. Kinsbourne Rep. at 4. Dr. Kinsbourne's report does not explain, however, *how much* oxidative stress is generated by vaccines generally (or the vaccines in question specifically), nor does it propose what level of oxidative stress is necessary to cross the "tipping point" to cause clinical disease manifesting as autism. In addition, based on his CV, it does not appear that Dr. Kinsbourne has the specific experience in the fields of immunology, mitochondrial function, or metabolic disorders to opine credibly on these topics, despite his pediatric and neurologic expertise.

Dr. Kinsbourne also addressed the timeframe in which he thought sufficient post-vaccination oxidative stress could occur to cause autism. He opined that the byproduct of vaccine-induced oxidative stress "typically becomes evident by two weeks after the provocative event." Kinsbourne Rep. at 4. In this case (according to C.J.K's mother) C.J.K. began regressing three weeks after receiving the flu vaccine in October 2005, which he proposed was a reasonable timeframe. *Id*. To support his opinion, Dr. Kinsbourne cited approximately seven studies or articles that he maintained shed light on the timeframe necessary for such a process to occur.[21]

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[20] Cytokine is a generic term for non-antibody proteins released by one cell population on contact with a specific antigen. *Dorland's* at 466. Cytokines act as intercellular mediators and contribute to the immune response. "Proinflammatory" signifies that these cytokines are capable of stimulating inflammation. *Id.* at 1523.

[21] *See* K. Edmonds, *The Otolaryngological Manifestations of Mitochondrial Disease and the Risks of Neurodegeneration with Infection*, 128 Archives of Otolaryngology-Head & Neck Surgery 355, filed as Ex. 45 (ECF No. 81-2); Poling, et al., *Developmental Regression and Mitochondrial Dysfunction in a Child with Autism*, 21 J. Child Neurol. 170, 170-72 (2006), filed as Ex. 46 (ECF No. 81-3) ("Poling"); M. Phillips, et al., *Effect of Influenza Vaccination on Oxidative Stress Products in Breath*, 4 J. Breath Research 1 (2010), filed as Ex. 47 (ECF No. 81-4); J. Shoffner et al., *Fever Plus Mitochondrial Disease Could be Risk Factors for Autistic Regression*, 25 J. Child Neurol. 429, 429-34 (2010), filed as Ex. 48 (ECF No. 81-5) ("Shoffner"); S. Reuter, et al., *Oxidative Stress, Inflammation and Cancer: How are They Linked?*, 4 Free Radical Biology Medicine 16 (2010), filed as Ex. 49 (ECF No. 81-6); S. Rose, *Oxidative Stress Induces Mitochondrial Dysfunction in a Subset of Autism Lymphoblastoid Cell Lines in a Well Matched Case Control Cohort*, 9 PLOS 1, filed as Ex. 50 (ECF No. 81-7), D. Fein, et al., *Brief Report: Pervasive Developmental Disorder Can Evolve into ADHD: Case Illustrations*, 35 J. Autism and Developmental Disorders 525 (2005), filed as Ex. 51 (ECF No. 82-1).

3. *Dr. Richard Boles*

Petitioners' third expert was Dr. Boles, a medical geneticist, and his report addresses challenges by Respondent's experts about C.J.K.'s purported mitochondrial disorder and/or disease diagnosis. *See* Report, dated Mar. 18, 2016, filed as Ex. 53 (ECF No. 104-2) ("Boles Rep."). Dr. Boles opined that "[s]ince all aspects of [C.J.K.]'s regression and subsequent plateauing of development occurred shortly following vaccination, vaccine-triggered injury is highly likely." Boles Rep. at 9.

While a brief synopsis of his background was included in his expert report, Petitioners did not separately file a CV for Dr. Boles. Boles Rep. at 1. His report indicated that he attended the University of California, Los Angeles for medical school and completed a residency in Pediatrics there followed by a genetics fellowship at Yale University. *Id*. After serving on the faculty at the University of Southern California, he became the director of Courtagen Life Sciences, a biotechnology company in Woburn, Massachusetts. *Id*. Dr. Boles also maintains a private practice in Pasadena, California where his emphasis is in Mitochondrial Medicine and Clinical Genomics. *Id*. In addition, Dr. Boles has authored many publications, mainly in the field of genetics. *Id*. He has expertise in genetics and the clinical treatment of mitochondrial diseases.

Dr. Boles began his report with a summary of C.J.K.'s medical history, relying heavily on allegations made by the Petitioners themselves rather than on the contemporaneous medical history. Thus, Dr. Boles notes that after the April 2005 vaccinations, Mrs. Kreizenbeck *states* that she had observed C.J.K. to become "more prone to ear and throat infections," and then, after the December 2005 flu vaccine, she alleged that his "behavior changed, and he became more irritable and tired easier. He stopped interacting with those around him as he had previously." Boles Rep. at 3. Dr. Boles did, however, also point out some record evidence from three weeks post-vaccination, when C.J.K. was noted to have congestion, fever, and was not following commands, as consistent with his theory. *Id*. In addition, Dr. Boles noted that C.J.K.'s brother also suffers from a regressive autistic spectrum disorder, suggesting a genetic component to C.J.K.'s condition. *Id*. at 4.

In addition, in opining that C.J.K. had experienced a vaccine-induced reaction due to his underlying mitochondrial disorder, Dr. Boles stressed that C.J.K. had been seemingly normal (including developmentally) before receiving his April 2005 vaccinations, but thereafter had a history of gastrointestinal disorders plus a diagnosis of hypogammaglobinemia from Dr. Gupta. Boles Rep. at 3, 4. Dr. Boles also noted testing performed by Dr. Natowicz that he deemed had yielded results significant to a mitochondrial disease/disorder analysis. In particular, he noted the following results: (a) positive levels of ketones from urine analysis, (b) mildly-elevated levels of pyruvate, (c) elevated serum 3; and (d) the genetic testing demonstrating mutations consistent with

immunodeficiency. *Id.* at 5. Importantly, however, and as previously discussed, Dr. Natowicz found *only* the serum 3 levels as suggestive of a mitochondrial disorder, deeming the other results (including genetic testing) inconclusive.

Dr. Boles's characterization of C.J.K.'s alleged metabolic condition was inconsistent. Throughout his report, Dr. Boles refers to both mitochondrial disorders and diseases, as if they are interchangeable concepts. *See, e.g.*, Boles Rep. at 1, 5. He ultimately opines that C.J.K.'s condition is "suggestive" of mitochondrial *disease* – but also states that "there is nothing in the records that argues against a mitochondrial *disorder*." *Id.* at 9 (emphasis added). He later opines that "it is appropriate to assign a diagnosis of probable mitochondrial *disorder*" to C.J.K. – and yet he also believes that "a diagnosis of mitochondrial *disease* can [in this case] be established far above" the relevant preponderance standard applicable to Program claims. *Id.* (emphasis added). Because Dr. Boles's expert report does not distinguish between disease and disorder, it is difficult to ascertain whether he means to conflate the terms or not (and as discussed below, there is sound reason to distinguish between the two).

The remainder of Dr. Boles's report was dedicated to rebutting various assertions made by Respondent's experts. *See generally* Boles Rep. at 6-8. In so doing, Dr. Boles reiterated his opinion that the testing performed on C.J.K. by Dr. Natowicz was sufficient to support the diagnosis of an underlying mitochondrial disease. Boles Rep. at 6-7. The "disease-disorder" dilemma repeats itself in this section of his report; thus, Dr. Boles maintains that (contra Dr. McCandless) in fact C.J.K. *does* bear "cardinal manifestations" of mitochondrial disease, while also deeming him to suffer from a "mitochondrial disorder." *Id.* at 6. Dr. Boles grants that some test results are not strongly supportive of the mitochondrial disease/disorder diagnosis, although he questioned whether tests that did not confirm the diagnosis should be given the same weight as the positive results. *Id.* at 6-7.

Dr. Boles's report made little attempt to explain how vaccines – whether the ones C.J.K. received or others – might aggravate an underlying, asymptomatic mitochondrial condition enough to produce immunodeficiency, developmental problems, or any other injury. He did maintain that vaccines could worsen underlying genetic propensities toward immunodeficiency or metabolic disorders – citing in support recent (albeit unspecified) studies on Dravet syndrome (a rare, catastrophic form of epilepsy that begins in infancy)[22] that found that the genetic factors

[22] *See Dravet Syndrome*, NIH, https://rarediseases.info nih.gov/diseases/10430/dravet-syndrome (last accessed on May 31, 2018). Dravet syndrome is not an illness or condition that would generally be helpful to *any* Program petitioner attempting to argue that an underlying genetic-caused condition could be exacerbated by vaccine – as a line of well-reasoned decisions stand for the proposition that because of the disease's well-recognized genetic etiology, it cannot be exacerbated by vaccine. *Stone v. Sec'y of Health & Human Servs.,* 676 F.3d 1373, 1384 (Fed. Cir. 2012), *rehearing den'd en banc,* 690 F.3d 1380 (Fed. Cir. 2012), *cert. den'd,* 133 S.Ct. 2022 (2013); *see also Oliver v. Sec'y of Health & Human Servs.*, No. 10-394V, 2017 WL 747846, at *25 (Fed. Cl. Spec. Mstr. Feb. 1, 2017), *aff'd*, 133

responsible for it could create susceptibility for "vaccine-related complications." *Id.* at 5. In addition, Dr. Boles noted that in his clinical experience "the most common trigger, by far, of acute/subacute deterioration in patients with mitochondrial disease is an infectious illness, usually viral or bacterial." *Id*. at 6. He also proposed that the precise mechanism for how a vaccine would result in exacerbation of an underlying mitochondrial disease remained unknown, although he speculated that it was likely immune-mediated, and (consistent with Dr. Kinsbourne) suggested that elevated cytokines or a reactive oxygen species-mediated process might be to blame. Dr. Boles did not, however, offer a single piece of medical literature in support of these contentions – or in support of *any* contention in his report, for that matter.[23]

B. Respondent's Experts

1. *Dr. Shawn McCandless*

Dr. McCandless authored two reports in the case. *See* Expert Report, dated Sept. 29, 2015, filed as Ex. F (ECF No. 88-1) ("McCandless Rep."); Supplemental Expert Report, dated Aug. 23, 2016, filed as Ex. U (ECF No. 107) ("McCandless Supp."). He received his medical degree from Temple University School of Medicine in 1988. *See* CV of Dr. McCandless, dated Sept. 29, 2015, filed as Ex. G (ECF No. 88-2) ("McCandless CV"). Dr. McCandless completed his residency in pediatrics at the University of Wisconsin Hospital and Clinics, followed by a second residency in pediatrics at Gloucestershire Royal Hospital. *Id*. at 1. He is currently an associate professor of genetics, pediatrics, and pathology at Case Western Reserve University, and also serves as a director for several centers at the University. *Id.* In addition, and importantly for the present case, he is a director of the Center for Inherited Disorders of Energy Metabolism ("CIDEM") (affiliated with University Hospitals Cleveland Medical Center) in Cleveland, Ohio. McCandless Rep. at 1.

At the outset, Dr. McCandless stated that he does not believe that C.J.K. has any mitochondrial disease, dysfunction, or an inborn error of metabolism. McCandless Rep. at 5. Rather, the "extensive testing described in these records confirms *the absence* of almost all known inborn errors of metabolism, and certainly all of those that are known to present with the clinical findings described in CJK." *Id*. (emphasis added).

Fed. Cl. 341, 353 (2017), *appeal docketed*, No. 17-2540 (Fed. Cir. Sept. 13, 2017); . Indeed – and somewhat contrary to Petitioners' significant aggravation claim - Dr. Boles referenced case and animal studies that have found that *irrespective* of vaccinations, humans and animals with the gene variation that C.J.K. has often exhibit clinical features including immunodeficiency, developmental delay, and hearing loss as a natural progression of their condition. Boles Rep. at 5.

[23] Dr. Boles's report was filed in this case in March 2016, after several requests to extend the time in which to do so. Given the amount of time that has since passed, Petitioners have no excuse for not filing any such materials by the present date.

