In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS
No. 17-236V
Filed: April 5, 2024

MATTHEW RODELA and CASANDRA HOGAN as legal representatives of the estate of V.S.R.,

Petitioner,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

Special Master Horner

Curtis R. Webb, Monmouth, OR, for petitioner.
Tyler King, U.S. Department of Justice, Washington, DC, for respondent.

RULING ON ENTITLEMENT[1]

On February 17, 2017, Matthew Rodela and Casandra Hogan ("petitioners") filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. §300aa-10, *et seq.* (2018) ("Vaccine Act"),[2] on behalf of their deceased daughter, V.S.R. (ECF No. 1.) Petitioners allege that the Measles, Mumps, Rubella ("MMR") vaccination that V.S.R. received on February 20, 2015 caused her to suffer a Table Injury of encephalitis that ultimately resulted in her death. (*Id.*) For the reasons set forth below, I conclude that petitioners are entitled to compensation.

[1] Because this ruling contains a reasoned explanation for the special master's action in this case, it will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002. *See* 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). **This means the ruling will be available to anyone with access to the Internet.** In accordance with Vaccine Rule 18(b), petitioner has 14 days to identify and move to redact medical or other information the disclosure of which would constitute an unwarranted invasion of privacy. If the special master, upon review, agrees that the identified material fits within this definition, it will be redacted from public access.

[2] All references to "§ 300aa" below refer to the relevant section of the Vaccine Act at 42 U.S.C. § 300aa-10-34.

I. Applicable Statutory Scheme

Under the National Vaccine Injury Compensation Program, compensation awards are made to individuals who have suffered injuries after receiving vaccines. In general, to gain an award, a petitioner must make a number of factual demonstrations, including showing that an individual received a vaccination covered by the statute; received it in the United States; suffered a serious, long-standing injury or death; and has received no previous award or settlement on account of the injury. Finally – and the key question in most cases under the Program – the petitioner must also establish a *causal link* between the vaccination and the injury.

In some cases, the petitioner may simply demonstrate the occurrence of what has been called a "Table injury." That is, it may be shown that the vaccine recipient suffered an injury of the type enumerated in the "Vaccine Injury Table," corresponding to the vaccination in question, within an applicable time period also specified in the Table. If so, causation is presumed and the petitioner is automatically entitled to compensation, unless it is affirmatively shown that the injury was caused by some factor other than the vaccination. § 300aa-13(a)(1)(A); § 300 aa-11(c)(1)(C)(i); § 300aa-14(a); § 300aa-13(a)(1)(B). As relevant to this case, the Vaccine Injury Table lists "encephalitis" as a Table injury if it occurs within 5-15 days of a vaccine containing measles, mumps, and/or rubella. § 300aa-14(a); 42 C.F.R. § 100.3(a).

What constitutes a Table Injury is ordinarily defined by "qualifications and aids to interpretation" ("QAI") that accompany the Vaccine Injury Table. § 300aa-14(b); 42 C.F.R. § 100.3(b). In this case, however, no such guidance is available. Under the Vaccine Act, the Secretary of Health & Human Services is responsible for promulgating regulations to update the Vaccine Injury Table. § 300aa-14(c). The secretary's modifications to the Table "apply only with respect to petitions for compensation under the Program which are filed after the effective date of such regulation." § 300aa-14(c)(4). In early 2017, the Secretary issued rulemaking to, *inter alia*, amend the Vaccine Injury Table to include QAI criteria for "encephalitis." However, that rule went into effect on March 21, 2017 (82 Fed. Reg. 11321 (Feb 22, 2017)), whereas the petition in this case was filed about a month earlier on February 17, 2017. Thus, the Vaccine Injury Table applicable in this case is the prior Table that became effective on July 23, 2015. 80 Fed. Reg. 35848 (June 23, 2015).

Prior to the March 2017 amendment, the Vaccine Injury Table did not include any definition of "encephalitis," though it otherwise provided criteria for "encephalopathy." *E.g.*, *Nuttall v. Sec'y of Health & Human Servs.*, No. 07-0810V, 2015 WL 691272, at *9 (Fed. Cl. Spec. Mstr. Jan. 20, 2015), *motion for review denied*, 122 Fed. Cl. 821 (2015), *aff'd per curiam*, 640 Fed. App'x 996 (Fed. Cir. 2016). Although encephalopathy and encephalitis can sometimes overlap and are not always distinguished in the literature, they do represent distinct pathophysiologic processes. (A. Venkatesan et al., *Case Definitions, Diagnostic Algorithms, and Priorities in Encephalitis: Consensus Statement of the International Encephalitis Consortium*, 57 CLINICAL INFECTIOUS DISEASES 1114 (2013) (Ex. H-2).) Whereas encephalopathy can refer broadly to altered mental status

resulting from a number of conditions, encephalitis refers specifically to an inflammatory process affecting the brain. (*Id.*) Thus, both parties agree that there is no regulatory definition of "encephalitis" available in this case. (ECF No. 120, p. 4; ECF No.122, n. 3.) The definition of "encephalitis" that will therefore be applied is addressed at length in section V, *infra*.

If no injury falling within the Table can be shown, petitioners could still demonstrate entitlement to an award by instead showing that the vaccine recipient's injury or death was caused-in-fact by the vaccination in question. § 300aa-13(a)(1)(A); § 300aa-11(c)(1)(C)(ii). To successfully demonstrate causation-in-fact, petitioners would bear a burden to show: (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 proximate temporal relationship between vaccination and injury. *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005). In this case, however, petitioners have not asserted any claim based on causation-in-fact, leaving their Table claim dispositive. (ECF Nos. 1, 93, 120, 124.)

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. § 300aa-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 ex rel. Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010) (alterations in original); *see also Snowbank Enters., Inc. 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). However, petitioners may not receive a Vaccine Program award based solely on their own assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. § 300aa-13(a)(1).

II. Procedural History

Petitioners filed their petition for compensation on February 17, 2017. (ECF No. 1.) It was subsequently reassigned to my docket on August 29, 2019. (*See* ECF Nos. 35, 70.) Petitioners filed V.S.R.'s medical records, several affidavits, and videos, between March 30, 2017, and August 17, 2017. (*See* ECF Nos. 8-9, 13, 19, 22-24; Exs. 1-15.) Petitioners then filed an expert report by neurologist Marcel Kinsbourne, M.D., and pathologist Robert Shuman, M.D., in April of 2018. (ECF Nos. 39-43; Exs. 16-37.) In November of 2018, respondent filed his Rule 4(c) report recommending against compensation, along with expert reports by neurologist Elaine Wirrell, M.D., pathologist Brent Harris, M.D., and infectious disease specialist Hayley Gans, M.D. (ECF Nos. 48-56; Exs. A-F.) Petitioner then filed responsive reports by Drs. Kinsbourne and Shuman (ECF Nos. 57-59, 62-64; Exs. 38-55) and respondent filed further reports from Drs. Wirrell and Harris (ECF No. 72; Exs. G-H). A three-day entitlement hearing

was held beginning on May 24, 2022. (Transcript of Proceedings ("Tr."), at ECF Nos. 113-15.) Thereafter, the parties filed post-hearing briefs. (ECF Nos. 120, 122, 124.) Accordingly, this case is now ripe for resolution of entitlement.

III. Factual History

V.S.R. was born at Blessed Beginnings Midwifery ("BBM") on January 1, 2014 full-term without complications. (Ex. 4, pp. 11-15.) Her head circumference at birth was measured at 35.6 centimeters. (Ex. 5, p. 2.) She was observed to be quite alert, active, and crying with a normal physical exam on January 3, 2014. (Ex. 4, p. 11.) V.S.R. was regularly examined at BBM until January 5, 2014, without any cause for concern. (*Id.* at 1-11.) On January 16, 2014, V.S.R. presented to pediatrician Dr. Maria Clara Plum at Kaiser Permanente ("Kaiser") for her 15-day well baby exam. (Ex. 5, pp. 1-4.) V.S.R. was in the 74th percentile for height and weight, and the 70th percentile for head circumference. (*Id.* at 3.) Specifically, her head circumference was measured at 36 centimeters. (*Id.* at 11.) Her physical exam did not reveal any abnormalities, and she was observed to be developing within normal limits. (*Id.* at 3.) V.S.R. was again seen by Dr. Plum on March 3, 2014, for her two-month well baby exam and Rotavirus ("RV"), Haemophilus Influenzae Type B ("Hib"), Pneumococcal ("Prevnar"), and combined Diphtheria, Tetanus, Pertussis, Hepatitis B, and Polio ("Pediarix") vaccinations. (*Id.* at 13-15.) At her two-month exam, V.S.R. was in the 63rd percentile for weight, 27th percentile for height, and 40th percentile for head circumference. (*Id.* at 14.) Specifically, her head circumference was measured at this appointment as being 40 centimeters. (*Id.* at 13, 20.) She showed no abnormalities on exam and her growth and development was noted to be within normal limits. (*Id.* at 14.)

V.S.R. was brought to Kaiser on April 12, 2014, with a complaint of fever. (Ex. 5, p. 23.) She had been irritable since the previous day and was being treated with Tylenol. (*Id.*) Petitioners denied any upper respiratory symptoms, vomiting, rash, ear pain, or urinary issues. (*Id.*) Her exam was generally normal aside from a dull, red right eardrum and congestion with clear mucus. (*Id.* at 24.) V.S.R. was diagnosed with fever and right acute otitis media (middle ear infection/inflammation) and prescribed amoxicillin and continued Tylenol as needed. (*Id.*) V.S.R. returned two days later, on April 14, with complaints of continued fever lasting four days. (*Id.* at 30.) Petitioners denied any cold symptoms or rash and believed that V.S.R. continued to suffer from the ear infection diagnosed at her previous visit. (*Id.*) V.S.R.'s physical exam was normal, with her ear inflammation and congestion having resolved. (*Id.* at 30-31.) The physician did not believe that V.S.R. suffered from an ear infection but explained that if V.S.R.'s fever persisted, then she should be brought back to check for a urinary tract infection. (*Id.*)

It does not appear that V.S.R. continued to experience any significant health issues following her ear infection in April of 2014 as her next available records document a visit to Dr. Plum on August 29, 2014, for her six-month well child exam. (Ex. 5, p. 35.) V.S.R. was observed to be in the 40th percentile for weight, 4th percentile for height, 69th percentile for head circumference. (*Id.* at 36.) Specifically, her head

circumference was measured at 44 centimeters. (*Id.* at 35, 41.) Her physical exam was normal, and she was noted to be developing within normal limits. (*Id.* at 35-36.) Specifically, V.S.R. was observed as able to roll both ways, transfer objects, reach to objects, sit with support, turn to sound, and engage in vocal play. (*Id.*) She also had good head control and showed pleasure when interacting with her parents. (*Id.*) At this encounter, V.S.R. received additional doses of the Pediarix, Prevnar, and Hib vaccines. (*Id.* at 36-37.)

V.S.R.'s was seen by Dr. Plum again on October 24, 2014, for her nine-month well baby exam and further immunizations. (Ex. 5, p. 44.) She was observed to have been feeding well, responding to quiet sounds, sitting without support, crawling on her hands and knees, and holding a bottle. (*Id.* at 44-45.) She was further observed to be in the 36th percentile for weight, 30th percentile for height, and 76th percentile for head circumference. (*Id.* at 45.) Specifically, her head circumference was measured at 45.1 centimeters. (*Id.* at 44, 54.) Her physical exam was normal, and her growth and development were within normal limits. (*Id.* at 45.) It was noted that V.S.R. was "at risk for dental decay," and a topical fluoride varnish was applied. (*Id.* at 44, 46.) V.S.R. was administered additional Pediarix, Hib, and Prevnar doses, as well as a seasonal influenza ("flu") vaccine. (*Id.* at 46.)

V.S.R. was brought to Kaiser's acute care department on January 9, 2015, with complaints of upper respiratory symptoms and cough. (Ex. 5, p. 56.) Petitioners reported that V.S.R. "began developing [a] cough and runny nose with mild fussiness about 3 weeks ago with low grade tactile fever. Runny nose improved over 5 days, cough persisted but improved some. However, a few days later [she] developed runny nose and cough again with fever to 102.4." (*Id.*) By this point, V.S.R.'s fever had been ongoing for about two days while her cough and runny nose had persisted for two weeks. (*Id.*) She was also eating less but drinking and taking normal levels of breast milk. (*Id.*) V.S.R.'s physical exam revealed an inflamed and bulging right ear drum, a right middle ear effusion, mucosal edema, rhinorrhea, and congestion with thick yellow mucus in V.S.R.'s nose. (*Id.* at 57.) Her left ear drum was not observed due to ear wax. (*Id.*) V.S.R. was diagnosed with right acute otitis media and acute sinusitis. (*Id.* at 57-58.) She was again prescribed amoxicillin. (*Id.* at 58.)

V.S.R. returned to Kaiser on January 24, 2015. (Ex. 5, p. 64.) She presented with fever, fatigue, macular rash, congestion, and cough, and she exhibited mucosal edema, rhinorrhea, and pharynx erythema. (*Id.* at 64-65.) V.S.R. was diagnosed with an upper respiratory infection and her rash was assessed as being consistent with dry skin. (*Id.* at 65-66.) Thereafter, several videos have been filed into evidence showing VSR's usual state in February of 2015, just prior to the vaccination at issue.[3] V.S.R. was seen by Dr. Plum on February 20, 2015, for her 12-month well baby exam and

[3] Specifically: a February 8, 2015 video shows V.S.R. walking around a shopping center; a February 10, 2015 video shows V.S.R. playing at a McDonald's playground; a February 13, 2015 video shows V.S.R. giving her older sister kisses; a February 14, 2015 video shows V.S.R. and her sister on a ride at Toys R Us; a February 14, 2015 video shows V.S.R. with the whole family; a February 15, 2015 video shows V.S.R. playing on an iPad. (Ex. 13, video 2; Ex. 15, videos 1-5.)

additional immunizations. (*Id.* at 70.) There was no discussion of V.S.R.'s prior infection and no report of any lingering symptoms. V.S.R. was observed to be in the 20th percentile in weight, 7th percentile in height, and 71st percentile in head circumference. (*Id.* at 71.) Specifically, her head circumference was measured at 46.1 centimeters. (*Id.* at 70, 77.) V.S.R.'s physical exam was normal, and she was observed to be growing and developing within normal limits. (*Id.* at 70.) Specifically, she was observed as being able to crawl, pull to stand, walk alone, sit alone, feed herself, babble, say "mama" and "dada," and gesture "[b]ye-bye/pat-a-cake/peek-a-boo." (*Id.*) During this visit, V.S.R. received doses of the Prevnar, Varicella, Hib, and Hepatitis vaccines, as well as the MMR vaccine at issue in this case. (*Id.* at 72.) This was V.S.R.'s last medical encounter prior to her death.

Several videos have been filed into evidence, showing V.S.R. during the period between the vaccination at issue and her death.[4] Petitioner's pathology expert, Dr. Shuman, opined that some of these videos, beginning with the video of V.S.R. playing at a shopping center play area on February 26, 2015, show V.S.R. exhibiting general confusion consistent with encephalitis (Tr. 213-15), though respondent's neurology expert disagrees (*Id.* at 442). Dr. Shuman also opined that a video of February 26 showed V.S.R. falling backward (as opposed to forward), which is unusual for a toddler. (*Id.* at 216-27.) He opined that it appeared to be consistent with a myoclonic jerk or seizure. (*Id.* at 218.) Again, respondent's neurology expert disagrees. (*Id.* at 435-36.) Dr. Shuman did not otherwise opine that the videos through February 26 showed any personality change. (*Id.* at 219.)

Mr. Rodela, who was V.S.R.'s primary day-time caregiver, presented a video from February 27, 2015, which he avers he recorded specifically because he found the behavior concerning and out of character. (Ex. 12, p. 2; Tr. 7-8, 18-20.) The video shows V.S.R. on the floor of petitioners' living room, having difficulty standing up and showing frustration as a result. (Ex. 13, video 1; Ex. 12, p. 2; Tr. 19.) Dr. Shuman opines the video shows evidence of symptoms consistent with encephalitis. (Tr. 162-66.) In particular, he opines the video likely shows V.S.R. either experiencing a simple motor seizure or a postictal state following a seizure. (*Id.* at 164-65, 207-08.) Respondent's neurology expert disagrees. (*Id.* at 431-32.) Mr. Rodela testified that he did not ultimately share the video with Ms. Hogan because V.S.R. eventually calmed down. (*Id.* at 23-24.) Although Mr. Rodela described his general impression of how V.S.R.'s behavior changed after the vaccination, he was unable to provide specifics apart from his presentation of the February 27 video. (*Id.* at 12-15, 22.)

[4] Specifically: a February 21, 2015 video shows V.S.R. at a McDonald's playground; a February 22, 2015 video shows V.S.R. on the phone; a February 26, 2015 video shows V.S.R. playing at a shopping center play area; a February 26, 2015 video shows V.S.R. watching cartoons; a February 26, 2015 video shows V.S.R. walking around a shopping center; a February 26, 2015 video shows V.S.R. at a shopping center play area; a February 27, 2015 video shows V.S.R. on the living room floor unable to stand and frustrated; a February 28, 2015 video shows what is asserted to be unusual behavior; a March 2, 2015 video shows V.S.R. playing "what's in the basket?" with her sister; a March 7, 2015 video shows V.S.R. riding in a wagon, and a set of four videos from March 7, 2015 shows V.S.R. on the dance floor at a wedding. (Exs. 13, 15.)

On March 4, 2015, V.S.R. suffered a likely seizure witnessed by her mother. Specifically, Ms. Hogan described an episode wherein V.S.R. appeared to "zone[] out," was unresponsive to her mother's voice and touch, and then seemed to be dazed afterward. (Ex. 1, pp. 2-3; Tr. 68-70, 91-92.) There is no record of this event as it happened at home and no medical attention was sought (Tr. 68-70); however, both parties' experts credit Ms. Hogan's description as identifying a seizure. (*Id.* at 161-62, 392, 447; Ex. 16, p. 2.) Specifically, the parties' neurology experts agree that the description is consistent with a focal seizure originating in the temporal lobe. (Tr. 205, 392, 447.)

About a week later, V.S.R. was found by her mother unresponsive, not breathing, and without a pulse. She was brought to Kaiser's emergency department ("ED") on March 11, 2015. (Ex. 6, p. 7; Ex. 8, pp. 3-6, 10-12; Tr. 76-79.) V.S.R. was noted to have been last observed as normal at 3:00 PM earlier that day. (Ex. 6, pp. 7-8.) She arrived to Kaiser's ED unresponsive, with no pulse and no spontaneous breathing. (*Id.* at 8.) Attempts to resuscitate were made but were ultimately unsuccessful. (*Id.*) She was pronounced dead at 8:38 PM on March 11, 2015. (*Id.*) According to Ms. Hogan, V.S.R. had been cranky and not nursing well the day before she died. (Ex. 1, p. 3; Tr. 70-71.) Ms. Hogan testified that she first noticed V.S.R. consuming less milk about a week before she died. (Tr. 67-68, 102.) According to Mr. Rodela's affidavit, on the day she died, V.S.R. felt as though she had a fever and could not be comforted. (Ex. 2, p. 4.) He had difficulty getting her to sleep prior to her final nap. (*Id.*) During the hearing, however, he indicated that he did not recall V.S.R. being ill on the day that she died and that the day was an otherwise ordinary day. (Tr. 24-25.)

The Irvine police were dispatched to petitioners' home at approximately 8:03 PM on March 11, 2015, but located petitioners at the hospital. (Ex. 8, p. 3.) After arriving at the hospital, the police interviewed petitioners and V.S.R.'s treating physicians. (*Id.* at 3-5.) Dr. Mueller, the treating physician indicated that V.S.R. never exhibited any vital signs upon arrival. (*Id.* at 3-4.) V.S.R.'s father, Mr. Rodela, explained that he had spent the day watching V.S.R. and that it had been a normal morning where she played as she usually did. (*Id.* at 4; Tr. 24-25.) He noted that he laid V.S.R. down for her first nap of the day at approximately 1:00 PM which lasted around 20 to 30 minutes. (Ex. 8, p. 4.) He reported that V.S.R. appeared to "be sweating just a little bit" when he woke her from her nap and that he believed this may have been because she caught his recent illness. (*Id.*) V.S.R.'s father further reported that she spent the afternoon playing and that he did not notice anything unusual about her. (*Id.*) He stated that he laid V.S.R. down for a second nap around 4:00 PM, at which point he also laid down because he was not feeling well. (*Id.*) He reported that he woke up around 6:00 PM and that V.S.R.'s mother had already returned home from work. (*Id.*)

V.S.R.'s mother, Ms. Hogan, explained that she left for work at approximately 6:30 AM on March 11, 2015, and returned around 4:30 PM. (Ex. 8, p. 4; Tr. 73.) Upon arriving home, she went in to check on V.S.R., who appeared to be breathing based on the rise and fall of the blankets she was under. (Ex. 8, p. 4; Tr. 73-74.) V.S.R.'s mother again checked on her at around 6:30 PM but did not notice whether the blankets were

moving up and down. (Ex. 8, pp. 4-5.) Around 8:00 PM, V.S.R.'s mother attempted to wake her in order to feed her. (*Id.* at 5; Tr. 75-76.) She noticed that V.S.R. was lying at about a 45 degree angle, "not quite on her stomach and not quite on her side," and attempted to wake her by tickling one of her feet which was sticking out from under the blanket. (Ex. 8, p.5; Tr. 76.) However, V.S.R. did not react to her mother tickling, at which point, her mother began to unwrap her blankets. (Ex. 8, p. 5; Tr. 76.) Once she had removed the blankets, V.S.R.'s mother noticed that she appeared to be lifeless and attempted to wake her. (Ex. 8, p. 5; Tr. 76.) She attempted to dislodge any potential airway obstructions and took her to the dining room table to begin CPR. (Ex. 8, p. 5; Tr. 77.) V.S.R.'s father had already called 911 at this point, and after their attempts to resuscitate V.S.R. through CPR had failed, went down to the street to wait for first responders. (Ex. 8, p. 5; Tr. 77-78.)

Forensic pathologist Etoi Davenport, M.D., performed V.S.R.'s autopsy. (Ex, 7, p. 1.) V.S.R.'s autopsy report listed her cause of death as "undetermined" and noted that she appeared to be "a normally developed, well-nourished, normocephalic female infant appearing consistent with the listed age of 1 year and 2 months." (*Id.* at 1, 3.) At the time of her death, V.S.R.'s head circumference was measured at 47.4 centimeters. (*Id.* at 3.) Dr. Davenport did not observe anything out of the ordinary upon physical exam. (*Id.* at 3-4.) V.S.R.'s body cavity exam was normal, and her heart appeared to be of normal size and shape with no noticeable defects. (*Id.* at 5.) Dr. Davenport also observed that V.S.R.'s lungs appeared normal. (*Id.* at 5-6.) V.S.R.'s liver appeared to be "mildly enlarged", but otherwise normal. (*Id.* at 6.) Her gallbladder and pancreas also appeared to be normal. (*Id.*) Dr. Davenport also found no abnormalities in V.S.R.'s endocrine, gastrointestinal, genitourinary, and musculoskeletal systems. (*Id.* at 6-7.) V.S.R.'s head examination did not reveal any evidence of hemorrhage. (*Id.* at 7.) Her brain was recorded as weighing 1040 grams (versus a reference of 944 grams) with a "slightly flattened gyral pattern over the bilateral superior surfaces," indicating "possible cerebral swelling." (*Id.*) Dr. Davenport was unable to identify any evidence of herniation, and the arteries at the base of V.S.R.'s brain were found to be "intact and free of significant antherosclerotic changes or aneurysms." (*Id.*) Dr. Davenport's pathologic diagnosis found that V.S.R. was a "normocephalic, well-nourished female child" in the 95th percentile for head circumference, 25th percentile for height, and 5th to 10th percentile for weight. (*Id.* at 10.) It was further noted that V.S.R.'s father had recently exhibited flu-like symptoms. (*Id.*)

A microscopic examination of V.S.R.'s heart found "generalized bubbly degeneration of the myocytes, patchy areas of myocyte contraction bands, and a few small foci of interstitial red blood cells." (Ex. 7, p. 12.) Her neck contents revealed "generalized dense tracheal submucosal lymphocytes with associated patchy areas of edema." (*Id.*) Dr. Davenport reported signs of lymphocytes infiltrating the mucosa "[i]in a few areas." (*Id.*) V.S.R.'s liver, diaphragm, kidneys, pancreas, adrenal glands, thymic gland, gastrointestinal system, and spleen all appeared normal on microscopic examination. (*Id.* at 12-13.) Sections of her brain had "general edematous changes surrounding the vessels and within the parenchyma," along with "a single focus of lymphocytic perivascular cuffing, but . . . no significant evidence of associated

parenchymal infiltration." (*Id.* at 13.) There appeared to be "a few small foci of perivascular and parenchymal red blood cells," with no evidence of meningitis. (*Id.*) V.S.R.'s toxicology reports were negative for ethanol, benzodiazepines, cocaine, phenethlamines, opiates, oxycodone, cannabinoids, zolpidem, alkaline drugs, and strong acid/neutral drugs. (*Id.* at 14.) However, her bloodwork revealed elevated levels of bismuth (3.2 µg/L versus a reference of .50 µg/L, mercury (6.4 µg/L versus a reference of 3.0 µg/L), selenium (160 µg/L versus a reference of 20 µg/L), and lead (3.8 µg/L versus a reference of .50 µg/L). (*Id.* at 18.) V.S.R.'s comprehensive metabolic panel showed critically high levels of potassium; critically low levels of glucose; high levels of chloride and AST; and low levels of CO2, creatine, calcium, total protein, albumin, and alkaline phosphatase. (*Id.* at 22.) V.S.R.'s various virology and bacteriology reports were negative for influenza A, B, and viral cultures. (*Id.* at 23-30.) Petitioners' also sought genetic testing for V.S.R. and themselves with the Sudden Unexplained Death in Childhood Registry and Research Collaborative; however, the testing did not reveal any remarkable genetic variants that could have contributed to V.S.R.'s sudden death. (Ex. 9, p. 2.)

IV. Summary of Expert Opinions

a. The parties' pathology experts

i. Robert Shuman, M.D., for petitioners[5]

Although V.S.R.'s autopsy concluded her death was undetermined, Dr. Shuman does not agree that her death falls under the category of Sudden Infant Death Syndrome ("SIDS") or Sudden Unexplained Death in Childhood ("SUDC"). (Tr. 514.) Instead, he opines that V.S.R. suffered a fatal encephalitis, which he opines began one to two weeks prior to her death.[6] (Ex. 43, p. 2; Ex. 38, pp. 7-8; Tr. 122, 165-66.) He

[5] Dr. Shuman has been proffered without objection as an expert in neurology, neuropathology, pediatric neurology, and neuroimaging. (Tr. 121.) Dr. Shuman received his bachelor's degree in experimental psychology from Cornell University in 1963 and his medical degree from Stanford University School of Medicine in 1968. (Ex. 35, p. 1.) He completed his internship and residency in pediatrics at the University of Colorado Medical Center in Denver, Colorado in 1970, after which he completed a second residency in pathology at the University of Washington Affiliated Hospitals in Seattle, Washington in 1972. (Ex. 35, p. 1; Tr. 116-17) Dr. Shuman held a fellowship in neuropathology at the University of Washington from 1972 to 1974 and completed a third residency in pediatric neurology at the University of Kentucky in 1985. (Ex. 35, p. 1; 117-18.) Dr. Shuman has held a number of academic appointments, with professorships in neurology and pathology at the University of Pittsburgh School of Medicine, the University of Nebraska Medical center, Creighton University Medical School, and the University of Oklahoma. (Ex. 35, pp. 1-2.) After leaving the academic realm, Dr. Shuman spent a number of years in private practice as a pediatric neurologist before eventually retiring in 2006. (*Id.* at 2; Tr. 120, 182.) He is board certified in neuropathy; neurology, with a subspecialty in pediatric neurology; and neuroimaging, and he maintains his medical license in Indiana. (*Id.* at 2; Tr. 120-21.) Dr. Shuman has published 49 articles on neurology and pathology, 2 textbooks, and 38 invited papers and abstracts. (Ex. 35, pp. 6-12.)

[6] To be clear, Dr. Shuman does cite some literature regarding SUDC and Sudden Unexplained Death in Epilepsy ("SUDEP") for the proposition that an unwitnessed terminal seizure is a known phenomenon. (Ex. 34, p. 3.) However, he is patently not relying on these concepts insofar as he is very clear in opining that V.S.R. suffered a fatal encephalitis, rather than an unexplained death. *See also infra* note 21. In his

suggests several findings were missed in V.S.R.'s autopsy. Although Dr. Shuman is not directly critical of Dr. Davenport, he suggests that real world pressures and limitations on medical examiners can result in some findings being missed. (Tr. 300-01.)

Regarding the gross examination, Dr. Shuman finds significance in several features. First, at 1040 grams, V.S.R.'s brain weight was unusually heavy in general and heavier than would be expected in an unexplained death. (Ex. 34, p. 1.) Accordingly, he opines the brain weight supports his conclusions regarding inflammation edema (*i.e*. swelling due to fluid collection).[7] (*Id*.; Ex. 38, p. 12.) Second, and relatedly, Dr. Shuman notes that V.S.R.'s head circumference on autopsy was measured at 47.4 centimeters, which was observed to be at the 95th percentile. (Ex. 38, p. 12.) In contrast, V.S.R.'s medical records generally showed her head circumference to be in a lower percentile throughout her infancy and her final medical appointment indicates a head circumference of 46.1 centimeters. This indicates that her head circumference increased by 1.3 centimeters over the course of 19 days, which he opines is not explained by normal growth. (*Id*.; Tr. 123.) According to Dr. Shuman, the cranial sutures of a 14-month old are still elastic, such that V.S.R.'s skull expanded to accommodate the edematous brain. (Ex., 38, p. 12.) Thus, he opines the heavy brain weight and increased head circumference support cerebral edema and associated swelling. (*Id.*) This is also confirmed by the finding of flattened gyri upon gross examination at autopsy, which is a finding that the normal contours of the outside of the brain have been flattened from pushing against the skull. (Tr. 123-24; Ex. 34, p. 1.) Dr. Shuman also observed edema upon microscopic examination and provided testimony during the hearing further showing that his microscopic examination confirmed tissue compression. (Tr. 123-24, 128, 166-68.) Although Dr. Shuman acknowledges that the autopsy report did not indicate any signs of herniation upon gross examination, he opines that the unfixed brain of a 14-month old is more gelatinous than a more mature brain and therefore does not retain signs of herniation once the skull is breached. (Ex. 34, p. 1.) However, during the hearing, he also testified that he had identified an uncal groove. (Tr. 124, 249-51.) He opines that this is clear evidence of herniation at the brain stem.[8] (*Id.* at 160.)

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first report, Dr. Harris characterized Dr. Shuman as agreeing that V.S.R.'s death is appropriately designated as SUDC (Ex. A, p. 6), but this is not entirely accurate. What Dr. Shuman stated was that some deaths labeled SUDEP may actually be explained by encephalitis. (Ex. 34, p. 3.)

[7] Initially, Dr. Shuman indicated that the mean brain weight for 14-month-old female is 655.1 grams, suggesting that V.S.R.'s brain weight of 1040 grams was three standard deviations above the mean. (Ex. 34, p. 1.) However, Dr. Harris cited a different source that identified 944 grams as the average brain weight for a 14-month-old child. (Ex. A, p. 4.) Incidentally, this is the same figure that Dr. Davenport used as a reference. (Ex. 7, p. 7.) Thus, Dr. Harris characterized V.S.R.'s brain as only "mildly heavier than expected for age." (Ex. A, p. 4.) In his second report, Dr. Shuman agreed that 655.1 grams is not the average brain weight for a 14-month-old (Ex. 38, p. 12, n. 1), but still maintained based on additional references that V.S.R.'s brain weight was statically significantly heavy (Ex. 38, pp. 10-12). Subsequently, Dr. Harris continued to disagree the brain was "statistically significantly heavy," but agreed the brain was increased, with the additional question of whether it was mildly or moderately so being unimportant absent evidence the increase was severe enough to result in herniation. (Ex. G, pp. 1-2.)

[8] Dr. Shuman explained that cerebrum sits on an anatomical feature called the tentorial notch, which is a wedge-shaped feature of bone and fibrous tissue near the brain stem. When the brain swells, downward

In addition to the gross findings, Dr. Shuman explained that the autopsy materials include four slides of fixed brain tissue – one each of the hippocampus, midbrain, cerebellum, and medulla. Among these samples, he identified several findings on microscopic examination that he opines are indicative of inflammation affecting all four portions of the fixed tissue samples. (Tr. 123-25.) According to Dr. Shuman, either resident or infiltrating immune cells constitute evidence of inflammation consistent with encephalitis, specifically noting that the presence of either type of immune cell is incompatible with SIDS. (*Id.* at 514.) Thus, he opines that "four out of four is 100 percent," meaning that there is evidence to support widespread inflammation in V.S.R.'s brain. (*Id.* at 202, 302.) Because the inflammation was present in the midbrain and medulla, which controls respiration and autonomic function, Dr. Shuman opined that the inflammation and edema he observed alone are sufficient to have been fatal. (*Id.* at 166-68, 170.) Dr. Shuman noted that there are no tissue samples available for the brainstem itself, but the samples from the midbrain and cerebellum show areas of the brain close to the brainstem that were inflamed. (Ex. 38, p. 10.) Because the brainstem controls vital functions, "inflammation of the brainstem is highly dangerous" and "[o]ne must not trivialize the importance of encephalitis as a cause of death *sui generis*." (*Id*.) However, Dr. Shuman also opined that the hippocampus was the most affected of the four samples. (Tr. 124.) Thus, he opines that the extent of the inflammation specifically affecting the hippocampus also supports an unwitnessed seizure as a further contributing factor. (*Id.* at 137-38, 166, 169.)