To support his conclusion, Dr. McCandless engaged in a detailed review of C.J.K.'s medical testing results. Based upon that review, he opined that the record did not establish "any cardinal symptoms of [primary] mitochondrial disease." McCandless Rep. at 3; R. Haas, et al., *Mitochondrial Disease: A Practical Approach for Primary Care Physicians*, 120 Pediatrics 1326 (2007), filed as Ex. H (ECF No. 88-3) ("Haas"). Specifically, Dr. McCandless noted that (a) C.J.K. never displayed elevated lactate and pyruvate in blood, urine, or cerebrospinal fluid ("CSF"); (b) did not manifest increased alanine in blood or CSF; (c) tests revealed no evidence of significant increase in tricarboxylic acid; and (d) no other amino acids in blood (proline or lower than normal citrulline or arginine) were detected. McCandless Rep. at 3; J. Smeitink, et al., *Mitochondrial Medicine: A Metabolic Perspective on the Pathology of Oxidative Phosphorylation Disorders*, 3 Cell Metabolism 9 (2006), filed as Ex. I (ECF No. 88-4) ("Smeitink"). Dr. McCandless acknowledged that C.J.K. had slightly elevated serum 3 levels, but considered that to be a "non-specific finding," especially in the absence of other persuasive indicators of a primary mitochondrial disease. McCandless Rep. at 3; Ex. 26 at 7.

Dr. McCandless then addressed other testing performed on C.J.K. McCandless Rep. at 3. First, he considered the fibroblast test that measured the lactic and pyruvic acids accumulated in skin cells. C.J.K. was found to be within a normal result of 14; true cases of mitochondrial dysfunction, by contrast, would show a ratio higher than 20. *Id.*; Ex. 37 at 2. Second, he reviewed the test of C.J.K.'s individual components of the mitochondrial respiratory chain. These components are measured individually, and the results of each such test for C.J.K. was normal. McCandless Rep. at 3; Ex. 37 at 3.

The final fibroblast test Dr. McCandless discussed was the Ox Phos, which according to Dr. McCandless measures "the ability of the mitochondria to take up the compounds, to normally metabolize the substrates added by extracting the energy from the chemical bonds in the compounds, and to measure the respiratory chain's ability to use that energy to make ATP." McCandless Rep. at 3.[24] Unlike the other fibroblast tests, Dr. McCandless admitted (consistent with the view of Dr. Natowicz) that this result *did* reveal mild dysfunction in the first part of the electronic transport chain (complex 1). *Id*. However, Dr. McCandless posited, its significance needed to be evaluated against the overall context of C.J.K.'s other clinical and laboratory findings – which were *not* supportive of the conclusion that C.J.K. had any mitochondrial disease or disorder. *Id*. When given its proper weight, this somewhat significant positive result was, Dr. McCandless proposed, most likely "not due to a specific underlying defect of mitochondrial electron transport chain itself," but instead reflected "some secondary suppressor of the electron transport chain either found in the patient, or [caused by] . . . a problem in the laboratory," and

[24] For a definition of ATP, see footnote 17 above.

therefore was not supportive of the conclusion that C.J.K. had any mitochondrial dysfunction. *Id*. at 3-4; Ex. 33 at 7.

Although admittedly not an immunologist, Dr. McCandless attempted to rebut Dr. Kinsbourne's theory of oxidative stress caused by vaccines. McCandless Rep. at 6. Mitochondria, Dr. McCandless maintained, have the ability to defend against injury, so only those individuals with severe defects in mitochondrial function are likely to develop symptoms as a result of an environmental insult. *Id*. at 5. Indeed, mitochondria are "exposed to oxidative stress constantly," rendering "without merit" the argument that an environmental factor like a vaccine could be sufficient to result in significant injury as is alleged in this case. *Id*.

Dr. McCandless also offered a second expert report aimed at responding to points made by Dr. Boles. *See generally* McCandless Supp. In it, Dr. McCandless noted Dr. Boles's concession that there was an "absence of proof" supporting the conclusion that C.J.K. suffered from "primary" mitochondrial disorder (i.e. a known mitochondrial disease), adding that Dr. Natowicz (with whom Dr. McCandless frequently interacts professionally) had himself never so proposed, given his use of the term "secondary phenomenon." McCandless Supp. at 1-2. Placing greater emphasis on the lab findings generated by Dr. Natowicz, and relying on his own expertise at CIDEM interpreting tests aimed at evaluating mitochondrial function, Dr. McCandless disputed Dr. Boles's attempt to define "trivial" increases in certain biomarkers as "highly abnormal." *Id.* at 2. The Ox Phos result was also "ambiguous at best" in Dr. McCandless's estimation – and, when considered in light of the lab's own discussion of that result (in connection with the other fibroblast results) could not properly be deemed "diagnostic of a primary mitochondrial disease." *Id.* at 3, 4; *see also* Ex. 31 at 4.

2. *Dr. Dean Jones, Ph.D.*

Dr. Jones offered an opinion based on his expertise in redox biology[25] and mitochondrial metabolism. He authored one report for Respondent, which was limited to addressing Dr. Kinsbourne's report. *See* Expert Report, filed as Ex. J, dated Sept. 29, 2015 (ECF No. 89-1) ("Jones Rep.").

Dr. Jones is currently employed as a professor at the Emory University of School of Medicine. *See* CV, filed as Ex. K, dated Sept. 29, 2015 (ECF No. 89-2) ("Jones CV"). He studied biochemistry and the University of Illinois in Urbana, Illinois, prior to obtaining his Ph.D. in

[25] Redox Biology is the study of reactive species, such as superoxide, hydrogen peroxide, and nitric oxide. *See Redox Biology (RB)*, Ctr. for Cancer Research, NIH, https://ccr.cancer.gov/training/trainee-resources/courses-workshops/rb (last accessed on May 31, 2018). Specialists in redox biology typically analyze how redox-active species are generated, and their effects on the cellular and physiological parts of the body. *Id.*

biochemistry at Oregon Health Sciences University in Portland, Oregon. *Id*. at 1. His research has been focused on mitochondrial metabolism, oxidative stress, and redox biology. Jones Rep. at 1. Dr. Jones acknowledges that he does not have clinical training in immunology, neurology, gastroenterology, or genetics. *Id*.

Dr. Jones, like Dr. McCandless, opined that C.J.K. does not have a mitochondrial disease or disorder, based on the "cumulative laboratory results." Jones Rep. at 2. He particularly disputed whether the Ox Phos test was sufficient by itself to conclude that C.J.K. had a mitochondrial disease, without additional controls and repeat measurements. *Id*. C.J.K. also lacked some of the "major deficits" that would characterize an individual suffering from a mitochondrial disease or disorder, making it more difficult to conclude that there could be any causal connection between vaccination and injury. *Id*. at 4. He referenced a case study cited by Dr. Kinsbourne - Poling, et al., *Developmental Regression and Mitochondrial Dysfunction in a Child with Autism*, 21 J. Child Neurol. 170, 170-172 (2006), filed as Ex. 46 (ECF No. 81-3) ("Poling") – to illustrate his point, noting the vast differences in test results relating to mitochondrial function as reported in Poling versus what C.J.K. displayed. Jones Rep. at 4.

Dr. Jones also took specific issue with Dr. Kinsbourne's descriptions of oxidative stress, stating they "represent[] a very non-professional write-up or a nearly complete ignorance of the concepts." Jones Rep. at 5. In connection with this contention, Dr. Jones referenced several studies that have been unable to find a statistically significant role for oxidative stress in initiating a pathogenic process or causing neurologic harm (autism or developmental problems). *Id*. at 5-6; M. Goodman, et al., *Clinical Trials of Antioxidants as Cancer Prevention Agents: Past, Present, and Future*, 51 Free Radical Biology & Med. 1068 (2011), filed as Ex. M (ECF No. 94-2). Rather, recent studies have suggested that reactive oxidants produced in response to oxidative stress have a beneficial role, acting as major components of growth and development. *Id*. at 6; M. Lampl, *Human Growth from the Cell to the Organism: Saltations and Integrative Physiology*, 36 Annals of Human Biology 478-95 (2009), filed as Ex. P (ECF No. 84-5). Dr. Jones also proposed that the signaling of certain cytokines (TNF alpha and IL-6 and IL-1 beta) encouraged by vaccines was common to normal physiology rather than the component of a pathologic process. *Id*. at 7.

3. *Dr. Max Wiznitzer*[26]

For his third expert report, Respondent offered the opinion of a pediatric neurologist, Dr. Wiznitzer. *See* Expert Report, filed as Ex. A, dated Sept. 29, 2015 (ECF No. 87-1) ("Wiznitzer

[26] Because Petitioners have formally represented that they are no longer pursuing the claim that vaccines caused C.J.K.'s autism, I am setting forth an abbreviated summary of Dr. Wiznitzer's opinion – although (as discussed below) I do not find fully credible Petitioners' assertions that they have fully abandoned developmental problems as an alleged result of the vaccinations at issue.

Rep."). Dr. Wiznitzer's overall impression was that C.J.K. had clinical features of autism prior to his influenza vaccination, and that none of those developmental problems "were caused or aggravated by his 10/12/05 influenza vaccination." *Id*. at 8.

Dr. Wiznitzer graduated from the honors program in medical education at Northwestern University, where he received a bachelors of science in medicine in 1975 and then his medical degree in 1977. *See* CV of Dr. Wiznitzer, filed as Ex. B, dated Sep. 29, 2015 (ECF No. 87-2) ("Wiznitzer CV"). *Id*. at 1. He completed a three-year internship and residency in pediatrics at Cincinnati Children's Hospital, followed by a one-year fellowship in child development and developmental disorders at the Cincinnati Center for Developmental Disorders. *Id*. He also completed a three-year child neurology fellowship at the University of Pennsylvania and Children's Hospital of Philadelphia, followed by a two-year National Institute of Health fellowship in disorders of higher cortical function in children at the Albert Einstein College of Medicine in the Bronx, New York (which involved working with children with autism spectrum disorders). *Id*. Dr. Wiznitzer currently works at the University Hospitals of Cleveland in Cleveland, Ohio. *Id.* at 2. Dr. Wiznitzer holds board certifications in pediatrics and neurology. *Id.* at 5.

Dr. Wiznitzer does not dispute that C.J.K. was accurately diagnosed with autism in March 2006. Wiznitzer Rep. at 7. However, Dr. Wiznitzer opined that C.J.K.'s clinical history was consistent with "the trajectories reported in the autism population," rather than the product of a disease process initiated by vaccines. *Id*. Dr. Wiznitzer did emphasize that C.J.K. was never diagnosed with developmental regression; rather, the records reveal that Mrs. Kreizenbeck, in association with certain of C.J.K.'s pediatricians, expressed concern that he was not *progressing* as expected. *Id*. The distinction (between regression and a plateau in development) Dr. Wiznitzer deemed significant, and related directly to his opinion that vaccines were not the cause of C.J.K.'s autism. *Id*. Indeed, Dr. Wiznitzer highlighted the fact that some indications in the medical records suggested that C.J.K.'s autism began *prior* to his vaccinations (although he made this point relying on records in which C.J.K.'s medical history was recounted after the fact, rather than in contemporaneous records). *Id.*

III. Factual Witness Statements

Filed with Dr. Kinsbourne's report was an affidavit from Mrs. Kreizenbeck, dated May 29, 2015, describing the changes she witnessed in C.J.K.'s condition following his receipt of the vaccines at issue. *See generally* Ex. 42. In it, Mrs. Kreizenbeck maintained that C.J.K.'s health worsened after his April 2005 vaccination, beginning with a fever. Ex. 42 at 2 ¶¶ 4-5. Although admitting that she could not precisely recall a similar reaction in October, she nevertheless asserted that C.J.K. commonly had post-vaccination fevers, and therefore he likely experienced one after the October 2005 vaccination as well. *Id.* at ¶ 7. She recalled observing more serious health and

behavioral changes after receipt of the October flu vaccine. *Id*. at ¶ 8. Mrs. Kreizenbeck also asserted that she first learned that C.J.K. might be autistic in December 2005, at a visit to an ENT doctor, and that the behaviors he displayed had not existed before October of that year (an assertion belied by the medical record, which places onset of behavioral changes as early July 2005). Ex. 42 at 3 ¶1; Ex. 4 (Part 1) at 20.