Dr. Shuman identified evidence of resident immune cells, namely activated microglia, in all four sections of brain tissue. (Tr. 124-25.) He indicated this is the most extensive finding of inflammation in V.S.R.'s tissue. (*Id.* at 124, 156.) Activated microglia respond to insults within the brain by losing their fixed position within the brain and migrating to the affected area. (*Id.* at 133.) Dr. Shuman opines that they are the earliest responding component of neuroinflammation. (*Id.* at 135.) According to Dr. Shuman's examination, there is evidence that these cells were not merely present, but active and proliferating in V.S.R.'s brain tissue, resulting in patchy neuronal loss. (*Id.* at 133-34.) He described three findings that he indicated show an active resident immune response. First, he explained that, in response to inflammation, microglia migrate to distressed cells. As the microglia surround a distressed neuron, they form a visible cluster, which is known as a microglia nodule. (*Id.* at 148-50.) During the hearing, Dr. Shuman explained that he observed one of these nodules in the midbrain around the top of the brain stem. (*Id*.) Second, once the microglia arrive at the cell, they phagocytose affected neurons – a process that he indicates he observed in the fixed tissue from the hippocampus. (*Id.* at 152-55.) Third, Dr. Shuman identified reactive astrocytes. Reactive astrocytes are brain cells that have become visible on microscopic imaging because they have developed fibril or glial sheathes in response to distress.

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pressure is exerted on the temporal lobe by the cerebrum. (Tr. 249-51.) This pushes the temporal lobe against the tentorial notch, which acts like a knife, cutting the outer casing ("pia") of the brain tissue. (*Id.*) This results in a small protrusion of brain tissue through the resulting defect. (*Id.*) According to Dr. Shuman, this defect is visible on V.S.R.'s pathology and is "a typical histologic feature of an uncal groove. It's in the right place. It has the right histopathology." (*Id.* at 250.)

(*Id.* at 156-57.) Reactive astrocytes are not inflammation in themselves, but they are evidence of damage caused by inflammation. (*Id.* at 158, 292.) It takes between 7-14 days for astrocytes to develop. (*Id.* at 157, 291.) Accordingly, this finding supports a course of inflammation in V.S.R.'s case of at least seven days. (*Id.* at 158, 291-92.)

Dr. Shuman also identified immune cell (lymphocyte) infiltration into the brain in the form of perivascular cuffing. Perivascular cuffing refers to a finding that shows these immune cells ringing, *i.e.*, "cuffing," the vascular walls within the brain. (Tr. 139-41, 274.) Within V.S.R.'s four tissue samples, he identified two such cuffs, one in the cerebellum and one in the hippocampus. (Tr. 138-39, 145-46.) Dr. Davenport had also located a focus of lymphocytic cuffing but appeared not to find it significant without additional indication of further parenchymal infiltration. (Ex. 7, p. 14.) However, Dr. Shuman opined that, especially where there are multiple foci of cuffing as he had observed, the alternative causes of perivascular cuffing are few and limited. (Tr. 268, 519.) Accordingly, he opined that any degree of perivascular cuffing is an abnormal finding that constitutes "the definition of brain inflammation." (*Id.* at 145, 147-48, 303-04.)

Despite asserting video evidence of encephalitis, Dr. Shuman also opined that the histopathologic diagnosis of encephalitis stands on its own even in the absence of clinical correlation. (Tr. 126-27.) Dr. Shuman further stressed that in addition to being epileptogenic, damage to the hippocampus and temporal lobe would typically result in learning and memory difficulties, which would not be readily detected in a 14-month-old. (*Id.* at 137.) Accordingly, he suggested that opportunities for clinical correlation apart from seizures could be more limited. (*Id.* at 135-37.)

ii. Brent Harris, M.D., for respondent[9]

Like Dr. Shuman, Dr. Harris observed evidence of edema on microscopic examination; however, he felt it was only mild. (Ex. A, p. 6; Tr. 336.) In that regard, he disagreed that the gross pathology supports significant edema/brain swelling. Dr. Harris

[9] Dr. Harris has been proffered without objection as an expert in anatomic pathology and neuropathology. (Tr. 314.) Dr. Harris received his bachelor's degree in biology from Colby College in 1986 and his medical degree from Georgetown University School of Medicine in 1996. (Ex. I, p. 1.) He completed his internship and residency in the Department of Pathology at Stanford University Medical School in 1996 and 1997, respectively. (*Id.*) Dr. Harris also completed fellowships in the Departments of Neuropathology and Neurobiology at Stanford University Medical School in 1997 and 2002, respectively. (*Id.*) He also holds graduate degrees in biochemistry from Hahnemann University and in pharmacology from Georgetown University. (*Id.*) Dr. Harris is board certified in anatomic pathology and neuropathology, and he maintains an active medical license in D.C. (*Id.* at 3; Tr. 310.) He has held various teaching, research, administrative, and consulting positions throughout his career. (Ex. I, pp. 1-2.) He currently serves as director of the Georgetown Brain Bank and of neuropathology at MedStar Georgetown University Hospital, as well as positions as an associate professor of neurology and pathology at Georgetown University School of Medicine and of pathology at Howard University Medical School. (*Id.*; Tr. 309, 311-14.) Additionally, he is currently employed as a consulting neuropathologist for six different entities, including as the sole neuropathologist for the Office of the Chief Medical Examiner of DC. (Ex. I, p. 2; Tr. 309.) Finally, Dr. Harris has published roughly 200 peer-reviewed journals and meeting abstracts, including a number of publications in the field of pediatric neuropathology. (Tr. 310.)

agreed the brain was heavier than normal, but not significantly so. (Tr. 327.) Further to that, he felt the heavy brain weight was largely explained by V.S.R.'s naturally large head. Specifically, she had a relatively high percentile head circumference throughout her life and her final measurement at autopsy was at the 95th percentile which, while large, was still normocephalic. (*Id.* at 321-23.) Dr. Harris disagreed that the skull of a 14-month old is sufficiently elastic as to explain the increased head circumference. (Ex. A, p. 6.) Dr. Harris did agree that Dr. Davenport observed flattened gyri, but noted that this finding was in the forebrain, which is not an area that herniates. (Tr. 323-26; *see also* Ex. A, p. 4.) He also disagreed that there is evidence of herniation in the form of any uncal groove. First, he did not observe the finding on his own review of the slides. (Ex. A, pp. 4-5; Ex. G.) Second, because Dr. Shuman identified only the notch itself, and not any associated evidence of tissue damage, the finding is best viewed as a postmortem artifact.[10] (Tr. 326.) Dr. Harris does not agree with Dr. Shuman that the 14-month old brain would not retain evidence of herniation once released from the skull. (Ex. A, p. 6.) Considering all of this, Dr. Harris does not agree that V.S.R. was experiencing significant edema or intracranial pressure. (*Id.* at 4-6.)

Dr. Harris indicated that a "purist" would view only lymphocytic infiltration as any evidence of neuroinflammation consistent with encephalitis; however, he agreed that most neuropathologists would look to both infiltrating and resident immune cells to determine encephalitis. (Tr. 344-45.) Thus, Dr. Harris agreed that activated microglia and astrocytes are one acceptable definition of neuroinflammation. (*Id.* at 342.) However, in his own clinical judgment, he opined that he would need to see (1) lymphocytes infiltrating the parenchyma, and (2) some evidence of etiology, such as viropathic changes, before he would conclude that there is histopathologic evidence of encephalitis. (*Id.* at 343-44.) He also opined that clinical correlation is important, which he opined is lacking in this case. (*Id.* at 346-47, 377.)

Regarding the microscopic examination, Dr. Harris agreed with Dr. Davenport's conclusion that a singular focus of perivascular cuffing is not significant without further evidence of infiltrating lymphocytes into the parenchyma. (Tr. 343-44, 366; Ex. G, p. 3.) Nonetheless, he agreed that the finding technically constitutes an abnormal finding and is evidence of inflammation. (Tr. 306, 366, 374.) He disagreed that Dr. Shuman has located a perivascular cuff in the cerebellum, but confirmed that he identified a perivascular cuff in the hippocampus. (Ex. A, p. 6; Tr. 525-26.) Dr. Harris agreed with Dr. Shuman that there are activated microglia visible in all four tissue samples, but he characterizes them as only diffuse. (*Id.*; Tr. 339.) He disagreed that there is any evidence of nodules or neuro phagocytosis, but agrees that reactive astrocytes are present in the hippocampus, though to a lesser extent than the microglia. (Ex. A, pp. 5-6; Ex. G. pp. 2-3; Tr. 358, 376.) He opined that, in this case, the extent of the findings of microglia and astrocytes are consistent with one or more seizures having occurred during the weeks prior to V.S.R.'s death, rather than being evidence of an encephalitic

[10] Dr. Harris explained that if the notch had occurred premortem, then there would be evidence in the tissue of blood flow to the site. Without such evidence, the notch likely occurred after death when blood would no longer be circulating. (Tr. 326.)

process. (Ex. A, p. 5.) In that regard, he agreed that astrocytes take about 1-2 weeks to develop. (Tr. 381.) However, he did not agree that a terminal seizure is implicated. (Ex. A, p. 5; Tr. 524.)

Like Dr. Shuman, Dr. Harris also recognized that there were significant limitations regarding V.S.R.'s autopsy. (Ex. A, pp. 4-5; Tr. 319.) In fact, he specifically noted that V.S.R.'s autopsy was not sufficiently sampled for a full assessment of neuropathologic abnormalities. (Tr. 339.) In contrast to Dr. Shuman, however, he nonetheless characterized himself as being in agreement with the autopsy findings. (Ex. A, p. 4; Tr. 354.) In sum, Dr. Harris opined that the autopsy evidenced mild to moderate edema, some of which he felt may have been artifact; a slightly heavier than expected brain; one perivascular cuff; and very mild astrogliosis in the hippocampus with mild microgliosis in the other sections. (Ex. A, pp. 4-5; Tr. 339-40.) She had no malformations, no viropathic changes, and no infiltrating immune cells apart from the one perivascular cuff. (Ex. A, pp. 4-6; Tr. 340.) Thus, he agreed with the ultimate conclusion that V.S.R.'s death is best classified as undetermined. (Ex. A, p. 5; Tr. 346.)

b. The parties' neurology experts

i. Marcel Kinsbourne, M.D.[11]

Prior to having the benefit of Dr. Shuman's assessment of V.S.R.'s pathology, Dr. Kinsbourne's first report focused on the cerebral edema observed upon autopsy by Dr. Davenport, noting that a finding of cerebral edema is consistent with a phenomenon of Sudden Unexplained Death in Epilepsy ("SUDEP"). (Ex. 16, pp. 2-3.) Dr. Kinsbourne opined that seizures are capable of causing cerebral edema by "greatly increas[ing] metabolic demands," which can trigger hypoxia, breach the blood brain barrier, and move fluid from the circulation into the brain's extracellular space. (*Id.* at 5.) One major consequence of brain swelling, cited by Dr. Kinsbourne, is elevated intracranial pressure, which reduces cerebral blood flow and leads to metabolic compromise. (*Id.*) Cerebral edema has also been associated with deregulation of the brain vasculature,

[11] Dr. Kinsbourne was proffered without objection as an expert in neurology with special competence in child neurology. (Tr. 388.) Dr. Kinsbourne received his bachelor's degree from Oxford University in 1952, his medical degree from Oxford in 1952, his master's degree from Oxford University in 1956, and his doctorate degree from Oxford in 1963. He also received an American medical degree from the state of North Carolina in 1967. (Ex. 17, p. 1.) Dr. Kinsbourne has served as a house physician and/or house surgeon at six different hospitals in London, with a focus on pediatrics and neurosurgery in his most recent positions. He has also served as registrar and senior registrar for the Neurology Department at United Oxford Hospitals and as a registrar for the Neurology Department at the Hospital for Sick Children in London. Dr. Kinsbourne has held numerous academic positions, including lecturer in experimental psychology at Oxford University, professor of pediatrics and neurology at Duke University Medical Center, and professor of pediatric neurology at the University of Toronto. He currently serves as a senior fellow at the Center for the Study of Aging and Human Development at Duke University, an adjunct professor of neurology at Boston University School of Medicine, a research professor at the Center for Cognitive Studies at Tufts University, and a professor of psychology at New School University. (*Id.*at 1-2.) Dr. Kinsbourne has published 424 different articles on pediatrics and psychology. He has published his own book on child psychology and has edited 8 different books on pediatrics and psychology. (*Id.* at 5-39.)

which leaves the brain exposed to blood pressure fluctuations and may lead to increased cerebral blood volume that further contributes to brain expansion. (*Id.*) Dr. Kinsbourne cited a paper explaining that increased intracranial pressure can induce a reduction in cerebral blood flow, hypoxia, and brain coning, which may cause irreversible impairment of nerve function and, in the worst cases, death. (*Id.* (citing Shotaro Michinaga & Yutaka Koyama, *Pathogenesis of Brain Edema and Investigation into Anti-Edema Drugs*, 16 INT'L J. MOLECULAR SCIS. 9949 (2015) (Ex. 24)).) Another study found that 35% of patients with SUDEP had cerebral edema at autopsy. (*Id.* (citing Sergio A. Antoniuk et al., *Sudden Unexpected, Unexplained Death in Epilepsy Autopsied Patients*, 59 ARQ NEUROPSIQUIATR 40 (2001) (Ex. 18)).)

After review of Dr. Shuman's opinion, Dr. Kinsbourne's second report additionally incorporated an opinion based on widespread inflammation, *i.e.*, encephalitis, affecting V.S.R.'s brain. (Ex. 39, p. 1.) Dr. Kinsbourne agreed with Dr. Shuman's opinion that such widespread inflammation of the brain could result in potentially fatal seizure activity. (*Id.*) For example, he noted that a study by Weibel et al. found that 36 out of 48 children who experienced encephalopathies following MMR vaccination reported seizures. (*Id.* (citing Robert E. Weibel et al., *Acute Encephalopathy Followed by Permanent Brain Injury or Death Associated with Further Attenuated Measles Vaccines: A Review of Claims Submitted to the National Vaccine Injury Compensation Program*, 101 PEDIATRICS 383 (1998) (Ex. 40)).) Dr. Kinsbourne opined that the existing evidence is "quite sufficient to enable an opinion to a reasonable degree of medical probability" that V.S.R. "suffered an encephalitis; that encephalitis probably caused a seizure which caused [her] death; and the MMR vaccine probably caused the encephalitis." (*Id.* at 2.) Further, Dr. Kinsbourne concluded that V.S.R.'s encephalitis would have developed between 5 and 12 days after her MMR vaccination, based on Dr. Shuman's finding that the astrocytic gliosis observed in V.S.R.'s brain would have taken one to two weeks to develop. (*Id.* at 1-2.) This would place the onset of V.S.R.'s encephalitis "within the 5 to 15 day risk interval for a Table encephalitis after an MMR vaccination in the Vaccine Injury Table." (*Id.* at 2.)

During the hearing, Dr. Kinsbourne further highlighted Dr. Shuman's explanation of inflammation affecting the hippocampus and ultimately concluded that V.S.R. likely suffered an encephalitis that in turn caused fatal seizures. (Tr. 390.) Thus, V.S.R.'s death was an acute complication of her encephalitis. (*Id.* at 393.) In reaching this conclusion, he relied on (1) at least one "clear" seizure occurring prior to death; (2) increased head circumference upon autopsy; (3) edema; (4) flattening of the gyri; (5) histologic evidence of inflammatory cells, including activated microglia, lymphocytes, and astrocytes; and (6) marked findings of inflammation, specifically in the hippocampus. (*Id.* at 389-90.) Although Dr. Kinsbourne opined that a fatal seizure is probable, he also opined that the edema alone was sufficient to be fatal by interfering with the circulation of blood to the brain. (*Id.* at 394-95.)

Dr. Kinsbourne stressed that the postmortem evidence is the most persuasive evidence in this case and that it paints a "coherent picture" of an encephalitis. (Tr. 400.) Dr. Kinsbourne opined that a "firm" diagnosis of encephalitis can be made based on

postmortem pathology alone, even if the outward clinical history is confusing or unclear. (*Id.* at 405-07.) He agreed that, in this case, the outward clinical evidence alone is not sufficient to diagnose encephalitis and that "[t]he key is the autopsy." (*Id.* at 409.) Nonetheless, he stressed that evidence of aberrant neurologic behavior is not completely absent, expressing that "the evidence is miscellaneous, but it is there." (*Id.* at 408-09.)

ii. Elaine Wirrell, M.D.[12]

Consistent with Dr. Harris's assessment of the pathology, Dr. Wirrell opined that V.S.R.'s death is most consistent with the phenomenon of Sudden Unexplained Death in Childhood ("SUDC"). (Ex. C, p. 10.) She indicated that "some SUDC deaths may be seizure related" and potentially overlap with SUDEP. (*Id.* at 11 (citing Dale C. Hesdorffer et al., *Sudden Unexplained Death in Childhood: A Comparison of Cases with and Without a Febrile Seizure History*, 56 EPILEPSIA 1294 (2015) (Ex. C- 5)).) Dr. Wirrell stressed the prevalence of hippocampal malformation among SUDC cases and the Kinney et al. hypothesis that such malformation is causally relevant. (*Id*. (citing Hannah C. Kinney et al., *Hippocampal Formation Maldevelopment and Sudden Unexpected Death Across the Pediatric Age Spectrum*, 75 J. NEUROPATHOLOGY & EXPERIMENTAL NEUROLOGY 981 (2016) (Ex. C- 6)).) Notably, however, she acknowledged there is no evidence in this case that V.S.R. had any hippocampal malformation. (*Id*. at 12.)

Dr. Wirrell also opined that V.S.R. was suffering some sort of undetected infection in the days preceding her death.[13] (Ex. C, p. 12.) She noted that prior to her death V.S.R. was clingy, more irritable, and not feeding as well as normal. (*Id.*) V.S.R.'s father reported that she "felt sweaty" and that he was concerned that she was "coming down with something" after her nap on March 11. (*Id.*) Although the autopsy report documented no evidence of pneumonia, Dr. Wirrell noted that it did comment on lymphocytic infiltration and tracheal edema, which is consistent with an upper respiratory viral illness. (*Id.*) Dr. Wirrell further noted that V.S.R. was "significantly hypoglycemic," with a blood glucose level upon presentation to the ER of 30 and a postmortem glucose level of 1. (*Id.*) She therefore suggested that metabolic disorders of organic acid metabolism or fatty acid oxidation may be considerations in this case. (*Id.* at 13.) She noted that metabolic crisis can be provoked by intercurrent illness or

[12] Dr. Wirrell was proffered without objection as an expert in pediatrics, pediatric neurology, and pediatric epilepsy. (Tr. 419.) Dr. Wirrell received her bachelor's degree in biochemistry from Simon Fraser University in 1985, and her medical degree from the University of British Columbia in 1989. (Ex. D, p. 1.) She completed an internship and residency in pediatrics, as well as a fellowship in pediatric neurology, at IWK Hospital for Children. Dr. Wirrell is board certified in pediatrics and neurology. (Id.) She has served as an assistant and associate professor of pediatrics in the division of neurology at the University of Saskatchewan and the University of Calgary, and she is currently employed as the chair of child neurology and director of pediatric epilepsy at Mayo Clinic. (*Id.* at 2-3; Tr. 413-14.) She has served as a journal reviewer for numerous publications since 2001, has completed 180 different presentations on pediatric neurology at medical conferences, and authored 161 peer-reviewed articles on neurology and pediatrics. (Ex. D, pp. 17-55.)

[13] Dr. Wirell noted that blood cultures were positive for Klebseiella pneumonia and Citrobacter freundi, but ultimately concluded that they were likely contaminants. (Ex. C, p. 12.)

fasting. (*Id.*) However, she stopped short of actually opining that any metabolic condition contributed to V.S.R.'s death.

In her first report, Dr. Wirrell agreed that "it is difficult to definitely exclude a seizure disorder," but she was doubtful that the "staring episode" reported by V.S.R.'s mother was "truly a seizure." (Ex. C, p. 13.) However, during the hearing, Dr. Wirrell later agreed that the March 4 event was a seizure, specifically a focal seizure originating in the temporal lobe. (Tr. 447.) Nonetheless, she did not agree that the February 27 event identified as a seizure by Dr. Shuman was, in fact, a seizure. (Tr. 431-32.) Dr. Wirrell also doubted that the seizures, if they occurred, would have been directly caused by the vaccination. (Ex. C, pp. 14-15.) And, while Dr. Wirrell agreed it is possible, albeit speculative, that V.S.R. suffered a fatal seizure, she would not attribute the seizure to any encephalitis. (Ex. H, p. 3.)

Dr. Wirrell did not agree that an encephalitis was present, because V.S.R. was showing normal motor skills, alertness, and coordination, with no significant cognitive decline, prior to her death. (Ex. C, p. 15.) Dr. Wirrell stressed that V.S.R. did not satisfy the diagnostic criteria for encephalitis which requires there be an "altered mental status for 24 hours or longer without an alternate cause" in addition to at least two other minor criteria. (Ex. H, p. 2 (emphasis omitted).) The minor criteria include: "(1) temperature of [38 degrees Celsius] or higher within 72 hours, (2) seizures, ([3]) new focal neurological findings, (4) CSF pleocytosis, (5) Neuroimaging showing brain parenchymal changes and (6) EEG consistent with encephalitis." (*Id.* (citing A. Venkatesan et al., *Case Definitions, Diagnostic Algorithms, and Priorities in Encephalitis: Consensus Statement of the International Encephalitis Consortium*, 57 CLINICAL INFECTIOUS DISEASES 1114 (2013) (Ex. H-2)).) Because the record does not conclusively document the existence of any of these criteria, Dr. Wirrell concluded that it is unlikely V.S.R. actually suffered from encephalitis. (*Id.*) Dr. Wirrell noted that "children with encephalitis have a high severity illness," with nearly all cases requiring hospitalization and 40% of cases requiring intensive care. (*Id.* (citing Kevin Messacar et al., *Encephalitis in US Children*, 32 INFECTIOUS DISEASE CLINICS N. AM. 145 (2018) (Ex. H-1)).) Because V.S.R. did not appear to suffer from any severe illness or symptoms of encephalitis prior to her death, Dr. Wirrell opined she was not encephalitic. (*Id.* at 2-3.) During the hearing, Dr. Wirrell also provided testimony rebutting Dr. Shuman's assessment of the video evidence. (Tr. 428-47.) She concluded that the videos do not show signs of encephalitis and disagreed that episodic neurologic dysfunction would support a diagnosis of encephalitis, especially without a period of at least 24 hours of sustained altered mental status. (*Id*. at 428-48.)

Further, Dr. Wirrell noted that neither the initial pathologist nor Dr. Harris made a diagnosis of encephalitis. (Ex. H, p. 3.) She noted that Dr. Harris found microglial and astrocytic activation in the hippocampus and mild subpial gliosis, but no microglial nodules or viropathic cellular inclusion. He also noted no evidence of neutrophilic inflammation. (*Id.*) Taken together, the findings were consistent with acute or subacute seizure activity, but insufficient to support any conclusion about V.S.R.'s cause of death. (*Id.*) Dr. Wirrell also disagreed that V.S.R.'s head circumference was substantially

excessive for her weight and age. (*Id.* at 4.) Dr. Wirrell opined that values between the 75th and 95th percentiles are within normal limits for V.S.R.'s age and that values in excess of the 97th percentile are considered abnormal. (*Id.* at 1.) Further, Dr. Wirrell noted, V.S.R.'s prior growth percentiles for weight and height were in the lower portion of the growth chart while her head circumference was substantially higher, in the 75th percentile, suggesting that the discrepancy between V.S.R.'s height/weight and head circumference was typical for how she was growing. (*Id.*; Tr. 425.)

c. Respondent's infectious disease expert, Haley Gans, M.D.[14]

Dr. Gans suggested that V.S.R. suffered an "episodic viral illness" leading to her death. (Ex. E, p. 4.) Although there are no medical records for the period between February 20, 2015, and March 11, 2015, she opined the parental accounts are consistent with reports of V.S.R.'s prior illnesses, which "show a pattern of protracted course of symptoms, with intermittent fevers and irritability associated with decreased appetite." (*Id.*) Dr. Gans explained that "[t]hese are classic symptoms seen in infants and toddlers when they are sick with viruses, which predominantly result in repeated upper respiratory tract infections at [V.S.R.'s] age." (*Id.* (citing Terho Heikkinen & Asko Järvinen, *The Common Cold*, 361 LANCET 51 (2003) (Ex. E-1); Sara S. Long, *Distinguishing Among Prolonged, Recurrent and Periodic Fever Syndromes: Approach of a Pediatric Infectious Diseases Subspecialist*, 52 PEDIATRIC CLINICS N. AM. 811 (2005) (Ex. E-2); Diane E. Pappas & J. Owen Hendley, *The Common Cold and Decongestant Therapy*, 32 PEDIATRICS REV. 47 (2011) (Ex. E-3); Matthew Thompson et al., *Duration of Symptoms of Respiratory Tract Infections in Children: Systematic Review*, 347 BMJ f7027 (2013) (Ex. E-4).) "In infants, fever and nasal discharge occur commonly with additional manifestations including fussiness, difficulty feeding, decreased appetite, and difficulty sleeping." (*Id.* (citing Heikkinen & Järvinen, *supra*, at Ex. E-1; Thompson et al., *supra*, at Ex. E-4).) She also noted that it is common for infants of V.S.R.'s age to experience around 10 viral illnesses per year with an average length of illness being 15 days. (*Id.*) Dr. Gans noted that the autopsy report provides further support for this opinion as "the only positive finding on the autopsy report which is not consistent with resuscitation is the 'lymphocytic infiltration of tracheal submucosa with associated edema and mucinous gland hyperplasia.'" (*Id.* (citing Ex. 7, p. 12).)

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[14] Dr. Gans was proffered without objection as an expert in pediatrics and pediatric infectious diseases. (Tr. 471.) Dr. Gans received her bachelor's degree in biochemistry from Connecticut College in 1987 and her medical degree from SUNY Health Science Center (Syracuse Upstate) in 1991. (Ex. F, p. 1; Tr. 465-66.) She completed her internship and residency in pediatrics at Stanford University School of Medicine ("Stanford") in 1992 and 1994, respectively, and a fellowship in pediatric infectious diseases at Stanford in 1998. (Ex. F, p. 1; Tr. 465-66.) Dr. Gans currently serves as a clinical associate professor in the Department of Pediatrics at Stanford, and she has previously held positions as a clinical instructor/research associate, clinical educator, acting assistant professor, and assistant professor in the same department. (Ex. F, p. 1.) She also currently holds the following appointments at Stanford: co-director of Pediatric Infectious Diseases Program for Immunocompromised Host, director of Fellowship Education in the Department of Pediatrics, and fellowship association program director of Pediatric Infectious Diseases. (*Id.*) Dr. Gans is board certified in both pediatrics and pediatric infectious diseases, and she maintains her medical license in California. (*Id.* at 2; Ex. E, p. 1.) In pertinent part, she has published 29 different peer-reviewed articles on pediatric infectious diseases. (Ex. F, pp. 5-7.)

Dr. Gans explained that "[t]he most common cause of fever and nonspecific illness in infants is viral infection." (Ex. E, p. 4 (citing Heikkinen & Järvinen, *supra*, at Ex. E-1; Pappas & Hendley, *supra*, at Ex. E-3).) Viral infections have also been associated with febrile seizures. (*Id.* (citing Brian Chung & Virginia Wong, *Relationship Between Five Common Viruses and Febrile Seizures in Children*, 92 ARCHIVES DISEASE CHILD. 589 (2007) (Ex. E-8); Helen M. Lewis et al., *Role of Viruses in Febrile Convulsions*, 54 ARCHIVES DISEASE CHILD. 869 (1979) (Ex. E-9); J. Gordon Millichap & John J. Millichap, *Role of Viral Infections in the Etiology of Febrile Seizures*, 35 PEDIATRIC NEUROLOGY 165 (2006) (Ex. E-10); J.H. van Zeijl et al., *The Pathogenesis of Febrile Seizures: Is There a Role for Specific Infections?*, 12 REV. IN MED. VIROLOGY 93 (2002) (Ex. E-11)).) Dr. Gans cited a literature review of 6,790 patients between 1929 and 1964, which identified the cause of fever in 7,036 different febrile episodes, with viral infection being recognized in 2.6% of those episodes. (*Id.* (citing Millichap & Millichap, *supra*, at Ex. E-10).) Dr. Gans noted that, in young children, the proportion is much higher, with one study finding that 76% of children evaluated for their first febrile seizure showed evidence of a viral illness and another study finding viral illness in 50% of febrile seizures. (*Id.* (citing Lewis et al., *supra*, at Ex. E-9; van Zeijl et al., *supra*, at Ex. E-11).)

Dr. Gans explained that rhinovirus and respiratory syncytial virus (RSV) account for up to 50% and 15%, respectively, of upper respiratory illness in infants and children. (Ex. E, p. 4 (citing Heikkinen & Järvinen, *supra*, at Ex. E-1; Thompson et al., *supra*, at Ex. E-4).) Rhinovirus has been associated with seizure in 23% of patients with rhinovirus infection. (*Id.* (citing Kelvin K.W. To et al., *Pulmonary and Extrapulmonary Complications of Human Rhinovirus Infection in Critically Ill Patients*, 77 J. CLINICAL VIROLOGY 85 (2016) (Ex. E-12)).) RSV is the second most common cause of upper respiratory infection. Up to 70% of all infants contract RSV within their first year of life and that infection manifests with fever in 75% of cases, cough in 98% of cases, wheezing in 65% of cases, otitis media in 58% of cases, and various neurologic symptoms in 1.2-20% of cases. (*Id.* (citing Caroline Breese Hall et al., *The Burden of Respiratory Syncytial Virus Infection in Young Children*, 360 NEW ENG. J. MED. 588 (2009) (Ex. E-14); Terho Heikkinen et al., *Clinical and Socioeconomic Burden of Respiratory Syncytial Virus Infection in Children*, 215 J. INFECTIOUS DISEASES 17 (2017) (Ex. E-15); Nathaniel Kho et al., *Respiratory Syncytial Virus Infection and Neurologic Abnormalities: Retrospective Cohort Study*, 19 J. CHILD NEUROLOGY 859 (2004) (Ex. E-16); John J. Millichap & Mark S. Wainwright, *Neurological Complications of Respiratory Syncytial Virus Infection: Case Series and Review of Literature*, 24 J. CHILD NEUROLOGY 1499 (2009) (Ex. E-17); Laura L. Sweetman et al., *Neurologic Complications Associated with Respiratory Syncytial Virus*, 32 PEDIATRIC NEUROLOGY 307 (2005) (Ex. E-18); Kazuhiro Uda & Katsuhiko Kitazawa, *Febrile Status Epilepticus Due to Respiratory Syncytial Virus Infection*, 59 PEDIATRICS INT'L 878 (2017) (Ex. E-19)).) Further, febrile seizures were recorded in 20% of children with RSV. (*Id.* (citing Chung & Wong, *supra*, at Ex. E-8).) Dr. Gans noted that diagnosing a viral illness via viral culture is especially difficult when the test is done late in the course of the illness, which she believed to be

the case here. (*Id.*) Thus, the limited investigation for viral etiology fails to explain V.S.R.'s illness, according to Dr. Gans. (*Id.*)

Dr. Gans also provided testimony at the hearing that was consistent with her report. (Tr. 471-504.)

V. Definition of "Encephalitis"

As discussed above, the parties agree that there is no regulatory definition of "encephalitis" applicable in this case. (ECF No. 120, p. 4; ECF No.122, n. 3.) However, they disagree with respect to what definition should therefore be used. Relying on principles of statutory construction, petitioners argue that the "common, ordinary, and accepted meaning" of encephalitis should be applied. (ECF No. 120, p. 4 (citing *Nuttall*, 2015 WL 691272, at *15; *Sebelius v. Cloer*, 569 U.S. 369, 376 (2013)).) They argue that the ordinary meaning of encephalitis is simply "inflammation of the brain." (*Id.* at 5.) Respondent argues, however, that petitioners' proposed definition is overbroad and that a clinical definition of encephalitis is required. (ECF No. 97, pp. 14-15.) Otherwise, respondent argues that petitioners would be granted a "presumption on top of a presumption," *i.e.*, not only a presumption of causation, but also a presumption of injury as well. (*Id*. at 15.)

As a starting point, I agree with the reasoning in *Nuttall v. Secretary of Health & Human Services*, No. 07-0810V, 2015 WL 691272, at *15 (Fed. Cl. Spec. Mstr. Jan. 20, 2015), *motion for review denied*, 122 Fed. Cl. 821 (2015), *aff'd per curiam*, 640 Fed. App'x 996 (Fed. Cir. 2016). (*See also* ECF No. 109, p. 2.) Like in this case, the *Nuttall* petitioner argued that the special master should apply the "ordinary" meaning of encephalitis, which she urged to simply be "inflammation of the brain." 2015 WL 691272, at *10. The special master accepted this understanding as a matter of statutory interpretation, but explained that, if the alleged injury is to also capture the sequela of the encephalitis, then petitioners must make additional showings that support the inflammation as the source of the vaccinee's symptoms. *Id*. In this case, that means linking the alleged brain inflammation to V.S.R.'s death. Specifically, the conclusion reached by the *Nuttall* special master was that a petitioner alleging encephalitis prior to the March 2017 table amendment was obligated to prove four points: (1) that the vaccinee did in fact experience brain inflammation; (2) that the impact of the alleged inflammation was severe enough to result in the injuries experienced; (3) that the location of the inflammation could have caused the symptoms experienced; and (4) that there is evidence to support the necessary timing of onset consistent with the Vaccine Injury Table. *Id. But see Abbott v. Sec'y of Health & Human Servs.*, No. 14-907V, 2018 WL 11227323, at *4-5 (Fed. Cl. Spec. Mstr. July 9, 2018) (finding that "'inflammation of the brain' is an adequate definition for 'encephalitis'" in light of, *inter alia*, the special master's analysis in *Nuttall*).