IV. Procedural History and Evolution of Petitioners' Claim

This action was initiated over ten years ago, and for large periods of its existence Petitioners unquestionably sought to establish that C.J.K.'s autism was the result of his 2005 vaccinations. Thus, the original 2008 petition alleged that C.J.K. "suffered from gastrointestinal disease, immune dysfunction, encephalitis, heavy metal poisoning, nutritional, metabolic, and mitochondrial dysfunction . . . by the multiple vaccinations [C.J.K.] received on April 1, 2005, and the thimerosal based Flu vaccine received on Oct 12, 2005. . . . [P]etitioners believe that the vaccinations that [C.J.K.] received . . . resulted in [a]utism." Petition, dated March 26, 2008, at ¶ 14.

The Kreizenbecks began as *pro se* petitioners. During the case's first eighteen months, very little occurred. Because autism was alleged as an injury in this case, it was included within the Omnibus Autism Proceeding ("OAP")[27], and was stayed pending the results of the six OAP test

[27] In the OAP, thousands of petitioners' claims that certain vaccines caused autism were joined for purposes of efficient resolution. A "Petitioners' Steering Committee" was formed by many attorneys who represent Vaccine Program petitioners, with about 180 attorneys participating. This group chose "test" cases to represent the entire docket in the OAP, with the understanding that the outcomes in these cases would be applied to cases with similar facts alleging similar theories.

The Petitioners' Steering Committee ultimately chose six test cases to present two different theories regarding autism causation. The first theory alleged that the measles portion of the MMR vaccine precipitated autism, or, in the alternative, that MMR plus thimerosal-containing vaccines caused autism, while the second theory alleged that the mercury contained in thimerosal-containing vaccines could affect an infant's brain, leading to autism.

The first theory was rejected in three test case decisions, all of which were subsequently affirmed. *See generally Cedillo v. Sec'y of Health & Human Servs*., No. 98-916V, 2009 WL 331968 (Fed. Cl. Spec. Mstr. Feb. 12, 2009), *mot. for review den'd*, 89 Fed. Cl. 158 (2009), *aff'd*, 617 F.3d 1328 (Fed. Cir. 2010); *Hazlehurst v. Sec'y of Health & Human Servs*., No. 03-654V, 2009 WL 332306 (Fed. Cl. Spec. Mstr. Feb. 12, 2009), *mot. for review den'd*, 88 Fed. Cl. 473 (2009), *aff'd*, 605 F.3d 1343 (Fed. Cir. 2010); *Snyder v. Sec'y of Health & Human Servs*., No. 01-162V, 2009 WL 332044 (Fed. Cl. Spec. Mstr. Feb. 12, 2009), *aff'd*, 88 Fed. Cl. 706 (2009).

The second theory was similarly rejected. *Dwyer v. Sec'y of Health & Human Servs*., No. 03-1202V, 2010 WL 892250 (Fed. Cl. Spec. Mstr. Mar. 12, 2010); *King v. Sec'y of Health & Human Servs*., No. 03-584V, 2010 WL 892296 (Fed. Cl. Spec. Mstr. Mar. 12, 2010); *Mead v. Sec'y of Health & Human Servs*., No. 03-215V, 2010 WL 892248 (Fed. Cl. Spec. Mstr. Mar. 12, 2010).

After the OAP's conclusion, a total of 11 lengthy decisions by special masters, the judges of the U.S. Court of Federal Claims, and the panels of the U.S. Court of Appeals for the Federal Circuit had unanimously rejected the petitioners' claims. These decisions found no persuasive evidence that the MMR vaccine or thimerosal-containing vaccines caused autism. The OAP proceedings concluded in 2010.

cases. After the test cases were resolved (unsuccessfully for any of the relevant petitioners), the Kreizenbecks chose to continue with their claim, and were ordered to produce an expert report. Order, dated September 22, 2010 (ECF No. 9). By December 7, 2011 (almost four years after the petition was filed), however, no expert report had been filed (after seeking several extensions of time) although Petitioners had retained Mr. Richard Gage as their attorney. *See* Consented Motion to Substitute Richard Gage in Place of Pro Se, dated Dec. 7, 2011 (ECF No. 21).

On February 22, 2012, Petitioners refined their causation theory in an amended petition. *See generally* Amended Pet. They now alleged that the flu vaccine C.J.K. received on October 12, 2005 (rather than his April 1, 2005 childhood vaccines), had "adversely effected his immune system," including diarrhea and vomiting. *See* Amended Petition, dated Feb. 22, 2012 (ECF No. 27) ("Amended Pet."). Filed with the amended petition was a motion for an extension of time, which explicitly stated "[t]his case is now being prosecuted as an immune system injury case. *This case is no longer being prosecuted as an autism injury case*." *See* Motion for an Extension of Time, dated Feb. 22, 2012 (ECF No. 27) at ¶2 (emphasis added). However, Petitioners also subsequently informed the special master then responsible for the action that they had obtained "mitochondrial testing" for C.J.K., and that the results of that testing might shed light on the nature of his injuries. *See* Status Report, dated March 15, 2013 (ECF No. 46). Awaiting those results caused further delay in the case's adjudication.

While the results of that testing were pending, on July 31, 2013, Petitioners filed the expert report of Dr. Levin – and thereby revealed the *third* iteration of Petitioners' causation theory. As discussed above, Dr. Levin posited that C.J.K. "was born with asymptomatic inborn errors of metabolism which were triggered to become symptomatic in the form of immunological anomalies by the cytokines released by the vaccinations he received on April 1, 2005." Levin Rep. at 2. Thus (and in contrast to the Amended Petition), Dr. Levin's opinion renewed Petitioners' earlier argument that the April vaccines were significant, since he maintained they had triggered an initial reaction, although he added that "[C.J.K.'s] symptoms returned with a re-challenge vaccination on October 12, 2005, and remained significant until he was appropriately treated by his attending physicians." *Id.*

In the interim, Petitioners continued medical record collection, and were subsequently ordered in the fall of 2013 to file an additional expert report once the mitochondrial testing results had been obtained and filed. *See* Scheduling Order, dated Nov. 5, 2013 (ECF No. 57). The special master's order made clear that this expert report was specifically to address "how one or more vaccine(s) received by [C.J.K.] *can cause an autism spectrum disorder*." *Id.* at 1 (emphasis added). Thus, as of the fall of 2013, it appears that there remained some belief (albeit possibly mistaken)

on the part of the special master presiding over the case at the time that Petitioners *still* sought to connect C.J.K.'s autism to his vaccinations, despite their claims to the contrary the year before.

Another year and a half passed while additional genetic testing was performed, with multiple extensions of time requested for the filing of the supplemental expert report. Eventually the matter was assigned to me in September 2014. Almost eight months after that, Petitioners filed Dr. Kinsbourne's expert report, on May 30, 2015. However – and despite having plainly stated in 2012 (now three years earlier) that Petitioners were abandoning their autism injury claim, Dr. Kinsbourne's report directly identified autism as a likely "sequelae" of the significant aggravation of C.J.K.'s condition brought on by his receipt of the flu vaccine in October 2005. Kinsbourne Rep. at 5. The summation of his opinion was unequivocal in this regard, affirmatively opining that "[C.J.K.] developed Autistic disorder soon after his influenza vaccination" due to oxidative stress caused by vaccination. *Id.* at 3.

Over the next several months in 2015, Respondent obtained and filed expert reports from Drs. McCandless, Wiznitzer, and Jones (ECF Nos. 87-89). In addition, Respondent filed an amended Rule 4(c) Report. *See* Amended Rule 4(c) Report, dated October 2, 2015 (ECF No. 90). Respondent's experts attempted to address the breadth of Petitioners' intertwined theories, and thus offered opinions responding to (a) Dr. Kinsbourne's causation theory regarding autism, (b) the lack of evidence C.J.K. had a mitochondrial disorder, and (c) the assertion that C.J.K. had an inborn metabolic error. *Id.* at 3-4.

I thereafter ordered Petitioners to file any supplemental expert report reacting to Respondent's experts' opinions by January 15, 2016. *See* Scheduling Order, dated Nov. 2, 2015 (Docket Entry). After two requests for additional time, Petitioners filed their third expert report, from Dr. Boles, on March 18, 2016. Like Dr. Kinsbourne, Dr. Boles also attributed C.J.K.'s autism and/or developmental problems to a reaction to the flu vaccine that exacerbated C.J.K.'s alleged underlying mitochondrial disorder, although he referenced many of C.J.K.'s other non-autism symptoms as vaccine-caused as well. Boles Rep. at 7, 9-10 (emphasis added). On August 23, 2016, Respondent filed a supplemental expert report from Dr. McCandless addressing Dr. Boles's conclusions. ECF No. 107.

By the fall of 2016, it appeared the matter was at long last ready for hearing, and I scheduled this to occur in the following year, on December 5-6, 2017. *See* Prehearing Order, dated Dec. 13, 2016 (ECF No. 112). In accordance with that Order, Petitioners filed their opening prehearing brief on May 5, 2017. *See* Prehearing Submission, dated May 5, 2017 (ECF No. 114) ("Pet. Prehearing"). In it, they set forth *yet another* variation in Petitioners' theory – now arguing (contrary to the 2012 amended petition) that the 2005 vaccinations "significantly aggravated [C.J.K.'s] pre-existing, but asymptomatic, mitochondrial disorder," resulting in virtually *all* of

C.J.K.'s symptoms after those respective dates. Pet. Prehearing at 6. Although reference to autism was nonexistent in this filing, Petitioners did propose that evidence of C.J.K.'s underlying mitochondrial dysfunction (exacerbated by vaccines) had manifested in the form of "neurological issues" (*Id.* at 9), and that within three weeks of his receipt of the flu vaccine C.J.K. was "no longer following commands and he had delayed speech." *Id.* at 9. The prehearing filing was vague in specifying which experts would be testifying and on what topics, making it difficult to conclude at this point that autism and/or developmental limits had in fact been completely eliminated as a complained-of injury in this case.

Respondent's pre-hearing brief, dated June 5, 2017, was accompanied by a separately-filed request for a ruling on the record dismissing this action (ECF Nos. 115 and 116) (collectively, "Mot.").[28] Noting that Petitioners' claim was dependent on a finding that C.J.K. had a preexisting metabolic disorder of some kind, characterized by mitochondrial dysfunction or disease, Respondent argued that neither the record nor the expert reports submitted in support of this concept supported it, and therefore asked for dismissal in light of a different case I had recently decided on the papers in which an injured party's alleged preexisting mitochondrial dysfunction was, as here, central to the claim. Mot. at 12, *citing Pope*, 2017 WL 2460503.

After the completion of prehearing briefing (which included additional filings reacting to Respondent's motion),[29] I held a status conference on October 4, 2017. *See* Scheduling Order, dated October 5, 2017 (ECF No. 120). Taking into account Petitioners' most recent expert reports (Drs. Boles and Kinsbourne) along with Respondent's Motion, and in light of the claim's similarity to other cases alleging that an underlying mitochondrial disorder had been exacerbated by vaccine (and resulting in autism or developmental regression as an injury), I determined that a ruling on the papers was preferable to a hearing as the most efficient means for resolving the case. *Id.* at 1.[30] I also expressed the view that (as of that time) the claim likely lacked reasonable basis in light of its deficiencies, and therefore even if a hearing were held, I would not be inclined to compensate Petitioners' counsel or experts for any work performed therein given my serious misgivings about the claim's substantive validity. *Id.* at 2.

[28] Respondent's actual motion (ECF No. 116) is a very short document that largely incorporates by reference the detailed analysis set forth in his pretrial filing (ECF No. 115). References herein to "Mot." shall therefore be to the substantive contents of the latter.

[29] Those filings are discussed below in the section of this Decision pertaining to the parties' respective arguments.

[30] I also noted in this Order that although Petitioners had formally stated that autism was not the complained-of injury (anymore), they appeared to be trying to reclassify the case in order to evade the overwhelming weight of negative precedent concerning autism injury claims. *Id.* at 1 n.1.

My October 5th Scheduling Order allowed Petitioners two weeks to determine how they would like to proceed. Petitioners ultimately conceded that the financial risk of their counsel not being compensated at a hearing outweighed their desire to have the matter heard, although they reiterated their objection to the hearing's cancellation. *See* Status Report, dated Oct. 20, 2017 (ECF No. 121). I thereafter set the deadline of December 8, 2017, for both sides to file final briefs in support of their positions, and each did so. The matter is ripe for resolution.