Further to this basic analytic starting point, the record of this particular case includes a 2013 consensus statement of the International Encephalitis Consortium ("IEC") on the definition of encephalitis. (Ex. H, p. 2 (citing Venkatesan et al., *supra*, at Ex. H-2).) The IEC defines encephalitis as "inflammation of the brain parenchyma

associated with neurologic dysfunction." (Venkatesan, *supra*, at Ex. H-2, p. 2.) This definition differs from the definition proposed by petitioner in that it specifically requires associated neurologic dysfunction. By requiring that brain inflammation be associated with resulting neurologic dysfunction, the IEC definition effectively agrees with the standard articulated by the *Nuttall* special master in that it treats *both* the inflammation *and* resulting neurologic dysfunction as constituent parts of an encephalitis. I find that the IEC definition is persuasive as an ordinary or common meaning of encephalitis and, further, that it supports application of the four-part *Nuttall* test on this record.

Petitioners argue that they should not be required to prove neurologic dysfunction. (ECF No. 120, p. 7.) However, use of the IEC definition appropriately squares the concerns raised by both parties, as well as the requirements of the Vaccine Act. Requiring that the inflammation at issue be associated with neurologic dysfunction addresses respondent's concern that the term encephalitis have some clinical significance. In fact, respondent agrees with its use in this case. (ECF No. 122, p. 24.) And, despite including a requirement of neurologic dysfunction, this definition does not meaningfully go beyond the ordinary meaning of encephalitis articulated by petitioners.[15] While petitioners observe that the dictionary definition of encephalitis is limited to discussing inflammation and does not specify neurologic dysfunction (ECF No. 99, p. 4; ECF No. 107, pp. 3-4), that does not mean a showing of neurologic dysfunction is inconsistent or incompatible with that definition. Under the statute, petitioners are required to plead (and ultimately prove) the vaccinee sustained an "illness, disability, injury, or condition" set forth in the Table and that the first "symptom or manifestation" occurred within the Table period. § 300aa-11(c). The associated neurologic dysfunction is the *sine qua non* of understanding an encephalitis, not merely as an abstract concept, but as an "illness, disability, injury or condition," leading to V.S.R.'s death.

In any event, the "severity requirement" of the Vaccine Act, as applicable in this case, also requires petitioners to show that V.S.R. "died from the administration of the vaccine." § 300aa-11(c)(1)(D)(ii). In *Wright v. Secretary of Health & Human Services*, the Federal Circuit explained that, with respect to the "residual effects" portion of this provision of the Act, traditional tort principles of causation apply, meaning the vaccine must be both a but-for cause and a substantial contributing factor of the alleged complications or residual effects. 22 F.4th 999, 1004-05 (Fed. Cir. 2022). Therefore, regardless of how "encephalitis" itself is defined for purposes of determining whether petitioners have established a Table injury, petitioners still have a burden of proving that V.S.R.'s alleged encephalitis contributed to her death in order to separately meet the statutory severity requirement. Ultimately, the same analysis – causally linking the alleged brain inflammation to V.S.R.'s death – is necessary regardless of whether it is

[15] The IEC definition does also arguably further refine the definition proffered by petitioners by specifically requiring inflammation of the parenchyma, which is the actual functional tissue of the brain. Dr. Shuman provided some testimony suggesting inflammation of the meninges could also be a relevant consideration, indicating that, in effect, both meningitis and encephalitis are often viewed by neuropathologists holistically as meningoencephalitis. (Tr. 267-68.) However, nothing in the analysis below turns on this distinction, and it is therefore not necessary to resolve that question.

included within the definition of encephalitis itself as evidence of associated neurologic dysfunction or addressed separately as a question of severity.

Nonetheless, the IEC definition itself does not fully resolve the parties' disagreements. There are still two disputes regarding the particular language employed by the IEC definition. First, the parties' briefs discuss two different understandings of what "inflammation" means in the context of encephalitis. Second, the parties disagree as to whether a showing of "neurologic dysfunction" requires at least a 24-hour period of altered mental status. These two issues are each addressed in turn below.

a. The meaning of inflammation

There are a number of pathologic findings – specifically, activated microglia (also referred to as microgliosis), reactive astrocytes (also referred to as astrocytosis or astrogliosis), neurophagocytosis, lymphocytic perivascular cuffing, and infiltrating lymphocytes – that both parties agree are elements or indicators of inflammation and that the experts discussed extensively. (ECF No. 120, pp. 8-14; ECF No. 122, p. 14.) However, they disagree on what elements are absolutely required to constitute the inflammation implicated by the term encephalitis. According to petitioners, demonstration of inflammation requires *either* activated resident immune cells from within the brain (*i.e*. activated microglia) *or* immune cells from general circulation infiltrating the brain (*i.e*. lymphocytic perivascular cuffing and/or infiltrating lymphocytes). (ECF No. 120, p. 8.) Respondent argues, however, that the expert testimony establishes that *both* are required. (ECF No. 122, p. 23.)

On petitioners' behalf, Dr. Shuman explained that "[i]nflammation is the infiltration of immune -- immunological directed cells, both from resident populations which migrate into the area and multiply in the area and from outside the locus from . . . being attracted to the tissue." (Tr. 135.) As he explained it, resident microglia within the brain are "a necessary part of inflammation. They're the first responders of inflammation." (*Id.* at 126.) Only later do nonresident immune cells such as lymphocytes, which are also components of inflammation, enter the brain. (*Id.*) Although Dr. Shuman separately testified that perivascular cuffing "is the definition of brain inflammation" (*Id.* at 145), this was a matter of emphasizing perivascular cuffing as highly conclusive, rather than definitionally essential, evidence of inflammation. According to Dr. Shuman, the microglia are the "very, very, very active, very first, most incredibly important component of inflammation." (*Id.* at 126.) Thus, Dr. Shuman explained, for example, that *either* perivascular cuffing *or* microglial activation would remove a child from the category of Sudden Infant Death Syndrome ("SIDS") and into the category of encephalitis. (*Id.* at 514.)

Dr. Harris, on the other hand, indicated that "the purists would recognize that cells coming in from the external blood really constitute the -itis, whereas neuroinflammation, I think, is a . . . broader term that encompasses both the immune cells coming in from the blood and the reactive cells within the brain itself. That's the way that I think most neuropathologists look at this." (Tr. 344-45.) That is, for a purist,

only infiltrating cells, and not the microglia otherwise relied upon by petitioners, constitute evidence of encephalitis. While Dr. Harris does not take the purist view, he expresses a conjunctive, rather than disjunctive, view of the two aspects of inflammation being discussed. Explaining his own clinical judgment, he testified that "[f]or me, I would want to see infiltrating lymphocytes . . . before I would call it an encephalitis." (*Id.* at 344.) However, notwithstanding this personal clinical judgment, Dr. Harris also specifically agreed that activated microglia and astrocytes alone can be viewed as sufficient to evidence neuroinflammation. (*Id.* at 342 (agreeing that "one definition of inflammation" is "the innate cells of that tissue reacting to some abnormal problem").)

Based on the experts' discussion, findings such as activated microglia, reactive astrocytes, neurophagocytosis, lymphocytic perivascular cuffing, and infiltrating lymphocytes, are *all* informative of whether inflammation of the parenchyma is present. Each finding constitutes *some* evidence of inflammation in itself. Moreover, Dr. Harris specifically agreed that, even if it is not preferred, neuroinflammation can be identified by resident immune cells without infiltrating immune cells. Thus, based on the above, I am not persuaded that any of these specific findings is dispositive of the meaning of "inflammation" as applied to encephalitis or singularly dispositive of whether such inflammation was present in this case.

b. Neurologic dysfunction and altered mental status

To the extent petitioners acknowledge the IEC definition of encephalitis requires neurologic dysfunction, they argue that the seizures and death that they alleged to be sequela of V.S.R.'s condition substantiate this requirement. (ECF No. 124, pp. 8-9.) They argue that to further read into this requirement the specific need to demonstrate a preceding altered or reduced consciousness would, in effect, place a burden on petitioners to satisfy the QAI requirements for encephalopathy, which are not applicable in this case. (*Id*.) Respondent disagrees. (ECF No. 122, pp. 24-27.) He contends that encephalitis is not identified by histopathology alone, but that clinical correlation is required. (*Id*.) In particular, respondent stresses that his neurology expert, Dr. Wirrell, opined that encephalitis necessarily includes an encephalopathic state, which itself would involve altered consciousness or focal neurologic deficits. (*Id*. at 27 (quoting Tr. 448).)

The IEC's consensus statement does indicate that a greater than 24-hour history of altered mental status is a "major" and "required" diagnostic criterion for encephalitis. (Venkatesan et al., *supra*, at Ex. H-2, p. 3 tbl.1.) Importantly, however, this ruling accepts the *definition* of encephalitis articulated by the IEC for purposes of understanding the ordinary meaning of the term, rather than applying its specific *diagnostic criteria* intended for clinical use. After all, "the function of a special master is not to 'diagnose' vaccine-related injuries, but instead to determine 'based on the record as a whole and the totality of the case, whether it has been shown by a preponderance of the evidence that a vaccine caused the child's injury.'" *Andreu ex rel. Andreu v. Sec'y of Health & Human Servs*., 569 F.3d 1367, 1382 (Fed. Cir. 2009) (quoting *Knudsen ex rel. Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 549 (Fed.

Cir. 1994)). Table injuries in particular are not necessarily coextensive with the full range of diagnostic considerations applied by clinicians. *Nuttall*, 2015 WL 691272, at *10 (explaining that QAI definitions of Table injuries are specialized definitions for Program purposes, rather than commonly used definitions, albeit typically being narrower); *Durham v. Sec'y of Health & Human Servs.*, No. 17-1899V, 2023 WL 3196229, at *13 (same).

While the IEC characterizes the mental status requirement as a "caveat" regarding the definition itself, the publication also makes clear that neurologic dysfunction encompasses much more than altered mental status. Thus, for example, Dr. Wirrell agrees that seizures, which are alleged by petitioners, are a form of neurologic dysfunction associated with encephalitis. (Tr. 464.) Explaining the reasoning behind the altered mental status requirement, the consensus statement indicates that "some infections or conditions related to infections may cause central nervous system (CNS) dysfunction without affecting consciousness (eg, post-varicella cerebellar ataxia), and our case definition would not capture these entities." (Venkatesan et al., *supra*, at Ex. H-2, p. 2 (citation omitted).) Importantly, however, this explanation points to the fact that the proffered definition is intended to be complementary to a separately included diagnostic testing algorithm (*Id.*), the intended purpose of which is to aid clinicians in the initial evaluation and management of suspected encephalitis patients (*Id.* at 3). In that context, clinical symptoms of ongoing associated neurologic dysfunction, such as altered mental status, combine with various diagnostic tests that act as surrogate markers of inflammation, in order to determine *inferentially* whether encephalitis is present. (*Id.* at 2; *see also* Messacar et al., *supra*, at Ex. H-1, p. 2 (explaining that "[b]rain parenchymal inflammation associated with neurologic dysfunction is the strict definition of confirmed encephalitis. However, due to the rarity of pre-mortem brain biopsy specimens available for histopathologic confirmation (particularly in children), clinical correlates are used to infer evidence of probable brain inflammation." (footnote omitted)).) But that is not the context of this case.

Following a fatal encephalitis, there is no further ongoing clinical history, confirmatory postmortem pathology becomes available, and, logically, the death itself is associated neurologic dysfunction. *Accord Jay v. Sec'y of Health & Human Servs.*, 998 F.2d 979, 983 & n.6 (Fed. Cir. 1993) (finding error where the special master failed to consider death as evidence of an encephalopathy and noting that "there is no more profound and permanent change in level of consciousness than death"). Thus, separate from its diagnostic criteria, the IEC consensus statement otherwise explains that "pathologic examination and testing of brain tissue is considered to be the 'gold standard' diagnostic test" for encephalitis." (Venkatesan et al., *supra*, at Ex. H-2, p. 2.) It is generally in the absence of such testing – which typically is not done premortem – that clinical, laboratory, electroencephalographic, or neuroimaging are used to identify encephalitis. (*Id.*) This makes sense for two reasons. First, the presence of demonstrable inflammation is the key difference between encephalitis specifically and the broader category of encephalopathy. (*Id.*) The type of histopathologic evidence discussed herein represents the detection of fixed, physical evidence of inflammation.

In a given case, this type of evidence would not cease to exist, or would not lose all meaning, if, for example, the period prior to death was to be entirely unobserved. Second, several of the available diagnostic criteria that could otherwise help substantiate a diagnosis, such as neuroimaging or EEG, are not available, or not routinely investigated, in a postmortem context. (*Id.* at 3 tbl.1.)

While Dr. Harris suggested it is "dangerous" to offer a histopathologic diagnosis without a clinical history (Tr. 319), Dr. Shuman explained that pathologists often do not have access to clinical history (*Id.* at 127). He explained that, while pathology does not *per se* diagnose neurologic dysfunction, it is possible to infer what neurologic dysfunction would have been present based on histopathologic findings. (*Id.* at 241-42.) Even if pathologists often incorporate clinical data into their conclusions, the histopathological assessment also stands on its own. (*Id.* at 240-41.) Dr. Shuman testified that, with regard to the type of histopathology available in this case, "[t]his sort of change tells you specifically and honestly and completely that it's inflammation. It doesn't tell you what caused the inflammation, but it tells you that it's inflammation. It tells you that it's encephalitis." (*Id.* at 127.) Petitioners' neurology expert, Dr. Kinsbourne, likewise opined on petitioners' behalf that postmortem findings are the most persuasive type of evidence of encephalitis. (*Id.* at 390.) He explained that postmortem findings of inflammation are sufficient to justify a diagnosis of encephalitis and that clinical correlation is not absolutely necessary. (*Id.*) Notwithstanding her clinical judgment regarding the nature of the neurologic dysfunction expected in an individual suffering encephalitis, Dr. Wirrell likewise agreed that, in principle, it is true that encephalitis can be identified based on pathology alone in at least some (florid) cases. (*Id.* at 427.)

I agree with petitioners that, under the version of the Vaccine Injury Table applicable in this particular case, any strict requirement that petitioners specifically demonstrate 24-hours of altered or reduced consciousness would in effect require them to demonstrate a Table Injury of encephalopathy, which is not the injury that they have alleged. Instead, as also articulated in *Nuttall*, 2015 WL 691272, petitioners' obligation is to prove that the brain inflammation that they allege constitutes an encephalitis correlates to the neurologic dysfunction they allege to be the consequence of that encephalitis. Thus, for example, in *Nuttall*, the special master accepted a decrease in language and an episode of separation anxiety as evidence that would establish the onset of the alleged limbic encephalitis. 2015 WL 691272, at *5, 8. The *Abbott* special master went further, rejecting respondent's argument that the petitioner was obligated under the Table to prove the first symptom of the specific form of encephalitis at issue (Rasumussen's encephalitis) occurred within the Table period. Instead, he concluded petitioner was obligated merely to prove that some symptom of brain inflammation, as he had defined encephalitis, had occurred within the period.[16] 2018 WL 11227323, at

[16] To be sure, there are decisions prior to 2017, in which encephalopathy and encephalitis are either not distinguished or are treated as going hand-in-hand based on the clinical presentation at issue. Several prior decisions by special masters express that encephalitis is best interpreted as a form of encephalopathy. *Wilson v. Sec'y of Health & Human Servs.*, No. 02-1797V, 2005 WL 6117474, at *3-4 (Fed. Cl. Spec. Mstr. June 27, 2005); *Veasey v. Sec'y of Health & Human Servs.*, No. 90-776V, 1991 WL 81905, at *4-5 (Fed. Cl. Spec. Mstr. May 2, 1991); *Roedl ex rel. Roedl v. Sec'y of Health & Human Servs.*,

*6. While the presence of altered mental status would be crucial to diagnosing a patient suspected of having ongoing encephalitis, and could be strong evidence of encephalitis in any case, specific demonstration of altered mental status is not a requirement for the identification of encephalitis when assessing encephalitis in hindsight based on postmortem pathology. It therefore is not a *definitional* component of encephalitis to be strictly required to establish the fact of any encephalitis, even if it otherwise remains relevant to assessing the overall clinical picture as it relates most notably to the timing of onset.

VI. Analysis

a. V.S.R. suffered encephalitis

i. Evidence of inflammation of the parenchyma (also *Nuttall* prong one)

The first step in determining whether V.S.R. suffered encephalitis consistent with the above-discussed definition is whether she had inflammation of the brain parenchyma. Considering all of the points discussed below, I conclude that there is preponderant evidence that V.S.R. suffered inflammation of the brain parenchyma consistent with encephalitis.[17]

No. 90-1995V, 1993 WL 89221, at *4 n.9 (Fed. Cl. Spec. Mstr. Mar. 12, 1993), *aff'd*, 28 Fed. Cl. 740 (1993); *Waleryszak v. Sec'y of Health & Human Servs*., No. 95-356V, 1999 WL 199054, at *12 (Fed. Cl. Spec. Mstr. Mar. 9, 1999), *motion for review denied*, 45 Fed. CL. 57. (1999), *appeal dismissed*, 250 F.3d 753 (Fed. Cir. 2000). However, these decisions largely express that encephalopathy is simply a broader or "all encompassing" term that refers to basically any injury to the brain. *E.g.*, *Roedl*, 1993 WL 89221, at *4 n.9. In fact, this has sometimes been referenced as a point of confusion. *Veasey*, 1991 WL 81905, at *4-5. One prior decision specifically concluded that, despite not having its own definition, for program purposes the term encephalitis is "subsumed" by the term encephalopathy, suggesting petitioners do need to meet the Table elements of encephalopathy, even in the context of encephalitis. *Downing v. Sec'y of Health & Human Servs*., No. 90-1134V, 1993 WL 120641, at *14 (Fed. Cl. Spec. Mstr. Apr. 2, 1993). However, another later decision, while not reaching the specific question of encephalitis because it was not alleged, maintained the distinction between the two types of Table injury. *Miller v. Sec'y of Health & Human Servs*., No. 06-753V, 2012 WL 12507077, at *6 n.6 (Fed Cl. Spec. Mstr. Sept. 25, 2012). *The Downing* special master's specific suggestion that the Table injury of encephalitis is subsumed by the Table injury of encephalopathy is less persuasive given the subsequent *Miller*, *Nuttall*, and *Abbott* decisions. Moreover, respondent has not advanced such an argument in this case. The *Miller* special master also explained that not all viable clinical evidence of encephalopathy constitutes evidence of a Table encephalopathy. *Id*. at *5-6. Even if applying the diagnostic criteria from the IEC, the Table requirements for an acute encephalopathy are more stringent than the description of altered mental status described by the IEC diagnostic criteria. (*See* Venkatesan, *supra*, at Ex. H-2, p. 3, tbl. 1.) And, significantly, none of these prior cases involved an injury first brought to medical or scientific attention postmortem, which is an important distinction under the IEC discussion for the reasons discussed above.

[17] In his post-hearing brief, respondent quotes a portion of the transcript where I asked Dr. Harris, "How do I – how do I view [the histopathology]? I mean, on some level, the two of you are clearly looking at the same thing and coming to slightly different conclusions." (ECF No. 122, p. 22 (quoting Tr. 375).) Dr. Harris responded in part that the differences of opinion "can be borne out with literature." (*Id.* (quoting Tr. 376).) Respondent then notes that I denied respondent an opportunity to file (out of time) histopathology images from a textbook. (*Id.* at 22-23.) Respondent appears to imply that my question during the hearing reveals that I should have allowed respondent's proposed filing into the record after all. However,

1. Resident immune cells

As explained above, Dr. Shuman testified that activated microglia, immune cells resident in the brain, are an early and very important aspect of inflammation. (Tr. 125-26.) Upon his review of the pathology, he observed these cells to be "most affected" and explained that he found them in all of the sections of the brain available for examination. (*Id.* at 124-25.) Dr. Shuman discussed activated microglia repeatedly throughout his discussion of the pathology slides presented during the hearing. In his testimony, Dr. Harris agreed that V.S.R.'s brain histopathology evidenced activated microglia diffusely in multiple areas and that activated microglia are a component of brain inflammation. (*Id.* at 337, 339-42.) In fact, Dr. Harris agreed activated microglia were available in all four of the tissue samples available in this case. (*Id.* at 339.)

Dr. Harris testified that to his eye, the microglial activation was not severe or widespread. (Tr. 337.) However, Dr. Shuman stressed several features that he explained confirm that the microglia were not merely present, but active and proliferating. (*Id.* at 124-25.) Specifically, he discussed evidence of reactive astrocytes, glial shrubs (or nodules), and neuron phagocytosis, as evidence further supporting the significance of the microglial findings. (*Id.*) He explained that these findings are all indicative of neuronal damage. (*Id.* at 125, 134, 287.) Dr. Harris did not interpret the pathology as including either microglial nodules or neurophagocytosis, but did agree that reactive astrocytes were present. (*Id.* at 334, 337, 376.) Dr. Shuman explained that reactive astrocytes are not inflammation in themselves, but are a tissue response to inflammation. (*Id.* at 158.) Reactive astrocytes are an abnormal finding that indicates damage to the neurons. (*Id.* at 306.) Dr. Harris felt the finding of reactive astrocytes was "mild" and therefore characterized it as "not well established;" however, he acknowledged it to be an abnormal finding. (*Id.* at 306, 337.)

Because he interpreted the microgliosis and astrocytosis as mild and diffuse, Dr. Harris opined that these findings are consistent with the pattern of seizures discussed separately below. (Tr. 370-71, 378-81.) Dr. Shuman, however, disagreed. His disagreement is based largely on his differing interpretation of the extent of these findings. (*Id.* at 511-13, 515, 518.) Effectively, Dr. Shuman opines that, even if V.S.R.'s seizures explained some of the activated microglia and reactive astrocytes, they do not explain the full extent of these findings. When considering the record as a whole,

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respondent's quotation misses the point raised during the hearing. What respondent quotes was a portion of further explanatory commentary after Dr. Harris was unclear as to my initial question. The question posed during the hearing was: "[I]s it fair to say that there's at least some degree of a subjective component to this?" (Tr. 375.) While Dr. Harris did raise reference to literature as part of his response, the response was broader than that. And, in any event, the inquiry did not imply that Dr. Harris was being challenged to cross reference his case-specific opinion against literature. Rather, Dr. Harris was being asked to comment on the nature of the interpretive process itself. To the extent there is an element of subjective interpretation, respondent stresses his view that Dr. Harris's qualifications are superior to Dr. Shuman's with specific respect to interpreting brain pathology at autopsy given that he remains in active practice. (ECF No. 122, p. 23.) However, this fact alone does not explain differences in interpretive judgment and Dr. Shuman was proffered without objection as having the requisite training and experience as a neuropathologist necessary to interpret the pathology available in this case. (Tr. 121.)

including the other findings discussed below, Dr. Shuman is persuasive on this point. Dr. Shuman's emphasis during the hearing that "four out of four is 100 percent" is persuasive as an expression that these findings are reasonably interpreted as likely to represent widespread inflammation notwithstanding the limitations of the available tissue samples. (Tr. 202, 302.)

Thus, there is preponderant evidence that V.S.R.'s postmortem pathology showed activated resident immune cells within all of the brain samples available for examination and with associated neuronal damage. This is evidence of neuroinflammation. (Tr. 126, 342, 514.)

2. Infiltrating immune cells

As discussed above, the other aspect of inflammation is infiltration of immune round cells, such as lymphocytes, which infiltrate the brain parenchyma from across the blood brain barrier. (Tr. 125.) While the experts are clear in explaining that the presence of resident immune cells is itself neuroinflammation, they are also clear in expressing that the presence of infiltrating immune cells is the clearest and strongest evidence of inflammation – this is the finding that the "purist" seeks, according to Dr. Harris. In that regard, Dr. Shuman explains that perivascular cuffing is evidence of circulating immune cells infiltrating the brain. (*Id.* at 139-41, 274.) Dr. Shuman described it as "the definition of brain inflammation." (*Id.* at 145.) He indicated that any degree of perivascular cuffing is an abnormal finding. (*Id.* at 147, 303-04.) "There's nothing modest about perivascular cuffing." (*Id.* at 293.)

Dr. Shuman testified that he identified multiple foci of perivascular cuffing located in different areas of the brain. (Tr. 145-46.) During the hearing, he specifically discussed two: one located around an artery in the cerebellum (*Id.* at 138-39 (discussing Ex. 38, p. 5 (Image 4)) and another located in the hippocampus (*Id.* at 146). Additionally, Dr. Davenport's autopsy report also indicates the presence of a perivascular cuff, though the report is not detailed enough to determine whether it corresponds to any of the cuffs discussed by Dr. Shuman. (Ex. 7, p. 13; Tr. 146-47, 298-99.) Though Dr. Harris disagrees that Dr. Shuman located a perivascular cuff in the cerebellum, he did himself locate a single focus of lymphocytic perivascular cuffing in the hippocampus. (Tr. 333-34, 526.) Dr. Harris explained that "technically those lymphocytes should not be there and from that technical standpoint, a cuff of lymphocytes would constitute the definition of encephalitis." (*Id.* at 344.)

However, Dr. Harris indicated that the finding of perivascular cuffing is not exclusive to encephalitis. (Tr. 333-34.) Thus, in this case, he is not willing to conclude the perivascular cuffing (a single instance of such cuffing by his own interpretation) is significant without evidence of lymphocytes further infiltrating the parenchyma. (*Id.* at 344.) In the autopsy report, Dr. Davenport appears likely to have drawn the same distinction. (Ex. 7, p. 13 (stating "[t]here is a single focus of lymphocytic perivascular cuffing, but there is no significant evidence of associated parenchymal infiltration").) Dr. Shuman, however, indicated that the alternative causes of lymphocytic cuffing are few

and limited. He opined that, as a general rule, lymphocytic cuffing is specific to inflammation, especially where there are multiple foci of cuffing as he identified. (Tr. 268, 519.) Dr. Harris did not identify any other condition that would explain the cuffing in V.S.R.'s case, which he agreed is an abnormal finding, but noted only that he has observed isolated instances of cuffing during autopsies in which brain injury is not implicated. (*Id.* at 366, 525.)

Given the above, it is undisputed that V.S.R.'s postmortem pathology showed at least some evidence of infiltrating lymphocytes in the form of perivascular cuffing. Because Dr. Harris concludes there is only a single perivascular cuff, he does not accept this finding as significant, despite acknowledging it to be an abnormal finding. However, Dr. Harris's clinical judgment on this question effectively represents a floor when considering the record as a whole. Dr. Shuman opines in his own clinical judgment that there is further evidence of lymphocytic infiltration and identifies additional cuffs. Dr. Davenport also confirmed at least one cuff was present that may or may not be the same cuff Dr. Harris identified. Moreover, Dr. Harris himself stressed that the brain material available for review was limited. (Tr. 339 (stating, with regard to a different finding, that "in all of the areas of the brain that were sampled – *and it was not nearly enough* – but in the four areas that were sampled, there were activated microglia in each of those areas" (emphasis added)).)

3. Ultimate expert conclusion

According to Dr. Shuman, the above-discussed pathology findings constitute neuroinflammation indicative of encephalitis. (Tr. 123-27.) He explained that Dr. Davenport's autopsy report does include findings consistent with encephalitis, even as she failed to appreciate the above-discussed microglia involvement and stopped short of assessing an encephalitis. (*Id.* at 298-300.) Asked whether the pathology in this case is encephalitis, Dr. Harris acknowledged the presence of activated innate immune cells (microglia and astrocytes), which he separately agreed constitute neuroinflammation, but indicated that such findings can be "very different" from encephalitis. (*Id.* at 343.) He then explained that "[f]or me to call something an encephalitis, one, I would like to know what the etiology is, and I would like to see circulating immune cells in the brain parenchyma," *i.e.*, infiltrating immune cells beyond the undisputed perivascular cuffing. (*Id.* at 343-44.) He then further indicated more specifically that he would want to see viropathic changes. (*Id*. at 344.)

Dr. Harris appears to be focused on viropathic changes because he largely discussed the case through the lens of whether a viral encephalitis was present. (Tr. 334, 344, 370, 530.) And, to be clear, Dr. Shuman himself hypothesized viral entry into the brain as a mechanism of vaccine-caused encephalitis. (*Id.* at 193.) However, respondent's own filings confirm that viral invasion of the central nervous system is only one of several different pathogeneses for encephalitis. (Messacar et al., *supra*, at Ex. H-1, p. 3.) In addition to primary infectious encephalitis, other forms of immune mediated encephalitis exist whereby vaccinations or pathogens from without the central nervous system nonetheless cause inflammation within the central nervous system.

(*Id*.) But in any event, Dr. Harris's testimony that he would want to know the etiology of the undisputed brain inflammation before he would conclude it was encephalitis effectively creates a "chicken and the egg" conundrum that is in tension with the causal presumption petitioners are entitled to under this statutory scheme. That is, in order for Dr. Harris to willingly conclude the observed neuroinflammation constitutes what would be a Table encephalitis, he must first know the etiology, but relieving petitioners of the need to prove the precise cause or etiology of the encephalitis is the entire purpose of designating it as a Table Injury in the first place.

Because Dr. Harris withholds any judgment that the pathology at issue is consistent with encephalitis pending some knowledge of the underlying etiology, accepting his testimony on that point would impermissibly elevate petitioners' burden of proof. Therefore, I give greater weight to Dr. Shuman's ultimate conclusion that the specific histopathologic evidence of neuroinflammation at issue in this case constitutes evidence of encephalitis in particular. But in any event, even giving strictly equal weight to the testimony of the two expert pathologists, there is still *undisputed* evidence of neuroinflammation, consistent with the above-discussed IEC definition of encephalitis, notwithstanding Dr. Harris's declining to specifically label it as encephalitis.

ii. Neurologic dysfunction and death (also *Nuttall* prongs two and three)

The second step in determining whether V.S.R. suffered encephalitis consistent with the above-discussed definition is whether the demonstrated neuroinflammation can be associated with neurologic dysfunction. Regarding this aspect of the analysis, petitioners point to both seizures and death that they allege would constitute neurologic dysfunction caused by the neuroinflammation evidenced by V.S.R.'s pathology. That is, petitioners assert that V.S.R. suffered edema and brain herniation. According to their experts, these findings are due to the inflammation and alone can be lethal. Additionally, petitioners assert that there is sufficient evidence to reasonably conclude that an unwitnessed seizure attributable to the alleged encephalitis further contributed to V.S.R.'s terminal event.

Considering all of the points discussed below, I conclude that V.S.R.'s death is more likely than not explained by a combination of inflammation and swelling, though without preponderant evidence specifically confirming herniation. Further, a terminal seizure event acting in concert with the inflammation and edema, though obviously unwitnessed, is also more probable than not. However, the question of whether there was a fatal seizure is not dispositive given the presence of the inflammation and edema. Accordingly, there is preponderant evidence of neurologic dysfunction associated with the neuroinflammation evidenced in this case.

1. Edema and herniation

Upon autopsy, Dr. Davenport observed a "slightly" flattened gyral pattern that suggested possible cerebral swelling. (Ex. 7, p. 7.) She also observed edematous

changes in the brain parenchyma without specifying the severity. (*Id.* at 12; Tr. 332-33.) Additionally, both parties' experts agree that they likewise observed edema upon microscopic examination indicative of at least some degree of brain swelling. (Tr. 123 (Dr. Shuman), 335 (Dr. Harris).) Further to that, Dr. Shuman presented microscopic images during the hearing that he explained show the resulting compression. (*Id.* at 127-30 (discussing Ex. 38, p. 4 (Image 3).) Dr. Shuman associates this swelling/edema to the neuroinflammation he identified. (*Id.* at 166-68.) Moreover, Dr. Shuman and Dr. Kinsbourne both explain that, if severe enough, inflammation and edema can interfere with neurologic function and be fatal. (*Id.* at 166-68, 395, 407-08.)

However, whereas Dr. Shuman opined there is compressive and lethal edema affecting the entire brain (Tr. 129-31), Dr. Harris indicated that he observed only mild to moderate edema under the microscope (*Id.* at 335-36; Ex. A, p. 4). Moreover, the flattened gyral pattern observed by Dr. Davenport was in the forebrain, a location that is not in itself an area where herniation occurs. (Tr. 325.) And, some degree of edema is consistent with SUDC, which would not implicate an encephalitis. (Ex. 16, pp. 2-3.) Ultimately, the parties' disagreement regarding the severity and significance of the cerebral edema encompasses two separate underlying issues – (1) competing assessments of the gross pathology particularly with respect to brain weight and head circumference, and (2) specific evidence of brain herniation. If Dr. Shuman is credited, the former speaks to severe intracranial pressure caused by inflammation and edema, which inferentially support fatal brain dysfunction (with or without seizure activity) as indicated by Dr. Kinsbourne. The latter would constitute definitive evidence of death from the swelling.

Dr. Davenport recorded that she had not observed evidence of herniation on gross examination. (Ex. 7, p. 7.) However, as noted above, she did note possible cerebral swelling. (*Id*.) Dr. Davenport's gross examination of the brain upon autopsy indicated that V.S.R. had a heavy brain weight of 1040 grams (as compared to 944 grams as a reference). (*Id.*) Head circumference was 47.4 cm. (*Id*. at 3.) This head circumference was noted to be normocephalic but was observed to be within the 95th percentile for age and sex, whereas V.S.R.'s overall body length was noted to be in the 25th percentile for age and sex and her weight was noted to be in the 5-10th percentile for age and sex. (*Id*. at 11.) According to Dr. Shuman, these measurements, especially when combined with the other evidence of compression, indicate intracranial pressure due to edema. (Ex. 39, p. 9; Tr. 123-24.) Dr. Harris disagrees, concluding these are not abnormal or pathologic findings. Both parties' experts agree the brain weight was technically heavy for her age (Ex. 38, p. 13; Ex. G, p. 2), but Dr. Harris stresses that the brain weight is only about 10% above normal weight, which he opines is not statistically significant (Ex. G, p. 1; Ex. A, pp. 5-6). Some increase in brain weight may be consistent with SUDC, but not necessarily. (Ex. 16, pp. 2-3; Ex. A, p. 5.) Dr. Harris further opines that at least some of the excess weight is explained by her head circumference being at the 95th percentile. (Ex. A, p. 4; Tr. 327.) Critically, however, V.S.R.'s recorded head circumference in the 95th percentile, though not beyond normal range, was abnormal *for her*.