V. Arguments For and Against Dismissal

Respondent's Motion

Respondent argues that the record does not allow for the conclusion that C.J.K. had any kind of preexisting mitochondrial disease or dysfunction, drawing upon a detailed review of the medical record to illustrate his points. Mot. at 5-11. In connection with this argument, Respondent highlights my determination in *Pope* to dismiss on the record a case with a similar theory and similar facts, and also involving some of the same experts, such as Dr. Kinsbourne. Mot. at 12. There, as here, (a) the record did not establish the existence of a mitochondrial disorder, or evidence of a post-vaccination reaction, and (b) the claimants lacked a reliable and persuasive causation theory. *Id.* at 13-17. Respondent also maintains that Petitioners' experts relied on facts not corroborated by the record, but merely alleged by Mrs. Kreizenbeck. *Id.* at 17-22. And he challenges the reliability of Dr. Kinsbourne's opinion regarding the concept of oxidative stress brought on by vaccination. *Id.* at 23-27.[31]

Petitioners' Opposition

Petitioners responded to the dismissal motion on July 14, 2017 (ECF No. 118) ("Opp."). Petitioners deem their evidentiary showing "solid," pointing out the disparity between C.J.K.'s pre- and post-vaccination health. Opp. at 2. They maintain that it was "medically probable" that C.J.K. did have an underlying (but initially asymptomatic) mitochondrial or immune dysfunction, as corroborated by the diagnoses of several subsequent treaters like Drs. Gutpa or Natowicz. *Id.* They further argue that proof of aggravation is found in the illnesses C.J.K. experienced after receiving the vaccines. *Id.* at 2-4. Once his immune-compromised condition was understood and his treatment adjusted, he experienced an improvement in his health. *Id.* at 3. Petitioners also, however, maintain that the law relevant in the Vaccine Program does not require them to prove the nature of C.J.K.'s immune deficiency "to perfection" – meaning that it does not matter whether

[31] Respondent's motion also takes aim at the fact that Petitioners' alleged injury had been vaguely articulated, allowing for the possibility that they continued to allege some kind of autism/developmental injury in this case despite their claims to the contrary. Mot. at 1 n.1.

treaters and experts were correct in their assessment that C.J.K. suffered from mitochondrial dysfunction - and that the overall picture afforded by a review of the medical record in its entirety supports their claim. *Id.* at 4-5.[32]

Consistent with the Amended Petition, the Opposition to Respondent's motion does not discuss, or even mention, autism, regression, or developmental delay as C.J.K.'s claimed injury. However, it relies on the facts and analysis set forth in their earlier prehearing brief, which *did* contemplate that the vaccinations, at least initially, manifested themselves in a developmental issue, and/or that such issues (which today have evolved into ADHD) are a consequence of vaccination. *See, e.g.*, Pet. Prehearing at 3, 4, 6, 7, and 9.

Petitioners also argue in favor of holding a hearing in this case. To that end, they note that there was medical record evidence supporting components of their claim (for example, the illnesses he experienced in 2005), and maintain that a hearing would assist them in developing facts on disputed topics such as onset. Opp. at 3. Given that "[f]or every argument made, Petitioners have made a counter-argument" (Opp. at 6), only a hearing could provide Petitioners with a reasonable opportunity to "fully present evidence" supporting their claim. *Id.* at 1.

Respondent's Reply

Respondent subsequently filed a reply in support of his motion. Reply, dated July 19, 2017 (ECF No. 119) ("Reply"). He maintains his prior position that preponderant evidence does not support Petitioners' contention that C.J.K. suffered from any kind of mitochondrial dysfunction, as alleged – and that even if it were assumed otherwise, the record also did not support the conclusion that any of the vaccines he received exacerbated it. Reply at 1-2. He also notes that there were significant reliability problems with both Drs. Kinsbourne's and Levin's reports that Petitioners have ignored, and that Respondent's more comprehensive expert reports rebut Petitioners' expert contentions. *Id.* at 2-4. Petitioners also do not grapple with reliable record evidence that is contrary to their theory, such as Dr. Wright's determination that C.J.K. lacked an immune deficiency. *Id.* at 5. All in all, Respondent reiterates his point that (consistent with *Pope*)

[32] Notably, Respondent's motion seems to have inspired Petitioners to fine-tune their theory yet again. Thus, the causation theory articulated herein seems to have moved further away from the theories of Drs. Kinsbourne and Boles, who attributed C.J.K.'s autism to the flu vaccine, and instead emphasizes the April and October vaccines containing live viruses (flu, MMR, and varicella) as the source of the immune deficiency. Opp. at 3 ("[i]t is known that it is extremely dangerous to give live vaccines to someone who has an inborn error of metabolism"). Petitioners cite to Dr. Levin's opinion for this assertion – although the Levin Report does not *itself* contain this language or make this specific argument. *See generally* Levin Rep. Moreover, this theory would eliminate from consideration the flu vaccine C.J.K. received – which was *not* a live virus vaccine. *See Vaccine Information Statements (VIS): Inactivated Influenza VIS*, CDC, https://www.cdc.gov/vaccines/hcp/vis/vis-statements/flu html (last accessed on June 4, 2018) ("[t]here is no live virus in flu shots.").

I could rule in this case based upon the plain content of the expert reports filed, and thereby weigh the sufficiency of Petitioners' overall evidentiary showing without a hearing. *Id.* at 2, 5.

Final Memoranda

As noted above, after I determined that I would rule on the record in this case, I provided both sides the opportunity to file final memoranda summarizing their positions. Each did so on December 8, 2017 (ECF Nos. 126 ("Pet. Filing") and 125 ("Rep. Filing")).

Petitioners' filing emphasized that the claim (as it stood in December 2017) sought only to recover damages for injuries that had manifested "as an immune system anomaly, namely hypogammoglobulinemia." Pet. Filing at 1. Totally ignoring Dr. Kinsbourne's opinion, Petitioners stressed the illnesses C.J.K. experienced after his April and October 2005 vaccinations, and the immune deficiency diagnosis he received, along with Dr. Levin's opinion about C.J.K.'s purported "inborn errors of metabolism," bulwarked by Dr. Boles's opinion about the nature of the error (namely mitochondrial dysfunction). *Id.* at 2-5. Otherwise Petitioners reiterated their prior points from earlier filings. Respondent's final filing was even more succinct, and merely set forth a listed summary of points previously made in his motion about the deficiencies in Petitioners' overall showing. Rep. Filing at 1-2.

VI. Applicable Legal Standards

A. Claimant's Burden in Vaccine Program Cases

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury" – i.e., an injury falling within the Vaccine Injury Table – corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Human Servs*., 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs*., 440 F.3d 1317, 1320 (Fed. Cir. 2006).[33] In this case, Petitioner does not assert a Table claim.

[33] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Human Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Human Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd*, 104 F. App'x 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Human Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs*., 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Human Servs*., 165 F.3d 1344, 1352-53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Human Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim (which is the kind of claim asserted in this matter), a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005): "(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."

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, the petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id*. at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of*

Health & Human Servs., 121 Fed. Cl. 230, 245 (2015) ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)). But this does not negate or reduce a petitioner's ultimate burden to establish his overall entitlement to damages by preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as 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'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs.*, 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record – including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 119, 136 (2011), *aff'd*, 463 F. App'x 932 (Fed. Cir. 2012); *Veryzer v. Sec'y of Health & Human Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd,* 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 F. App'x 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant

proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id*. at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 2013 WL 1896173 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Standard for Significant Aggravation Claim

In this matter, Petitioners maintain that the relevant vaccines significantly aggravated a preexisting condition in C.J.K. – his purported mitochondrial disease or dysfunction. Where a petitioner so alleges, the *Althen* test is expanded, and the petitioner has additional evidentiary burdens to satisfy. *See generally Loving v. Sec'y of Health & Human Servs*., 86 Fed. Cl. 135, 144 (2009). In *Loving*, the Court of Federal Claims combined the *Althen* test with the test from *Whitecotton v. Sec'y of Health & Human Servs*., 81 F.3d 1099, 1107 (Fed. Cir. 1996), which related to on-Table significant aggravation cases. The resultant "significant aggravation" test has six components, which are:

> (1) the person's condition prior to administration of the vaccine, (2) the person's current condition (or the condition following the vaccination if that is also pertinent), (3) whether the person's current condition constitutes a 'significant aggravation' of the person's condition prior to vaccination, (4) a medical theory causally connecting such a significantly worsened condition to the vaccination, (5) a logical sequence of cause and effect showing that the vaccination was the reason for the significant aggravation, and (6) a showing of a proximate temporal relationship between the vaccination and the significant aggravation.

Loving, 86 Fed. Cl. at 144; *see also W.C. v. Sec'y of Health & Human Servs*., 704 F.3d 1352, 1357 (Fed. Cir. 2013) (holding that "the *Loving* case provides the correct framework for evaluating off-table significant aggravation claims"). In effect, the last three prongs of the Loving test correspond to the three *Althen* prongs.

Within the *Loving* analysis, it is necessary to evaluate the likely natural course of an injured party's preexisting disease, in order to determine whether the vaccine made the petitioner worse than he would have been but for the vaccination. *Locane v. Sec'y of Health & Human Servs.,* 685 F.3d 1375, 1381-82 (Fed. Cir. 2012) (upholding special master's determination that petitioner had failed to carry her burden of proof in establishing that her preexisting injury was worsened by the

relevant vaccine); *Hennessey v. Sec'y of Health & Human Servs.*, No. 01-190V, 2009 WL 1709053, at *41-42 (Fed. Cl. Spec. Mstr. May 29, 2009), *mot. for review den'd*, 91 Fed. Cl 126 (2010). In other words, the critical point of examination is "whether the change for the worse in [petitioner's] clinical presentation was aggravation or a natural progression" of the underlying condition. *Hennessey*, 2009 WL 1709053, at *42. The Federal Circuit has upheld the determinations of special masters that worsening was not demonstrated by a petitioner in connection with establishing her overall preponderant burden of proof for a non-Table causation-in-fact claim. *See, e.g., Snyder/Harris v. Sec'y of Health & Human Servs.,* 553 F. App'x 994, 999-1000 (Fed. Cir. 2014); *Locane*, 685 F.3d at 1381-82.[34]

The mere fact a vaccine might "trigger" a transitory negative response in an individual with an underlying condition is not proof of worsening if that individual would be expected to experience a similar course regardless. *Faoro v. Sec'y of Health &Human Servs.*, No. 10-704V, 2016 WL 675491, at *27 (Fed. Cl. Spec. Mstr. Jan. 29, 2016), *mot. rev. den'd*, 128 Fed. Cl. 61 (Fed. Cl. Apr. 11, 2016) (finding that "the vaccinations would not have changed her clinical course and thus, the vaccinations did not significantly aggravate her preexisting condition"). This point was emphasized in a subcategory of Program cases involving the claim that a child's Dravet syndrome (a rare seizure disorder now understood to be caused by the SCN1A gene mutation) was significantly aggravated by vaccination. *Faoro*, 2016 WL 675491, at *1. In such cases, special masters have repeatedly determined that petitioners failed to show that a child's expected outcome would have been different but-for the vaccination – even though it was not disputed that the child's first major seizure had in fact been triggered by vaccination. *Id.* at *2 ("[a]lthough H.E.F.'s vaccinations may have caused a low-grade fever or otherwise triggered her first seizure, neither the initial seizure nor her vaccinations caused or significantly aggravated her Dravet syndrome and resulting neurological complications"); *see also Snyder/Harris v. Sec'y of Health & Human Servs.*, 553 F. App'x 994 (Fed. Cir. 2014) (special master was not arbitrary in finding that petitioners' expert failed to show that the child's outcome would have been different had he not received the vaccinations at issue).