In contrast to her autopsy, which showed a head circumference in the 95th percentile, Dr. Shuman stresses that V.S.R.'s prior medical records from nine months of age up to just weeks prior to her death show a head circumference growing from 44cm in August of 2014 to 46.1 cm in February of 2015. (Ex. 38, p. 12 (citing Ex. 5, pp. 35-39, 44-49, 70-77).) Throughout her life, V.S.R.'s head was consistently measured at a higher percentile compared to the rest of her body measurements. However, these measurements were nowhere near the 95th percentile. At her final medical encounter on February 20, 2015, V.S.R.'s head circumference was noted to be at the 71st percentile. (Ex. 5, p. 72.) Dr. Shuman explains that, at age 12-15 months, head circumference should be expected to grow at about one centimeter per 12 weeks. (Ex. 38, p. 12.) However, comparing the autopsy finding to the prior medical records, V.S.R.'s head circumference increased 1.3 centimeters over the course of just the 19 days between her February 20 medical encounter and her March 11 death. Thus, V.S.R.'s head circumference at autopsy cannot be explained by normal growth. Instead, Dr. Shuman opines that, coupled with the other evidence of compressive edema, V.S.R.'s increased head size is evidence of substantial intracranial pressure. (*Id.*; Tr. 244.) At 14 months of age, Dr. Shuman opines that the skull is still somewhat elastic such that this is a reasonable conclusion. (Ex. 38, p. 12.)

During the hearing, Dr. Harris acknowledged that V.S.R.'s head circumference at autopsy, though within normal range, was "very large" and that this is not consistent with her prior medical records. (Tr. 321.) In response to my question, Dr. Harris observed that the contrast between V.S.R.'s head circumference (95th percentile) and her body weight (5th to 10th percentile) "caught my eye" and "caused me some question in thinking about this." (*Id.* at 321-22.) However, although Dr. Harris agreed that acute swelling would cause the brain to push against the bone, explaining the flattened gyri, he opined that at one year of age the skull is "really pretty much fused" such that intracranial pressure would not cause the skull to expand. (*Id.* at 327.) Thus, he concluded that this finding was likely due to differences in measuring technique. Notably, however, he himself characterized this as a "guess" and he was unable to explain what differences in measuring methodology he was invoking. (*Id.* at 322-23.) Without more, Dr. Harris's testimony as to this finding is speculative.[18] In his prior report, notwithstanding his separate statement that the cranial sutures were likely to be fused, Dr. Harris *had previously agreed* that V.S.R.'s head circumference at autopsy was suggestive of head swelling, either acutely or subacutely. (Ex. G, p. 1.) Moreover, because Dr. Harris's observation regarding brain weight was informed by his

[18] On one level, common sense suggests that a difference in measurements taken by two different people at two different times could easily be due to simple error or other difference in measurement, especially when it involves a discrepancy of a centimeter or so. Accordingly, Dr. Harris's speculation is not by any means unrealistic. However, it is also apparent that the difference at issue in this case would represent a very big discrepancy in terms of what is actually being measured – as the records reflect, from 71st percentile to the 95th percentile. (*Compare* Ex. 5, p. 72, *with* Ex. 7, p. 10.) It cannot merely be assumed that the medical professionals taking these measurements were unconcerned with the relative tolerance of these measurements, *i.e.*, that fractions of centimeters may change the significance of the finding. If the measurements were not taken with enough care and consistency to be accurate to a fraction of a centimeter, there would literally be little to no point in taking them at all.

assessment of the head circumference, his inability to effectively explain V.S.R.'s head circumference on autopsy also undercuts his opinion that the excess brain weight was likewise not significant.

Further to this, Dr. Shuman observed that there is an "uncal groove" or "notch" in the temporal lobe. (Tr. 244.) Dr. Shuman testified that this is evidence of herniation that was missed by Dr. Davenport.[19] (*Id.* at 168, 242, 244.) In contrast, Dr. Harris stressed that Dr. Davenport noted that there was no evidence of herniation upon gross examination. (*Id.* at 324-25 (discussing Ex. 7, p. 7).) He suggested that there were sufficient indicators of swelling that Dr. Davenport likely would have been aware of the need to examine for herniation.[20] Dr. Harris agreed that the uncal groove Dr. Shuman described is one of the "classic" areas for identifying herniation. (*Id.* at 325-26.) However, he suggested that when notching is the only finding, without corresponding disruption of the tissue, then that is better interpreted as a postmortem artifactual change. (*Id.* at 326.) In any event, Dr. Harris did not see this notching on his own review of the slides. (Tr. 326-27.) Apart from this specific finding, the experts have otherwise presented a difference in clinical judgment with respect to whether the unfixed 14-month-old brain would retain signs of herniation once the skull is breached. (Ex. 38, p. 9; Ex. A, p. 6.) While Dr. Shuman opined the signs of herniation would not be preserved due to the infant brain being more gelatinous than the mature brain, Dr. Harris disagreed. (Ex. 38, p. 9; Ex. A, p. 6.) However, Dr. Harris did separately stress the need to fix postmortem brains before dissecting precisely because the fresh tissue "has a lot of give to it." Tr. 360-61.) Dr. Shuman indicated that an absence of evidence of herniation reduces the likelihood of fatal cerebral edema, but does not eliminate it. (Ex. 38, p. 10.)

Dr. Kinsbourne explained that, because the cranial cavity is a closed compartment, the evidence of flattened gyri in V.S.R.'s forebrain can be taken as some indication of intracranial pressure throughout the brain, including the brain stem. (Tr. 395; *see also id.* at 248 (Dr. Shuman opining the whole brain is affected by edema).) Dr. Harris agreed that Dr. Davenport's observation of flattened gyri upon gross examination was a finding of abnormal brain swelling. (*Id.* at 323-24.) He also agreed that it is evidence the brain was pushing against the skull. (*Id.* at 327.) However, Dr. Harris never explained how his interpretation of the edema under microscope as being only mild squares with Dr. Davenports gross identification of flattened gyri and cerebral swelling, which is a finding he effectively agrees indicates there was sufficient swelling to cause the skull to deform the brain. Moreover, he never directly addressed Dr. Shuman's identification of compression on his own microscopic examination. Nor, especially given my resolution of the head circumference issue, has Dr. Harris

[19] Both experts agreed that the real-world pressures on medical examiners mean that forensic autopsies are not always as complete or thorough as would be ideal. (Tr. 300-01 (Dr. Shuman); Tr. 318-19 (Dr. Harris).) Both experts had criticisms of the autopsy performed in this particular case.

[20] However, when specifically asked whether we can "be reasonably certain that V.S.R.'s brain did not herniate," Dr. Harris responded "[w]ell, I can't, because I did not observe . . . [V.S.R.] in the gross state . . . and I don't have a picture." (Tr. 324.)

substantiated that the degree of edema and swelling in this case is actually consistent with SUDC. In that regard, respondent's own experts have highlighted the theory that SUDC happens at least in part due to vulnerability related to structural malformation within the hippocampus. (Ex. A, p. 5.) However, the experts agree there is no evidence in this case that V.S.R. had such a malformation, leaving this a less likely alternative explanation. (Tr. 296, 334.) Considering all of these factors, Dr. Harris has not refuted petitioners' experts' opinion that V.S.R. was experiencing significant intracranial pressure due to inflammation and edema.

In light of Dr. Harris's explanation regarding the uncal groove, I am not persuaded that Dr. Shuman has preponderantly established that there is pathologically confirmed herniation. I am, however, more persuaded by Dr. Shuman's explanation regarding the overall severity of V.S.R.'s edema and intracranial pressure than I am by Dr. Harris's denials that these findings are significant. Even without specific confirmation of herniation, Dr. Shuman and Dr. Kinsbourne explained that edema and inflammation can be lethal when they affect blood circulation and neurologic function, especially if the brain stem is included. (Tr. 166-67, 394-95.) In addition to the flattened gyri, Dr. Shuman also confirmed tissue compression within the microscopic slides. (*Id.* at 127-30, 242-47 (discussing Ex. 38, p. 4 (Image 3).) He further opined that the findings of neuroinflammation within the available tissue samples are sufficient to reasonably implicate the brain stem activity. (*Id.* at 248-51.)

2. Seizures

Based on the analysis above, petitioners have established through their experts that, even without specific confirmation of herniation, there is preponderant evidence that V.S.R. was experiencing inflammation and edema sufficient to compromise brain function. Dr. Shuman further explained that among those tissues sampled, it was the tissue of the hippocampus, which is the most epileptogenic tissue in the brain, that was the most affected by the inflammation. (Tr. 169.) He indicated that an insult to the hippocampus, like the neuroinflammation at issue in this case, is likely to lead to an epileptic response. (*Id.* at 190.) He specifically opined the damage visible in this case would be expected to cause seizures. (*Id.* at 137-38.) Moreover, a seizure originating in the hippocampus can affect the brain stem, which controls autonomic functions, such as breathing and cardiac function. (*Id.* at 192.) Dr. Kinsbourne further explained that seizures are more common during sleep due to a lower seizure threshold.[21] (*Id.* at

[21] Of note, Drs. Shuman and Kinsbourne did discuss literature regarding Sudden Unexplained Death in Epilepsy ("SUDEP"). (Ex. 38, p. 9; Tr. 294; Ex. 16, pp. 1-2.) They cited several papers indicating that unattended seizures may be an explanation for at least a subset of SUDC cases. During the hearing, respondent's counsel raised the point that where seizures have been suspected in SUDC, there has been hippocampal malformation. (Tr. 294.) Dr. Shuman explained, however, that V.S.R. did not suffer SUDC; she suffered a symptomatic seizure caused by encephalitis affecting the hippocampus. In either event, injury to the hippocampus results in a fatal, unwitnessed seizure. Dr. Shuman simply equates a "malformation" to one type of injury, allowing that encephalitis could result in similar compromise. (*Id.* at 295-97.) Importantly, petitioners are not asserting that V.S.R.'s vaccination caused SUDC or SUDEP. They are asserting that what they allege to be a pathologically confirmed encephalitis caused an unwitnessed, fatal seizure. The fact that encephalitis can cause seizures is not controversial. (*E.g.*, Tr.

394.) He explained that seizure activity increases the metabolic rate of the brain. (*Id.* at 395-96.) Where the brain is already compromised of blood supply by swelling, the seizure can "quite readily" compromise vital functions in the brain stem. (*Id.* at 396, 407-08.) Ultimately, any seizure can be dangerous or potentially fatal. (*Id.* at 171.)

Dr. Harris agreed that, especially in a child 14-months or younger, a seizure from the hippocampus can affect the structures in the brainstem involved in oxygen recognition, carbon dioxide recognition, and wakefulness. (Tr. 529-30.) Although Dr. Harris does not ultimately opine that a seizure caused V.S.R.'s death (*Id.* at 334, 375, 380), he agreed that the activated microglia in the hippocampus are consistent with seizure-related changes and he agreed that it is a possibility that V.S.R. was suffering seizures in the week or so leading up to her death (*Id.* at 370-71, 378, 381). To the extent he characterized the pathology as relatively mild, he opined that it is consistent with two or more seizures having occurred in the weeks prior to her death. (*Id.* at 379-80.) (By definition, however, the proposed terminal seizure could not explain the microglial activation. (*Id.* at 527.)) In that regard, it is also undisputed that V.S.R. suffered a witnessed seizure on March 4, 2015. (*Id.* at 67-68 (Ms. Hogan); 161, 204-07 (Dr. Shuman); 389, 396 (Dr. Kinsbourne); 447-48 (Dr. Wirrell).)

Dr. Wirrell agreed with Drs. Shuman and Kinsbourne that V.S.R.'s March 4 seizure was consistent with a focal seizure emanating from the temporal lobe (which is within the hippocampus) that she also correlated to the microglial activation discussed by the pathologists. (Tr. 447-49, 457-58.) Drs. Wirrell and Gans expressed skepticism that V.S.R.'s seizures would have been caused by her vaccination, both because of the timing relative to vaccination and because of the lack of fever. (Ex. C, pp. 14-15; Ex. E, pp. 4-5.) However, petitioners' experts are clear in explaining that the seizures at issue constitute symptomatic seizures. (Tr. 173, 396-97.) That is, the seizures are a symptom of the underlying encephalitis which, with an appropriate showing, can itself be presumed to have been caused by the vaccination. There is no need for petitioners to causally connect the seizures to the vaccination other than through the encephalitis. In that regard, Dr. Wirrell agreed that a temporal lobe seizure can be caused by inflammation and that seizures constitute neurologic dysfunction associated with encephalitis. (*Id.* at 458, 464.)

Notwithstanding Dr. Harris's ultimate conclusion (Tr. 334, 375, 380), respondent himself incorporates a fatal seizure into his explanation of V.S.R.'s death. (ECF No. 122, p. 34.) He simply argues the seizures should be attributed to a viral infection leading to an unspecified neurologic condition, rather than the encephalitis proposed by petitioners. (*Id*.) Respondent argues that petitioners have the sequence backward, suggesting that the mild pathology is a consequence of the seizures, not the cause. (*Id.* at 29.) However, Dr. Shuman disagreed that the seizures could have caused all of the microglial activation that was present. (Tr. 511-13.) This disagreement is interwoven with the experts' differences regarding the severity of the finding. (*Id.* at 518.) Dr.

464; Venkatesan et al., *supra*, at Ex. H-2, p. 3, tbl.1 (including generalized or partial seizures not attributable to a preexisting seizure disorder among diagnostic evidence supporting encephalitis).)

Shuman also stressed that the microglial activation was not limited to the hippocampus. (Tr. 515, 518.) Ultimately, respondent's argument is not persuasive, both because Dr. Harris's characterization of the activated microglia as merely mild does not control, and because activated microglia and reactive astrocytes are not the only evidence of injurious inflammation and swelling, for all the reasons discussed above. Thus, petitioners' experts' opinions do not depend on activated microglia as *the* cause of V.S.R.'s seizures as respondent suggests.

3. Ultimate expert conclusion

Taking all of this together, petitioners' neurology expert, Dr. Kinsbourne, persuasively opined that it is "much more likely than not" that V.S.R. suffered an encephalitis that caused death by seizure. (Tr. 390.) In reaching this conclusion, he relied on (1) at least one clear seizure occurring prior to death; (2) increased head circumference upon autopsy; (3) edema; (4) flattening of the gyri; (5) histologic evidence of inflammatory cells, including activated microglia, lymphocytes, and astrocytes; and (6) marked findings of inflammation specifically in the hippocampus. (Tr. 389-90.) All of these points are preponderantly established on this record. Dr. Kinsbourne did not specifically rely on Dr. Shuman's additional identification of herniation via uncal groove.

Dr. Kinsbourne explained that encephalitis is a known cause of seizures and that seizures are a common occurrence in encephalitis. (Tr. 397-98.) Although there is no direct evidence of the proposed terminal seizure, all of the above is sufficient to circumstantially demonstrate by a preponderance of the evidence that V.S.R.'s encephalitis was of sufficient severity to result in neurologic dysfunction, namely seizures and death. Even in the absence of a terminal seizure, the evidence of neuroinflammation and edema with intracranial pressure is sufficient to support Dr. Shuman's and Dr. Kinsbourne's conclusion that a fatal encephalitis occurred.

b. Onset occurred within the Table period (also *Nuttall* prong four)

Under the Vaccine Act, "the special master or court may find the first symptom or manifestation of onset or significant aggravation of an injury, disability, illness, condition, or death described in a petition occurred within the time period described in the Vaccine Injury Table even though the occurrence of such symptom or manifestation was not recorded or was incorrectly recorded as having occurred outside such period." § 300aa-13(b)(2). However, such determination must be based upon preponderant evidence. *Id*. The special master may not make a finding of entitlement to compensation "based on the claims of a petitioner alone, unsubstantiated by medical records or by medical opinion." § 300aa-13(a)(1). The special master must consider the entire record and is not bound by any specific medical judgment or conclusion contained within the medical records, though they must be considered. § 300aa-(b)(1).

Having established that there is preponderant evidence that V.S.R. suffered an encephalitis that led to her death, petitioners must also establish that onset of the encephalitis occurred within the timeframe designated by the Vaccine Injury Table. In

this case, that period is between 5- and 15-days post-vaccination. V.S.R. received the subject MMR vaccine on February 20, 2015, and died on March 11, 2015, which was 19 days later. (Ex. 5, p. 72; Ex. 6, pp. 7-8.) The fifteenth day post-vaccination was March 7, 2015. Therefore, petitioners must demonstrate that V.S.R.'s ultimately fatal encephalitis began at least four days prior to her death.