C. Law Governing Factual Determinations

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any

[34] This is consistent with the fact (well recognized by controlling precedent) that evidence of "worsening" relevant to Respondent's alternative cause burden may reasonably by evaluated by a special master in determining the success of a petitioner's prima facie showing. *Snyder/Harris*, 553 F. App'x at 1000, *quoting Stone*, 676 F.3d at 1380 ("no evidence should be embargoed from the special master's consideration simply because it is also relevant to another inquiry under the statute"); *see also de Bazan v. Sec'y of Health & Human Servs.,* 539 F.3d 1347, 1353 (Fed. Cir. 2008) ("[t]he government, like any defendant, is permitted to offer evidence to demonstrate the inadequacy of the petitioner's evidence on a requisite element of the petitioner's case-in-chief").

diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as "the results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such a determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd, Rickett v. Sec'y of Health & Human Servs*., 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Human Servs*., No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Human Servs*., 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms. It is equally unlikely that pediatric neurologists, who are trained in taking medical histories concerning the onset of neurologically significant symptoms, would consistently but erroneously report the onset of seizures a week after they in fact occurred").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Human Servs*., No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony – especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Health & Human Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff'd*, 968 F.2d 1226 (Fed. Cir.), *cert. den'd, Murphy v. Sullivan*, 506 U.S. 974 (1992) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral

testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, there are situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Human Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Human Servs.*, 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Human Servs*., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *La Londe v. Sec'y Health & Human Servs*., 110 Fed. Cl. 184, 203-04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records over contrary testimony, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

D. Analysis of Expert Testimony

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Human Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc*., 509 U.S. 579, 594-96 (1993). *See Cedillo v. Sec'y of Health & Human Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Human Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999)). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to

peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Human Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742-45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 146 (1997)); *see also Isaac v. Sec'y of Health & Human Servs.*, No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for review den'd*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. App'x 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339).

E. Consideration of Medical Literature

Both parties relied on a few pieces of medical and scientific literature in this case in support of their respective positions. I have reviewed all of the medical literature submitted in this case, although my decision does not discuss each filed article in detail. *Moriarty v. Sec'y of Health & Human Servs.*, No. 2015-5072, 2016 WL 1358616, at *5 (Fed. Cir. Apr. 6, 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted).

F. Determination to Resolve Case without Hearing

I have opted to decide entitlement in this case based on written submissions and evidentiary filings, including the expert reports filed by each side. The Vaccine Act and Rules not only contemplate but encourage special masters to decide petitions on the papers rather than via evidentiary hearing, where (in the exercise of their discretion) they conclude that the former means of adjudication will properly and fairly resolve the case. Section 12(d)(2)(D); Vaccine Rule 8(d). The choice to do so has been affirmed on appeal. *D'Toile v. Sec'y of Health & Human Servs.*, No. 15-85V, 2018 WL 1750619, at *2 (Fed. Cir. Apr. 12, 2018); *see also Hooker v. Sec'y of Health & Human Servs.*, No. 02-472V, 2016 WL 3456435, at *21 n.19 (Fed. Cl. Spec. Mstr. May 19, 2016) (citing numerous cases where special masters decided on the papers in lieu of hearing and that decision was upheld). I am simply not required to hold a hearing in every matter, no matter the preferences of the parties. *See Hovey v. Sec'y of Health & Human Servs.,* 38 Fed. Cl. 397, 402-03 (1997) (special master acted within his discretion in denying evidentiary hearing); *Burns*, 3 F.3d at 417.

Pope provides a good example (especially given its factual similarities to the present case) of the considerations that have in prior cases persuaded me to resolve a matter on the record rather than after hearing. There, a petitioner alleged that her son's developmental regression and autism were the result of a vaccine's exacerbation of the child's alleged underlying mitochondrial disorder. *Pope*, 2017 WL 2460503, at *1. The child had experienced many post-vaccination infections and illnesses, and the petitioner maintained that such a history of illness (plus reactions to the vaccines that the record did not set forth but petitioner alleged had nevertheless occurred) established exacerbation of the asymptomatic, underlying metabolic disorder. In addition, *Pope* featured some testing that suggested the existence of mitochondrial dysfunction, as here – and the petitioner also engaged Dr. Kinsbourne, who proposed a theory much like that offered in this case, based on vaccines stressing an individual with an underlying metabolic disorder. *Id.* at *8 – 10.

After consideration of the expert reports and record, I opted to rule on the record, denying entitlement and rejecting petitioner's request for a hearing. *Pope*, 2017 WL 2460503, at *27. In so doing, I noted that (a) I did not require live testimony to resolve a disputed fact, such as onset; (b) some fact disputes mainly involved distinctions between what the record said and what fact witnesses argued, and therefore were amenable to resolution on the papers; and (c) petitioner's experts over-relied on witness statements as opposed to the record itself. *Id.* at *26. I also determined that the petitioner's theory was too similar to theories already rejected in countless prior autism injury cases, and that I was able to weigh the reliability and ultimate persuasiveness of the expert opinions based on their written reports. *Id.*

ANALYSIS

Although Petitioners have affirmatively represented on several occasions that they no longer claim that C.J.K.'s autism or developmental problems were vaccine-caused, both the procedural history and the record – which includes the opinions of their own experts – belie their representations to a degree. As discussed above, Petitioners first asserted that they were releasing autism as the complained-of injury six years ago – but then, two years later, produced an expert opinion *in support* of that same injury (from Dr. Kinsbourne).[35] *See, e.g.*, Kinsbourne Rep. at 4 ("[a]fter the [October 2005] vaccination [C.J.K.] developed Autistic disorder"). And it is far from clear that Petitioners have actually abandoned their view that C.J.K.'s developmental problems (whether deemed a plateau or regression) were vaccine-caused – as both they and their experts continue to emphasize C.J.K.'s developmental issues as sequelae of a vaccine injury. *See, e.g.*, Boles Rep. at 3, 9; Pet. Prehearing at 3, 4, 6, 7, and 9.

It is not surprising that Petitioners might wish to distinguish this action from the host of others alleging autism as an injury – given the dismal track record of such claims. As noted above, *none* of the OAP test cases resulted in outcomes favorable to the relevant petitioners. Moreover, since the resolution of the OAP, *no* claimants have succeeded on a non-Table, causation-in-fact claim connecting autism to receipt of a vaccine. *See, e.g.*, *Hardy v. Sec'y of Health & Human Servs*., No. 08-108V, 2015 WL 7732603, at *4-5 (Fed. Cl. Spec. Mstr. Nov. 3, 2015) (referencing eleven autism claims unsuccessfully tried, plus six that were rejected (over the petitioners' objections) without trial).

Other Program claimants have attempted to recast their claim that a vaccine caused an autism injury as a claim that the vaccine precipitated *some other* initial form of injury, like an encephalopathy (more often than not autoimmune in nature), that *later* indirectly produced developmental problems due to the resulting neurologic injury. *See, e.g., Cunningham v. Sec'y of Health & Human Servs.*, No. 13-483V, 2016 WL 4529530 (Fed. Cl. Spec. Mstr. Aug. 1, 2016), *mot. for review den'd*, slip op. (Fed. Cl. Jan. 25, 2017). But such efforts have been understood as seeking to evade the weight of negative precedent involving autism claims. *Cunningham*, *slip op.* at *7-8 ("[r]egardless of petitioner's attempt to differentiate this case from other autism cases by creating this second step, the Special Master rightfully classified this case as an autism case"). Arguing that "neurologic" or other developmental problems (whether or not properly termed autism) are the product of a vaccine-aggravated mitochondrial disease or disorder is not a significantly different tactical approach. *See, e.g.*, *T.M. v. Sec'y of Health & Human Servs.*, No. 08-284V, 2016 WL 11087157, at *28 (Fed. Cl. Spec. Mstr. Aug. 9, 2016) (dismissing claim that

[35] If the prior special master's order to produce this report erred in assuming autism was still a component of Petitioners' claim, Petitioners made no effort to correct that misunderstanding.

vaccine caused mitochondrial disease/disorder resulting in developmental problems), *mot. for rev. den'd*, 133 Fed. Cl. 78 (2017).

Nevertheless – there is no question that Program claimants may refine their allegations, just as any civil action complainant might seek to conform their allegations to the evidence. *See, e.g., Nuttall v. Sec'y of Health & Human Servs.*, No. 07-810V, 2014 WL 643584, at *4 (Fed. Cl. Spec. Mstr. Jan. 23, 2014) ("[p]etitioners have the right to develop their own case, and if needed, to amend their petition and change their theory . . . ."). [36] Accordingly, I am for purposes of my analysis treating this matter as if Petitioners do *not* claim that C.J.K. experienced any developmental problems at all due to vaccination – whether deemed autism, developmental regression, or some other kind of neurologic deficiency with any behavioral symptoms. This leaves only the theory that C.J.K. had some underlying "inborn error of metabolism" – whether in the form of mitochondrial dysfunction, immunodeficiency, or something else - that was exacerbated by the 2005 vaccines, resulting in a litany of harmful symptoms thereafter. As the below analysis demonstrates, however, excising autism from this case in no way saves what remains of the claim.

I. Mitochondrial Disease vs. Dysfunction

As I previously noted in *R.V. v. Sec'y of Health & Human Servs.*, No. 08-504V, 2016 WL 3882519, at *26 (Fed. Cl. Spec. Mstr. Feb. 19, 2016), *mot. for review den'd*, 127 Fed. Cl. 136 (Fed. Cl. July 1, 2016), *appeal dismissed*, No. 16-2400 (Fed. Cir. Oct. 26, 2016), the concept of mitochondrial disease or dysfunction includes a number of disorders affecting the body's ability to metabolize energy. It can manifest with a multitude of symptoms, some of which are developmental in character, like autism – although autism has yet to be persuasively linked causally to the condition. *Id.*

True mitochondrial disease is distinguishable from a lesser form of dysfunction. The former (which may be more accurately described as "primary" mitochondrial disease) usually presents with severe, clinically-recognized symptoms, and is often conclusively diagnosed by genetic testing, while mitochondrial dysfunction (also called "secondary" mitochondrial disease) can be the byproduct of a different disease or environmental trigger, or merely reflect a transient metabolic problem. Haas at 1330; *R.V.*, 2016 WL 3882519, at *26; *Anderson v. Sec'y of Health & Human Servs.*, No. 02-1314V, 2016 WL 8256278, at *24 (Fed. Cl. Spec. Mstr. Nov. 1, 2016), *mot. for review den'd,* 131 Fed. Cl. 735 (2017), *aff'd,* 717 F. App'x 1009 (Fed. Cir. 2018). Examples of mitochondrial disease include Leigh disease, a progressive and typically terminal condition

[36] At a minimum, dropping autism or ADHD as a complained-of injury would mean that Petitioners could not recover for damages relating to those conditions, but could otherwise (if they established entitlement to damages) recover for the costs of treating C.J.K.'s immunodeficiency and the non-developmental sicknesses he has since experienced.

characterized by a subacute necrotizing encephalomyelopathy.[37] The presence of mitochondrial disease or dysfunction can be evaluated by consideration of the results of several lab tests, applied to different diagnostic frameworks. *See R.V.*, 2016 WL 3882519, at *26; *Anderson*, 2016 WL 8256278, at *7.

Secondary mitochondrial diseases have been linked to various underlying genetic disorders (including copper-metabolism disorders, lysosomal disorders, peroxisomal disorders, pantothenate kinase-associated neurodegeneration, holocarboxylase synthetase deficiency, molybdenum cofactor deficiency, and neonatal hemochromatosis), as well, as medications, toxins, and aging. Haas at 1331; Smeitink at 12. The diagnostic evaluation for secondary mitochondrial dysfunction is essentially the same as that conducted for primary mitochondrial disease (centering on a multi-tiered interpretation of clinical, imaging, metabolic screening, and biochemical markers). *See generally* Haas.

I have issued decisions in several cases in which petitioners claimed a child possessed an undiscovered or asymptomatic mitochondrial disorder that had been aggravated by vaccination. In each instance, I have not found that any secondary form of mitochondrial disease was successfully established. *See, e.g.*, *Anderson*, 2016 WL 8256278, at *24-25 (finding petitioner did not suffer from a secondary mitochondrial disorder where overall health history and medical testing did not support such a conclusion based on the dialogistic guidelines); *R.V.*, 2016 WL 3882519, at *33-34 (finding the same). Other special masters have reached the same conclusion. *Bast v. Sec'y of Health & Human Servs.*, No. 01-565V, 2012 WL 6858040 (Fed. Cl. Spec. Mstr. Dec. 20, 2012) (application of the Bernier criteria for mitochondrial dysfunction did not support a preponderant finding of a mitochondrial disorder), *mot. for review den'd*, 117 Fed. Cl. 104 (2014), *appeal dismissed*, 579 F. App'x 1001 (Fed. Cir. 2014). Common to all such cases were the following:

- the petitioners sought to identify a metabolic disorder they alleged had predated vaccination - based on testing performed long *after* the time of vaccination;

- no contemporaneous treater ever proposed at the time of vaccination, or even soon thereafter, based on any observed changes in the relevant child's health or other clinical indicia, that the child might be suffering from any form of mitochondrial disorder;

- the child in question was never diagnosed with a known primary mitochondrial disease – leaving only the possibility that a secondary form of mitochondrial disorder was present; and

[37] *Dorland's* at 538.

- testing performed on the child rendered ambiguous and inconclusive results, with some results supporting the diagnosis and others undermining it, making it impossible to conclude "more likely than not" that the child did have a secondary mitochondrial disease.

There are hardly any cases, by contrast, where a claimant obtained an entitlement award based on the allegation that a child's preexisting mitochondrial dysfunction was aggravated by a vaccine – and those rare instances that do exist are facially inapposite. For example, in *Poling v. Sec'y of Health & Human Servs.*, No. 02–1466V, 2008 WL 1883059 (Fed. Cl. Spec. Mstr. Apr. 10, 2008)[38], the child in question (who was later diagnosed with mitochondrial disease) had received several vaccines, and then within 48 hours developed a high fever that became low-grade over the next several days, along with inconsolable crying, sleeplessness, and significant, noticeable motor problems memorialized in the medical record that worsened over the next several days. Such facts are completely distinguishable from the present. Moreover, *Poling* involved a Table claim – and therefore the fact that Respondent conceded entitlement therein, based on Petitioner's evidentiary satisfaction of the Table elements, did not amount to a concession that causation had been established based on the criteria relevant to a non-Table case like the present.

In *Paluck v. Sec'y of Health & Human Servs*., 786 F.3d 1373 (Fed. Cir. 2015), the Federal Circuit affirmed a Court of Federal Claims's determination that a special master erred in denying compensation to petitioners claiming (in a non-Table case) that the MMR, varicella, and pneumococcal vaccines significantly aggravated their child's mitochondrial disease, resulting in severe neurodegeneration with evidence of developmental problems. However, the child's underlying mitochondrial disease diagnosis was not a contested fact (as is the case here). *Paluck* is also factually distinguishable for other reasons. The vaccinated child (a one-year-old) had experienced a persistently high fever in the two to seven days immediately after receiving the vaccines, and was soon thereafter diagnosed with possible neurologic problems confirmed by MRI results, among other things. *Paluck*, 786 F.3d at 1376. Nothing so severe is evident from the present evidentiary record.

II. Petitioners Have Not Shown that C.J.K. Had Any Mitochondrial Dysfunction

Petitioners were tasked with establishing that C.J.K. possessed some kind of underlying mitochondrial dysfunction that was aggravated by vaccination. Preponderant evidence does not support their contention.

[38] The Poling article referenced in Drs. Kinsbourne's and Jones's reports involves the same child as the *Poling* case.

First, I find that C.J.K. did *not* suffer from a "primary" mitochondrial disease. The best evidence that he had any kind of mitochondrial dysfunction comes from the treating records of Dr. Natowicz, and he was only willing to propose that C.J.K. was experiencing *at best* a "secondary phenomenon," or the secondary kind of mitochondrial disease. *See* Ex. 33 at 6-7. Dr. Boles's report could be read in places to suggest the contrary, but he was inconsistent in his use of terms, and ultimately opined that C.J.K. suffered from a "probable mitochondrial disorder" given the "absence of proof." Boles Rep. at 9. The record otherwise does not reveal that C.J.K. suffered from the kind of clinically recognized disease or illness that would be of sufficient progressive severity to constitute primary mitochondrial disease, as Dr. Jones's report makes clear when comparing testing results for C.J.K. with those for the child in Poling. Jones Rep. at 3-4.

Second, I do not find that preponderant evidence supports the conclusion that C.J.K. suffered from even a secondary form of mitochondrial dysfunction or some other condition that would negatively impact immune system function. Dr. McCandless has provided a persuasive close reading of the testing performed on C.J.K., and as he points out the results, when evaluated as a whole, do not support the conclusions urged by Petitioners. The sole positive fibroblast test result is insufficient, by itself, to support Petitioners' favored diagnosis. Indeed, Dr. Natowicz's diagnosis is itself hedging and tentative in character – and I need not accept it wholesale simply because he was one of C.J.K.'s treaters. *See, e.g.*, *R.V.*, 2016 WL 3882519, at *33-34.[39]

Another basis for questioning whether preponderant evidence supports the conclusion that C.J.K. had a secondary mitochondrial disease arises from the clinical standards used for determining if a person suffers from such a condition. In other cases, I have discussed the different relevant diagnostic criteria. *See, e.g., T.M.*, 2016 WL 11087157, at *30; *Anderson,* 2016 WL 8256278, at *24. Although those criteria have evolved, they generally require evidence that several different elements are present – some of which are established with testing, while others reflect clinical symptoms. It is evident here, by contrast, that C.J.K. only demonstrates (a) slightly elevated serum 3, (b) a slightly positive result in only one of several fibroblast tests, and (c) some evidence of other objective criteria (i.e. alleged muscle tone loss[40], gastrointestinal problems). But

[39] Although my primary grounds for giving Dr. Natowicz's diagnosis less weight are due to its somewhat tentative nature, plus Dr. McCandless's more persuasive interpretation of the same data points, I also observe that Dr. Natowicz's diagnosis was made *eight* years after the vaccinations in question. Because Petitioners allege C.J.K. suffered from a metabolic disorder, such long after-the-fact testing has somewhat less probative value than contemporaneous testing performed closer in time to vaccination or injury onset. Indeed, and as noted in other cases involving alleged mitochondrial disorders, testing performed on *different days* can produce wildly divergent results. *See, e.g., Anderson v. Sec'y of Health & Human Servs.*, No. 02-1314V, 2016 WL 8256278, at *24 (Fed. Cl. Spec. Mstr. Nov. 1, 2016), *mot. for review den'd,* 131 Fed. Cl. 735 (2017), *aff'd,* 717 F. App'x 1009 (Fed. Cir. 2018). It is therefore difficult to conclude that just because testing on C.J.K. produced *some* results supportive of a secondary mitochondrial disease diagnosis in 2013, that these findings can be reasonably applied to 2005.

[40] Hypotonia, or low muscle tone, can be a clinical indicia of a mitochondrial disorder. *See, e.g., R.V.*, 2016 WL 3882519, at *12. Mrs. Kreizenbeck's affidavit alleges C.J.K. displayed loss of muscle tone after his receipt of the flu

Dr. McCandless persuasively set forth the many *other* relevant clinical criteria that were not satisfied by testing performed on C.J.K., referencing valid medical support for his views. McCandless Rep. at 3, citing Smeitink and Haas. He also noted that even the few positive results suggestive of secondary mitochondrial disease were arguably of less significance than Petitioners urge. Dr. Boles, by contrast, did not set forth the criteria he was applying, and did not persuasively rebut Dr. McCandless's points.

There are scattered bits of reliable evidence in the record that C.J.K. might have suffered from some secondary form of mitochondrial disorder – but it mainly comes in the form of treater opinions that upon close inspection do not support the diagnosis all that strongly, since they rely on ambiguous testing data points based in turn on mildly elevated results. On the other hand, Dr. McCandless has provided an exhaustive review of the record, and his conclusions (bulwarked by his demonstrated familiarity with this kind of testing) are trustworthy and persuasive – and that opinion is better supported by the record. The record does not support the conclusion that it is "more likely than not" that C.J.K. suffered from a secondary mitochondrial disease or dysfunction.

III. Petitioners Have Not Demonstrated C.J.K. Experienced Vaccine-Caused Aggravation of an Underlying Metabolic Disorder or Secondary Mitochondrial Disease.

Even if my determination above were in error, and Petitioners were found to have offered sufficient preponderant evidence making it more likely than not that C.J.K. had a secondary form of mitochondrial disease, Petitioners' claim would founder on something more fundamental: their inability to establish that C.J.K.'s preexisting metabolic condition was aggravated by *any* of the vaccines he received.

Petitioners argue that merely because C.J.K. was healthy before his April 2005 vaccinations, but thereafter began to experience recurrent infections and then later manifested "immune system problems," that they have met this element of the *Loving* test. Pet. Prehearing at 7-8. But this is no different from arguing that a mere temporal relationship between vaccine and injury satisfies a petitioner's burden of proof – a proposition flatly rejected by the Federal Circuit. *See, e.g., LaLonde v. Sec'y of Health & Human Servs.*, 746 F.3d 1334, 1341 (Fed. Cir. 2014) ("[a] temporal correlation alone is not enough to demonstrate causation"). The law relevant to significant aggravation claims requires much more than that – petitioners must demonstrate that the underlying condition was worsened beyond what would be expected to occur otherwise/absent vaccination. *Hennessey*, 2009 WL 1709053, at *41-42.

vaccine in October 2005. Ex. 42 at 2 ¶8. However, the medical records do not corroborate this assertion – although Dr. Boles relied on it in his report. Boles Rep. at 3, 4.

The record in this case does not reflect circumstances in which a vaccine made a child with a preexisting metabolic condition markedly worse. It does not disclose any instances of a close-in-time reaction, and there is a lack of *contemporaneous* treater evidence or test results demonstrating the purported reaction was occurring in 2005 or in early 2006. To the extent Petitioners maintain that the vaccines later triggered some kind of immune deficiency, Dr. Gupta's 2008 diagnosis (Ex. 32 at 2) is conclusory and not supported by filed test results, while also being undercut by Dr. Wright's 2006 determination that C.J.K. did *not* suffer from immune dysfunction. Ex. 6 at 3-4. The overall record better demonstrates that Petitioner received some childhood vaccines in April 2005, suffered illnesses that similarly-situated infants experience (respiratory or gastrointestinal infections), and then later that fall received a flu vaccine – all without truly alarming incident. I cannot conclude from such a record that Petitioner's purported metabolic disorder produced a worse outcome for him than would be expected, simply due to the vaccines he received. *See, e.g.*, *Hennessey*, 2009 WL 1709053, at *41-52.

I also do not find persuasive Petitioners' efforts to supplement the contemporaneous record with assertions from Mrs. Kreizenbeck about changes she purportedly observed in C.J.K. post-vaccination, or her reporting of fever-oriented reactions that were closely followed by significant changes. Her claims of vaccine reactions do not find any corroboration in the record – and it is well understood in the Program that contemporaneous records are deemed accurate. *See Murphy*, 23 Cl. Ct. at 733.

IV. Petitioners Have Not Established a Reliable or Persuasive Causation Theory that Vaccines Could Exacerbate an Underlying Mitochondrial Disorder.

None of Petitioners' experts (some of whom unquestionably offered opinions intended to bolster Petitioners' allegedly-abandoned arguments that C.J.K.'s vaccines caused autism or developmental injury) provided sufficiently reliable and persuasive opinions to support the conclusion that vaccines *could cause* exacerbation of an existing secondary mitochondrial disease.

The most current iteration of Petitioners' claim leans heavily on the opinion of Dr. Levin. Facially, however, this opinion (a two-page letter) is the *least* effective of the three reports filed in this case by Petitioners, given its conclusory nature. *See generally* Ex. 28. For the assertion that C.J.K. suffered from "inborn errors of metabolism," Dr. Levin relies heavily on the hypogammaglobulinemia diagnosis of Dr. Gupta in 2008 (Levin Rep. at 1) – a diagnosis that not only was preceded in 2006 by the *contrary* diagnosis of Dr. Wright (Ex. 6 at 3-4), but also which is itself too perfunctory to give substantial weight, given the absence of corroborative medical records revealing the basis for Dr. Gupta's conclusions. Dr. Levin otherwise makes broad assertions about the capacity of vaccine-induced cytokines to stimulate the immune system pathologically that he offers little support for beyond his own *ipse dixit*, and which I do not deem

reliable on their face.[41] If Dr. Levin meant to expand on his conclusory views at a later date, he has missed his chance; Petitioners could have filed a supplemental report from him in the nearly *five* years since his report was first prepared, but they never did so.

Dr. Kinsbourne's opinion suffers from similar persuasiveness problems, given the factual assumptions and unreliable assertions underlying his conclusions. There are legitimate questions surrounding Dr. Kinsbourne's expertise to opine on the matters at issue at all, given his lack of direct experience with metabolic disorders.[42] But even putting qualifications aside, Dr. Kinsbourne's report on its face makes assertions about the capacity of vaccines to cause oxidative stress sufficient to result in disease or immune dysfunction that are weakly grounded in reliable science – deficiencies that have been recognized in other cases, when he has offered similar opinions. *See, e.g., Pope*, 2017 WL 2460503, at *8 (observing that Dr. Kinsbourne failed to explain "how much oxidative stress is generated by vaccination generally, . . . [or] what level of oxidative stress is necessary to cross the "tipping point" to cause clinical disease"); *Dwyer v. Sec'y of Health*

[41] I have in other cases questioned the theory that a vaccine-induced cytokine storm or cascade can sustain itself long enough (e.g., more than a few weeks) to precipitate harm to an individual at a later date. *See, e.g., Carda v. Sec'y of Health & Human Servs.*, No. 14-191V, 2017 WL 6887368 (Fed. Cl. Spec. Mstr. Nov. 16, 2017); *Dean v. Sec'y of Health & Human Servs.*, No. 13-808V, 2017 WL 2926605 (Fed. Cl. Spec. Mstr. June 9, 2017), *motion for rev. den'd*, slip op. (Fed. Cl. Sept. 26, 2017).

[42] As a pediatric neurologist, Dr. Kinsbourne has expertise in testifying about autism – but barely sufficient expertise to opine on the interplay between vaccines and underlying metabolic deficiencies sufficient (after prompting by a vaccine) to produce a neurologic injury like autism. He is also not an expert on the topic of mitochondrial disease or metabolic disorders, a central aspect of Petitioners' theory.

Dr. Kinsbourne has often testified in Vaccine Program cases on behalf of petitioners in a variety of contexts. *See, e.g., Hammitt v. Sec'y of Health & Human Servs.*, No. 07-170V, 2010 WL 3735705, at *8 (Fed. Cl. Spec. Mstr. Aug. 31, 2010) (alleging that the petitioner's DTaP vaccination caused her Dravet Syndrome), *on reconsideration*, 2011 WL 1135878 (Fed. Cl. Mar. 4, 2011), *mot. for review den'd*, 98 Fed. Cl. 719 (2011), *aff'd*, 676 F.3d 1373 (Fed. Cir. 2012). But other special masters have observed deficiencies in his capacity to opine on certain topics, due in part to his lack of clinical expertise in the past 30-plus years:

> A significant concern regarding Dr. Kinsbourne's reliability as an expert witness is that he has not maintained a "hospital based clinical pediatric neurology practice" since 1981. . . . Dr. Kinsbourne's testimony reflected his lack of recent clinical practice. His testimony was highly generalized and lacked any grounding in practice. While Dr. Kinsbourne may keep current with medical literature . . . his testimony amounts to little more than repeating snippets from that literature.
>
> He has no current experience or context outside of "behavioral aspects" of pediatric neurology with which to apply, question, or discuss an article's teachings. . . . Dr. Kinsbourne does not publish, research, teach, counsel, attend meetings or conferences, or have any special training in the field of genetics. . . . Nor does Dr. Kinsbourne have any "experience or training or knowledge in clinical genetics, molecular genetics, and neurogenetics." . . . The fact that for the past twenty-five years Dr. Kinsbourne has not focused his practice, research or teachings in the field of seizure disorders, and that Dr. Kinsbourne has no expertise in the field of genetics significantly limited his ability to offer reliable, persuasive, and cogent testimony in this case.

Hammitt, 2010 WL 3735705, at *8 (internal citations omitted).

& Human Servs., No. 03-1202V, 2010 WL 892250, at *163 (Fed. Cl. Spec. Mstr. Mar. 12, 2010) ("[w]itnesses with far better qualifications in research into neurodegenerative diseases and oxidative stress established that the cellular processes Dr. Kinsbourne described do not work the way he asserted"). He also relies heavily on Mrs. Kreizenbeck's unsubstantiated allegations of a vaccine reaction. Kinsbourne Rep. at 1-2. And Dr. Kinsbourne's opinion focused on C.J.K.'s autism/developmental injuries – issues which Petitioners maintain are no longer relevant to their claim.[43]

Dr. Boles's report was the most reliable of the three filed by Petitioners – but only because it was largely devoted to establishing the propriety of C.J.K.'s secondary mitochondrial disease diagnosis, a topic upon which Dr. Boles was eminently qualified to opine. But, as noted above, I find (based on a comparison of Dr. Boles's report with those of Drs. McCandless and Jones, as well as consideration of the relevant portions of the medical record) that he did not succeed in persuasively establishing that C.J.K. more likely than not *did* have a metabolic disorder that could have been exacerbated by vaccines. Moreover, even if my determination in this respect is wrong, the other components of his report bearing on causation are less well-founded. The aspects of Dr. Boles's opinion dealing with vaccine exacerbation not only exceeded his expertise somewhat, but were conclusory and unsubstantiated by even the limited medical literature that Dr. Levin offered.[44] And Dr. Boles placed too much emphasis on Mrs. Kreizenbeck's uncorroborated

[43] These parts of Dr. Kinsbourne's opinion are equally unpersuasive and unreliable. For example, Dr. Kinsbourne associates autism or developmental problems with mitochondrial dysfunction. Kinsborne Rep. at 3. But this assertion finds minimal scientific support, at least based on the literature filed in this case. At best, he offers a single study (J. Shoffner, et al., *Fever Plus Mitochondrial Disease Could Be Risk Factors for Autistic Regression*, 25 J. Child Neurol. 429 (2009) (filed as Ex. 64) ("Shoffner")), and the Poling case report, to bridge this analytical gap between vaccination and autism (see Kinsbourne Rep. at 3-4), but neither are able to do the work assigned.

Poling, for example, describes a single child later diagnosed with mitochondrial disease. The child had received several vaccinations, and then within 48 hours developed a high fever that became low-grade over the next several days, along with inconsolable crying, sleeplessness, and significant, noticeable motor problems that worsened over the next several days. Poling at 1. There, not only was the mitochondrial disease diagnosis supported, but the reaction to the vaccines was immediate, documented, and facially undeniable – unlike in this case.

Shoffner, while a legitimate piece of scientific literature, is also unhelpful given the present facts. That study looked at the relationship between autistic *regression* in patients with mitochondrial dysfunction and fever – not vaccination and fever and/or autism. Shoffner at 1. The evidence that C.J.K. regressed after any of the vaccines he received is fairly weak, by contrast, if not nonexistent. *See* Ex. 8 at 1; Ex. 4 (Part 3) at 13, 20; Ex. 9 at 2-4; Ex. 11 at 1-9. In addition, as Shoffner succinctly acknowledges, "[a]utistic regression was not associated with vaccination." Shoffner at 3, 4 ("[i]n our patients with mitochondrial disease and autistic spectrum disorders, the vaccines did not appear related to the neurologic regression.").

[44] I recognize that petitioners are not *required* to offer medical or scientific literature. But when a petitioner seeks to advance causation theories based on conclusory arguments that either lack substantiation from a credible and persuasive expert report, or reflect conclusory expert statements that are not themselves backed up with reliable scientific support, the absence of such evidence (which could corroborate or advance their theory) can be noted in evaluating if the petitioner has carried his burden of proof.

allegations of C.J.K.'s vaccine reactions in opining that proof of exacerbation was established, further diminishing the reliability of his opinion. Boles Rep. at 3; *see, e.g.*, *Hooker*, 2016 WL 3456435, at *28 (reliance on incorrect assumption of fact causes expert to lose evidentiary value).

Respondent's experts, by contrast, effectively rebutted the concept that vaccines could negatively interact with a metabolic disorder, while persuasively refuting Petitioners' contentions that C.J.K. had any kind of mitochondrial disease or metabolic disorder. Dr. Jones in particular - an expert in redox biology, unlike Dr. Kinsbourne - cogently demonstrated that Dr. Kinsbourne's theories about possible mechanisms by which a vaccine could stress an individual's underlying metabolic disorder sufficient to cause harm were outdated and unreliable. Jones Rep. at 5-6. This is not the first time this kind of theory has been persuasively rebutted by Dr. Jones. *See*, e.g., *Bast*, 2012 WL 6858040, at *6 (Dr. Jones "testified persuasively that the commonly induced but transient state of oxidative stress . . . cannot produce the type of permanent damage alleged").

Additionally, the Federal Circuit's decision in *Paluck* does not compel the finding that Dr. Kinsbourne's causation theory here was legally sufficient to meet Petitioners' burden, as Petitioners maintain. *See* Pet. Prehearing Brief at 8-10. Besides involving far more extreme facts than herein (as noted above), in *Paluck* the Federal Circuit made *no findings whatsoever* with respect to the reliability of the petitioners' medical theory – nor was it asked to by either party. By contrast, there are numerous apposite cases where the reliability of the medical theory connecting autism to mitochondrial disease has been successfully challenged. *See, e.g.*, *Bast*, 2012 WL 6858040, at *25-39; *R.V.*, 2016 WL 3882519, at *10-25.

The causation theory presented herein is strikingly similar to theories presented – and rejected – in many more previously-resolved cases. *See, e.g., Hardy*, 2015 WL 7732603, at *4-5 (petitioners failed to demonstrate that DTaP vaccine caused or significantly aggravated underlying mitochondrial disease resulting in ASD); *R.V.*, 2016 WL 3882519, at *42, *mot. for review den'd*, 127 Fed. Cl. 136 (2016) (factual record did not support contention that child suffered from a mitochondrial disease, or that the vaccine at issue had a causal connection to the development of ASD); *Miller v. Sec'y of Health & Human Servs*., No. 02-235V, 2015 WL 5456093 (Fed. Cl. Spec. Mstr. Aug. 18, 2015) (petitioners failed to demonstrate that several childhood vaccines caused encephalopathy or aggravated underlying mitochondrial disease/dysfunction); *Lehner v. Sec'y of Health & Human Servs*., No. 08-554V, 2015 WL 5443461 (Fed. Cl. Spec. Mstr. July 22, 2015) (petitioners failed to demonstrate that flu vaccine resulted in autoimmune encephalitis). Petitioners' experts herein offered opinions no more compelling than those who went before.

V. Petitioners Cannot Satisfy the *Althen* Prongs.

Give the above, it is evident that Petitioners have not met their burden under the analysis set forth in *Althen* (and subsumed in *Loving* for claims of significant aggravation[45]) for proving a causation-in-fact claim. With respect to the first, "can cause" prong, Petitioners have not provided sufficient reliable evidence, in the form of expert opinions or otherwise, that any of the vaccines C.J.K. received could exacerbate an underlying metabolic or mitochondrial disorder, resulting in immune dysfunction (or developmental problems). The expert views offered in support of these theories are thin and inadequately substantiated with either demonstrated expert knowledge of the subject, or scientific and medical literature bridging the gap between expert and theory. Certainly no direct evidence has been offered to establish the capacity of the vaccines at issue to interact with a metabolic disorder, but the circumstantial evidence offered is also insufficient.

Next, Petitioners have failed to make a preponderant case that C.J.K. *did* experience vaccine-caused immune dysfunction. There is some record support for the immune dysfunction diagnosis in the form of Dr. Gupta's 2008 diagnosis, but it is conclusory - and comes *after* an equally-valid diagnosis from Dr. Wright in 2006 finding no such dysfunction. Petitioners otherwise failed to offer any explanation for why Dr. Gupta's diagnosis is more credible than Dr. Wright's earlier diagnosis. The evidence supporting the secondary mitochondrial disease allegations is found in Dr. Natowicz's 2013 work-up, and it has more reliability – although, for the reasons highlighted by Dr. McCandless, the probative value of that diagnosis is fairly low when the evidence is viewed in totality. There is also no contemporaneous medical record evidence that C.J.K. suffered any reaction close-in-time to the April or October vaccinations, and nothing in the record that would circumstantially support the conclusion that a vaccine-induced process had

[45] Because I have concluded that Petitioners could not demonstrate several factual predicates of their significant aggravation claim (i.e., that C.J.K. had an underlying secondary mitochondrial disease, or that the vaccines he received did in fact aggravate it), I do not herein provide a point-by-point discussion of each *Loving* prong. To some extent, this reasonably flows from the fact that if a vaccine cannot be established to be causal of an injured person's condition (here, because a predicate of the claim is an unsubstantiated mitochondrial disease), then there is no need to evaluate if the person's underlying condition was worsened. *Hennessey v. Sec'y of Health & Human Servs.*, No. 01-190V, 2009 WL 1709053, at *42 (Fed. Cl. Spec. Mstr. May 29, 2009), *mot. for review den'd*, 91 Fed. Cl 126 (2010) ("[i]n most off-Table significant aggravation cases, it may be more logical to consider the last three *Loving* factors [the *Althen* factors] first").

I note, however, that Petitioners have largely failed to offer preponderant evidence for a significant *Loving* element: that C.J.K.'s underlying mitochondrial disease was worsened by vaccination. *Hennessey*, 2009 WL 1709053, at *42. The record does not reveal worsening; the "before and after" argument that Petitioner's illnesses manifested post-vaccination is not sufficient to satisfy this test. *See Locane v. Sec'y of Health & Human Servs.,* 685 F.3d 1375, 1381-82 (Fed. Cir. 2012) (upholding special master's determination that petitioner had failed to carry her burden of proof in establishing that her preexisting injury was worsened by the relevant vaccine). And Petitioners' three experts did little in their reports to make scientifically-reliable arguments regarding what worsening would look like, or how to compare outcomes of individuals with underlying metabolic disorders who received vaccines versus those who did not.

begun at either time. The infections C.J.K. suffered do not appear at the time to have been viewed by treaters as out of the ordinary for a child of his age. *See, e.g.*, *Anderson*, 2016 WL 8256278, at *19. And Mrs. Kreizenbeck's allegations that she observed immediate post-vaccination reactions are uncorroborated by the contemporaneous medical records.

Finally, with respect to the reasonableness of the timeframe in which C.J.K.'s vaccine injury occurred, Petitioners produced medical records (corroborated by Mrs. Kreizenbeck's affidavit) that C.J.K. began having health issues approximately three weeks after his flu vaccination in December 2005. *See, e.g.*, Ex. 8 at 1; Ex. 4 (Part 3) at 13, 20; Ex. 9 at 1-4; Ex. 11 at 1-19. However, among the first symptoms that he presented with were developmental issues - which as stated above have not been found to be associated with vaccination, and which I am (consistent with Petitioners' stated intent) treating for present purposes as *not* alleged to be vaccine-caused. In addition, there is contrary evidence suggesting that C.J.K.'s developmental problems first manifested as communication or attention issues as early as the summer of 2005, long before that vaccination. *See* Ex. 4 (Part 3) at 12; Ex. 8 at 1, 7; Ex. 4 (Part 1) at 20-21; Ex. 9 at 2-4; Ex. 11 at 4; Ex. 26 at 1. And there is even less evidence of a reaction after the April 2005 vaccinations. The after-the-fact 2008 immunodeficiency diagnosis cannot be linked to a 2005 vaccination event simply on the basis of C.J.K.'s different illnesses that summer, in the absence of reliable and persuasive evidence contemporaneous with those illnesses at the time (whether in the form of treater opinion or test result) that would suggest the illnesses were caused by the immune deficiency. This record simply does not support the conclusion that any of C.J.K.'s various alleged vaccine injuries began in a medically reasonable period after the vaccines he received – and Petitioners' experts provided no reliable explanation for the temporal period in which his alleged immune dysfunction would be expected to manifest, or its likely course.

VI. <u>This Case was Properly Resolved without a Hearing.</u>

In ruling on the record, I am declining Petitioners' request that I conduct a hearing. The choice of how best to resolve this case is a matter that lies generally within my discretion, but given Petitioners' objections I shall explain my reasoning.

Prior decisions have recognized that a special master's discretion in deciding whether to conduct an evidentiary hearing "is tempered by Vaccine Rule 3(b)," or the duty to "afford[] each party a full and fair opportunity to present its case." *Hovey*, 38 Fed. Cl. at 400-01 (citing Rule 3(b)). But that rule also includes the obligation of creation of a record "sufficient to allow review of the special master's decision." *Id*. Thus, the fact that a claim is legitimately disputed, such that the special master must exercise his intellectual faculties in order to decide a matter, is not itself grounds for a trial (for if it were, trials would be required in every disputed case). Special masters

are expressly empowered to resolve fact disputes *without* a hearing – although they should only so act if a party has been given the proper "full and fair" chance to prove their claim.

In this case, several factors counseled against holding a hearing. As Respondent pointed out in his motion, Petitioners' claim closely parallels numerous other cases asserting that an underlying secondary mitochondrial disease was exacerbated by vaccines and thereby causing injury. This remains so even if the "downstream" developmental or autism injuries initially alleged herein are ignored, leaving only the contention that an immune deficiency was the product of exacerbation of C.J.K.'s underlying condition. But the core components of such a claim – that vaccines could impact a possible, but unproven, mitochondrial condition – have been not only rejected after trial, but rejected *without* hearing. *See Pope,* 2017 WL 2460503, at *26-27. The congruence of Petitioners' theory and its factual predicates with numerous, previously-rejected variations on the same theme counseled against expending the time and effort necessary for a hearing.[46]

The specific expert opinions offered herein also did not suggest the need for live testimony in order to probe the bases for their opinions. Where experts provide equally plausible readings of a record, or opine on a matter of notable complexity, hearing their testimony live may well aid the special master in weighing the evidence. But this is not always the case – even novel causation issues may be resolved on the papers if deficiencies in the relevant theory can be identified based on careful reading of the relevant reports. *See D'Toile*, 2018 WL 1750619, at *2 (Fed. Cir. Apr. 12, 2018) (upholding determination on the record that flu vaccine had not been demonstrated to cause narcolepsy, even though issue was novel and had not been tried in the Program). Given my familiarity with the concepts at issue raised by both sides' expert reports, I was able to ascertain the weaknesses in Petitioner's theory based solely on the reports filed.

Admittedly, there is conflict in the record between Dr. Boles's interpretation of the mitochondrial function testing (which he deems supportive of the conclusion that C.J.K. had a mitochondrial "disease"), and Dr. McCandless's (which he argues does not). In some cases, this kind of dispute among similarly-qualified experts would be grounds for a hearing, so that credibility could be weighed and experts cross-examined. But the fact that experts dispute a point does not inexorably result in a hearing in all cases. I have found that Respondent's interpretation of the record is more persuasive. On its face, that record reveals that Dr. Natowicz himself – a primary treater with agreed expertise in mitochondrial diseases – felt that C.J.K.'s dysfunction was

[46] The decision not to hold a hearing based upon the similarity of the claim to previously-litigated claims is not something that would only ever inure to Respondent's benefit. The opposite circumstances – where a petitioner asserted a claim that has repeatedly *succeeded* in the past (for example, the allegation that the flu vaccine can cause Guillain-Barré syndrome) – would motivate me to act in the same manner, and propose to Respondent that either the case be settled or that *it* be resolved on the papers.

at best "secondary," and nothing in Dr. Boles's report undermines that conclusion. Indeed, as Dr. McCandless has pointed out, Dr. Boles himself seems to agree (in many places in his report) that C.J.K. did *not* suffer from a classic form of direct mitochondrial disease (and his confused and contradictory treatment of the terms "disorder" versus "disease" do not aid him on this issue). Boles Rep. at 1, 5, 9.

Similarly, I have found that the record better supports the conclusion, consistent with Dr. McCandless's reliable and persuasive opinion, that C.J.K. had no secondary mitochondrial disease at all. This conclusion stems from a weighing of the evidence (as supporting one diagnosis over the other) that I am empowered to make. I did not need to hear from an expert live to arrive at this determination – and this, plus the similarity of this case to other cases involving comparable theories and facts, strongly militated against holding a hearing that was overwhelmingly likely to yield the same result.

Another consideration pertaining to the expert opinions offered herein was the evidentiary *quality* of the reports filed. It is reasonable to expect experts to prepare reports accurately reflecting the opinion they intend to offer at trial, with all necessary evidentiary support to bulwark the opinions included, rather than as a "teaser," with the best and most persuasive parts withheld so they may be unfurled at hearing in dramatic fashion. *See, e.g.*, *Pope*, 2017 WL 2460503, at *26-27. Here, the Petitioners' reports were either self-evidently conclusory or unsubstantiated. In addition, some of Petitioners' experts (Dr. Kinsbourne in particular) lacked demonstrated expertise in the matters discussed in their reports. I did not require a hearing to know that, after reading Petitioners' reports, I did not find them sufficiently scientifically reliable (especially in the absence of a record that would, contemporaneously with the vaccinations in issue, corroborate their assertions).

Finally, and most importantly, I would reach the same determination herein even if I *accepted* Petitioners' argument (advanced by Dr. Boles's report) that C.J.K. had secondary mitochondrial disease – for the record does not at all support the conclusion that his vaccines exacerbated it enough to result in immune deficiency. Rather, the record establishes that (a) C.J.K. received vaccinations in April and October 2005, (b) had no recorded or memorialized reactions to them out of the ordinary, and (c) experienced illnesses and developmental problems temporally after them but which have not been persuasively demonstrated to have been vaccine-caused. This conclusion could be reached *without* hearing from Dr. Boles live – and if his expert report is insufficient on any matter, it is less on his interpretation of the mitochondrial testing and *more* on his conclusory views regarding causation in this case.

I also did not require hearing live from Mrs. Kreizenbeck to resolve fact disputes involving whether, and when, C.J.K. experienced a reaction to the April and October 2005 vaccines. As discussed above, there is a facial discrepancy between the actual medical records – which

memorialize no contemporaneous reaction, or one long preceding at least the October 2005 flu vaccine – and what Mrs. Kreizenbeck alleges in her short affidavit. She has offered no other evidence to corroborate her assertions. Controlling case law indicates that under such circumstances, the records are presumed correct. *See, e.g.*, *Murphy*, 23 Cl. Ct. at 733. Moreover, this is not the first case involving similar causation theories and where a petitioner recalled reactions after an infant's vaccinations that were not disclosed to a treater. *See, e.g.*, *Anderson*, 2016 WL 8256278, at *9-10*; R.V.*, 2016 WL 3882519, at *9-10; *T.M.*, 2016 WL 11087157, at *9-10. Nothing here suggests that a hearing would make it any more likely that I would find Petitioners' allegations on this subject more credible after a hearing, given the record as it stands.

At bottom, I return to the overall nature of Petitioners' claim. As noted above, my analysis has attempted to set aside the fact that the present claim has been, at different points of its existence, one alleging autism or developmental problems as a vaccine-caused injury. But even dropping autism, the claim remains highly similar - both in terms of the facts alleged as well as the theories offered to support it – to those adjudicated in *numerous* prior Vaccine Program cases. Over and over again, such cases have foundered on a petitioner's inability to establish that her child suffered from mitochondrial dysfunction, and/or that the relevant vaccine could interact with that dysfunction and cause injury (whatever that injury was). I see nothing in the record and expert reports offered in this case that suggests this matter's outcome would be any different after hearing– and therefore concerns about the wise husbanding of judicial resources impel me to resolve the claim on the papers. Given the number of filings flooding the Program's docket over the past several years, and the attendant inability of the special masters to resolve claims with the expediency they deserve, it is reasonable to give such concerns some priority.

CONCLUSION

The record does not support the Petitioners' contention that the vaccines C.J.K. received could, or did, injure him as alleged, nor have Petitioners established that it is more likely than not that he suffered from some form of underlying mitochondrial dysfunction. Petitioners have not established entitlement to a damages award, and therefore I must **DISMISS** their claim.

In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accordance with this decision.[47]

IT IS SO ORDERED.

/s/ Brian H. Corcoran
Brian H. Corcoran

[47] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by filing a joint notice renouncing their right to seek review.

Special Master