V.S.R. was not seen for any medical follow up between the time of her vaccination and her death. Accordingly, there are no medical records or treating physician opinions available to help identify the onset of her condition. Petitioners seek to identify the onset of V.S.R.'s encephalitis in three separate ways. First, Dr. Shuman opines that the nature of the pathologic findings indicates at least 7-14 days of inflammation at the time of death. Second, petitioners assert that the evidence indicates V.S.R. had prior seizures that were evidence of her encephalitis. At least one of these seizures was witnessed by V.S.R.'s mother on March 4, 2015. (Tr. 67-68.) Third, Dr. Shuman opines based on his review of the video evidence that V.S.R. was demonstrating neurologic dysfunction by no later than February 26. I am persuaded by the first and second of these points and find that together they are sufficient to place onset of V.S.R.'s encephalitis within the appropriate Table period, *i.e.*, by no later than March 7, 2015.

Dr. Shuman explained that the reactive astrocytes that he identified within V.S.R.'s pathology typically manifest about 7-14 days after microglial activation begins. (Tr 165-66.) Dr. Harris agreed. (*Id.* at 381.) Thus, with V.S.R.'s death having occurred on March 11, 2015, this finding alone would place onset of brain inflammation no later than March 4, 2015, and perhaps as early as late February.[22] This also corresponds with the date of V.S.R.'s one undisputed, witnessed, seizure that occurred on March 4, 2015. (*Id.* at 67-68 (Ms. Hogan); 161, 204-07 (Dr. Shuman); 389, 396 (Dr. Kinsbourne); 447-48 (Dr. Wirrell).) Dr. Harris specifically confirmed that V.S.R.'s activated microglia and astrocytes in the brain are consistent with a series of seizures beginning about a week to ten days prior to her death. (*Id.* at 381, 524.) And Dr. Wirrell agreed that the March 4 seizure was likely a focal seizure from the temporal lobe, though she would not attribute a single seizure to encephalitis absent additional indicators of an encephalopathic state. (*Id.* at 447-49; *accord* Messacar, *supra*, at Ex. H-1, p. 2.) She did, however, agree that the location of V.S.R.'s focal seizure corresponded to microglial activation observed by the pathologists. (Tr. 457.) Moreover, she agreed that the March 4 seizure could have been caused by inflammation in the temporal lobe. (*Id.* at 458.) These points are sufficient to preponderantly establish that V.S.R.'s encephalitis was present within the Table period and that the first outward symptom of encephalitis, namely her March 4, 2015 seizure, likewise occurred within that period.

[22] During the hearing, I asked Dr. Shuman to clarify whether the fixed tissue he examined was representative of the condition of the tissue at the time of death. He explained that changes would continue until tissue fixation, which occurred about 12-14 hours after death, but these changes would not be very significant. They would result in degrade more so than advance. (Tr. 150-52.)

The fact that, apart from a single seizure, V.S.R. was not in any obvious distress in the days leading up to her death is perhaps the most puzzling aspect of this case. It is not necessarily unreasonable for Dr. Shuman to view the available video footage with the benefit of hindsight, seeking out more subtle suggestions of neurologic dysfunction. However, based upon my own review of the videos with the benefit of expert neurologists' testimony, I do not find the videos provide any clear evidence of encephalitis. Although the points raised by Dr. Shuman with respect to the video footage cannot be entirely dismissed, neither Dr. Kinsbourne nor Dr. Wirrell supported his interpretation. Dr. Kinsbourne, in particular, as petitioners' own expert in neurology, opined that the video evidence alone is not diagnostic of encephalitis. (Tr. 409.) Thus, I find that the purported signs of encephalitis Dr. Shuman raises are inconclusive at best.[23] Respondent's experts' skepticism regarding the lack of progressive clinical symptoms of encephalitis is therefore well taken.

Nonetheless, Dr. Kinsbourne testified that, while clinical symptoms of progressive brain swelling would ordinarily be expected in most cases, they cannot necessarily be expected in all cases. (Tr. 408.) In that regard, Dr. Shuman testified that while V.S.R. had evidence of inflammation in several areas of the brain (including the hippocampus, midbrain, cerebellum, and medulla), the most severely affected area was the hippocampus. (*Id.* at 124-25.) Apart from having epileptogenic capacity, he explained that together the temporal lobe and hippocampus are responsible for language and memory. (*Id.* at 137.) Thus, while damage to this portion of the brain would result in a learning disability, for a 14-month-old like V.S.R., outward clinical signs would be more limited. (*Id.* at 136-37.) In that regard, Dr. Wirrell did leave open the possibility that inflammation could cause a temporal lobe seizure without signs of encephalopathy. (*Id.* at 458.)

Dr. Shuman's point is further supported by the literature filed by respondent, which observes that "[t]ypical alterations in speech, behavior, and cognition in older individuals with encephalopathy may be more challenging to detect in infants and young children, who present more commonly with irritability, lethargy, or loss of interest in feeding." (Messacar, *supra*, at Ex. H-1, p. 4.) Thus, the IEC does include personality change, and not only reduced consciousness, among the ways in which altered mental status can be evidenced. (Venkatesan, *supra*, at Ex. H-2, p. 3 tbl.1.) Although V.S.R. did not have any medical evaluation during the relevant period to specifically assess neurologic dysfunction, V.S.R.'s parents did testify to behavior changes, including fussiness and reduced feeding, which occurred during the week prior to her death. In fact, Dr. Wirrell did otherwise find significance in V.S.R.'s irritability and feeding difficulties shortly before death, though she attributed those behaviors to the ongoing infection she suspected. (Ex. C, p. 12.) Ultimately, while Dr. Kinsbourne would not diagnose encephalitis in this case based on clinical presentation alone, he was careful

[23] Respondent also argues that Dr. Shuman's assessment of onset occurring on February 27 is incompatible with his suggestion that viremia was the mechanism of V.S.R.'s encephalitis. (ECF No. 122, p. 30.) However, for all the reasons discussed herein, petitioners are not obligated to prove viremia as the underlying cause of V.S.R.'s encephalitis, and I have not credited Dr. Shuman's identification of onset beginning specifically on February 27. Accordingly, the issue raised by respondent is immaterial.

to note that there is not a complete absence of evidence of neurologic dysfunction leading up to V.S.R.'s death. (Tr. 408-09 ("[T]he evidence is miscellaneous, but it is there."))

While respondent's experts raise reasonable concerns regarding V.S.R.'s outward clinical presentation, the above-discussed factors temper the significance of V.S.R.'s potentially confounding clinical presentation in the days prior to her death. These uncertainties stand in contrast to the much more clear-cut relationship between V.S.R.'s postmortem brain pathology and her undisputed seizure activity. Moreover, as discussed below, respondent's own attempt at otherwise explaining V.S.R.'s history and death fails to make any better sense of the situation. For these reasons, I find that the onset of V.S.R.'s encephalitis is preponderantly evidenced by her witnessed seizure and postmortem pathology, notwithstanding that her outward clinical presentation alone is otherwise insufficient to identify an encephalitic child. This places onset of V.S.R.'s encephalitis no later than March 4, 2015, which is consistent with the period identified by the Vaccine Injury Table for an encephalitis following the MMR vaccine.

c. Respondent has not preponderantly established any factor unrelated to vaccination as the cause of V.S.R.'s death[24]

Once petitioners have met their own burden of proof, the government may still demonstrate that the injury is nonetheless "due to factors unrelated to the administration of the vaccine described in the petition." § 300aa-13(a)(1)(B). In order to meet his burden of proof, respondent must demonstrate by preponderant evidence "that a particular agent or condition (or multiple agents/conditions) unrelated to the vaccine was in fact the sole cause (thus excluding the vaccine as a substantial factor)." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347,1354 (Fed. Cir. 2008) (emphasis omitted). Comparable to what a petitioner must show in a cause-in-fact case, respondent must show a logical sequence of cause and effect linking the injury to the proposed factor unrelated. *Deribeaux ex rel. Deribeaux v. Sec'y of Health & Human Servs.*, 717 F.3d 1363, 1368-69 (Fed Cir. 2013). It need not be scientifically certain but must be legally probable. *Id*. Conditions or other factors that are "idiopathic,

[24] There is no question that respondent's post-hearing brief sets forth an alternative assessment of V.S.R.'s clinical history and death. (ECF No. 122, pp. 31-34.) However, respondent's post-hearing brief is a bit ambiguous with respect to how respondent's argument fits within the parties' respective burdens of proof. Based on my review of respondent's argument and the evidence of record, I conclude that respondent's position is best addressed as a question of his own shifted burden of proof to demonstrate that petitioner's Table encephalitis was caused by a factor unrelated to vaccination. There is an argument, however, that what respondent advances should be considered with respect to whether a Table encephalitis is actually present. In that context, what respondent argues is that, rather than any encephalitis at all, V.S.R. actually experienced a viral illness leading to an unspecified neurologic condition that then resulted in her seizures and death. In addition to the "factor unrelated" analysis below, I have considered respondent's argument from this other angle as well. However, particularly given respondent's inability to articulate what neurologic condition he is asserting, I do not find his arguments any more compelling as evidence countering the fact of an encephalitis than as evidence that V.S.R.'s death was due to a factor unelated to her vaccination.

unexplained, unknown, hypothetical, or undocumentable" cannot defeat a petitioner's claim. § 300aa-13(a)(2); *Knudsen*, 35 F.3d at 548-49.

In his post-hearing brief, respondent argues that "[p]etitioners ignore the clinical and pathological evidence that V.S.R. had a viral illness that could have caused her death." (ECF No. 122, pp. 31-34.) Specifically, respondent argues that, rather than encephalitis, V.S.R. suffered a viral illness that resulted in seizures and death. (*Id*.) In that regard, Drs. Gans and Wirrell opined that V.S.R.'s death was ultimately due to a respiratory tract infection. (Tr. 488; Ex. H, p. 4; Ex. E, p. 4.)

However, respondent's proffered infectious disease expert, Dr. Gans, effectively acknowledged that V.S.R. had no symptoms of infection. (Tr. 492-93.) She was clear in opining that she felt V.S.R.'s prior January infection had resolved and was unrelated. (*Id.* at 490.) Apart from a contemporaneous report that V.S.R. may have been sweaty on the day that she died (Ex. 8, p. 4), there is no clear evidence of any symptoms of illness. While Dr. Gans stressed that upper respiratory infections *can* exist in the absence of such symptoms, this still leaves a relative dearth of supporting evidence. Regarding any further detail, she noted she is not a pathologist. (Tr. 487-88.) In response to my questioning, she seemed to agree that the finding of lymphocytic infiltration in the trachea is of very limited utility without other evidence pointing to the cause of it. (*Id.* at 499-500.) She explained that certain viruses, notably RSV and rhinovirus, are associated with adverse neurologic events and sudden unexplained death, but did not point to any evidence that V.S.R. was infected with one of these specific viruses. (*Id.* at 492, 500-03.) Instead, much of the focus of her testimony seemed to be on what she viewed as the comparative implausibility that a vaccine would cause an encephalitis. (*Id.* at 471-81.) However, as discussed above, because this case resolves as a Table injury, petitioners bear no burden of proof with respect to the cause of V.S.R.'s encephalitis.[25]

Nor did Dr. Harris provide any significant support for Dr. Gans's opinion. He opined that V.S.R. had no significant abnormalities affecting the heart or lungs, with no evidence of bacterial infection, acute pneumonia, or aspiration, before she died. (Tr. 351-52.) He indicated the lymphocytic infiltration of the trachea "could speak to an upper airway respiratory illness . . . that could have been caused by a virus that possibly was going through the family at that time," but this is equivocal and he additionally stressed that he could not say more. (*Id.* at 354.) Dr. Harris indicated that "I think this is a tragically sad case that we don't have a specific reason to her death." (*Id.* at 373.)

[25] It should be noted that Dr. Shuman indicated that, based on Dr. Davenport's finding of lymphocytic infiltrate in the trachea, he agreed V.S.R. had an upper respiratory infection or some kind of reactive airway disease at the time of death and that this was likely due to the same virus that caused her encephalitis, suggesting the vaccine caused encephalitis via a viral infection. (Tr. 195.) While Dr. Gans's testimony would challenge the assumption underlying Dr. Shuman's testimony regarding the relationship between vaccination, viruses, and encephalitis, this is again of no moment in the context of a Table injury. Petitioners are not obligated to prove how the vaccine could have caused encephalitis. In that respect, Dr. Shuman's testimony on this point is effectively a nullity. Importantly, however, I do not understand Dr. Shuman's testimony to be conceding that V.S.R. suffered an infection unrelated to vaccination that caused her encephalitis and death.

Ultimately, he opined that sudden unexplained death in childhood is the best way to categorize V.S.R.'s death overall. (*Id.* at 354.) One particular factor informing Dr. Harris's opinion is the lack of any evidence of viropathic changes in the brain. (*Id.* at 334, 344, 370, 530.) Thus, respondent has little to no basis for urging that the infection proposed by Drs. Wirrell and Gans was the cause of the encephalitis that I have concluded was present.

To the extent Drs. Harris and Wirrell endorsed SUDC, rather than encephalitis, as the cause of V.S.R.'s death (Tr. 345-46, 530), I have already considered this, to the extent diagnostically applicable, in determining whether an encephalitis was present. *See Doe 11 v. Sec'y of Health & Human Servs*., 601 F.3d 1349, 1357-58 (Fed. Cir. 2010) (explaining that "[e]vidence of SIDS was just one factor among many that the special master relied on in concluding that 'the facts of this case' did not support Doe's theory of causation," an analysis distinct from respondent's shifted burden of proof with respect to demonstrating alternative causes). Regarding respondent's shifted burden of proof, Dr. Harris's endorsement of SUDC is based on his opinion that V.S.R.'s autopsy correctly determined that her cause of death is undetermined. (Tr. 354.) However, concluding that V.S.R.'s death is unexplained does not support respondent's burden of proof. § 300aa-13(a)(2); *Knudsen*, 35 F.3d at 548; *see also Doe 11*, 601 F.3d at 1357 (explaining that "alternative causes that are 'idiopathic, unexplained, unknown, hypothetical or undcoumentable' cannot overcome a petitioner's prima facie case").

For these reasons, respondent has not met his own preponderant burden of proof in seeking to establish that V.S.R.'s death was caused by factors unrelated to vaccination.

VII. This is not an unexplained death case

Finally, as discussed in Section I, *supra*, I emphasize that petitioners have pursued this case solely on the basis of qualifying for a presumption of causation under the Vaccine Injury Table. And, for all the reasons discussed in Section VI, *supra*, I have concluded based on the specific facts of this case that V.S.R.'s death was more likely than not explained by a Table encephalitis, notwithstanding that the autopsy report concluded that the cause of death was undetermined. Thus, I have concluded that this is *not* an instance of unexplained death consistent with any of the categorizations of sudden unexplained deaths in either infancy or childhood (*i.e.*, SUDC, SUDEP, SIDS or SUID).[26] In fact, Dr. Shuman explicitly testified that the pathology findings of

[26] Numerous petitioners in this program who have pursued cause-in-fact claims related to unexplained deaths have been unable to substantiate a medical theory supporting vaccine-causation as an explanation for these phenomena. *E.g.*, *Boatmon v. Sec'y of Health & Human Servs*., 941 F.3d 1351 (Fed. Cir. 2019). Nothing in this ruling is inconsistent with that history of litigation. I have myself dismissed several prior SIDS cases for lack of a *prima facie* showing of vaccine causation based on varying theories and autopsy findings. *Downing-Powers v. Sec'y of Health & Human Servs.*, No. 15-1043V, 2020 WL 4197303 (Fed. Cl. Spec. Mstr. June 2, 2020); *Brunson ex rel. T.A. v. Sec'y of Health & Human Servs*., No. 17-530V, 2020 WL 5755502 (Fed. Cl. Spec. Mstr. Sept. 3, 2020); *Bohn ex rel. G.B. v. Se'cy of Health & Human Servs.*, No. 16-0265V, 2021 WL 4302367 (Fed. Cl. Spec. Mstr. Aug. 23, 2021).

neuroinflammation he observed in this case are incompatible with these categorizations of unexplained death. (Tr. 514.) Moreover, consistent with the Table definition of encephalitis I identified in Section V, *supra*, the evidence of record was not limited to simply reflecting some evidence of inflammation affecting the brain. As discussed throughout the analysis, Dr. Harris explained that incidental findings consistent with neuroinflammation can occur and do not always point to encephalitis. However, in this case the evidence supported the conclusion that the findings of neuroinflammation were the likely cause of V.S.R.'s seizures and death for the reasons discussed above.

VIII. Conclusion

For all the reasons discussed above, I have concluded that petitioners have met their burden of proof by demonstrating by a preponderance of the evidence that V.S.R. suffered a Table injury of Encephalitis, the first symptom of which arose during the period prescribed by the Vaccine Injury Table. This relieves petitioners of any obligation to prove that the vaccination actually caused-in-fact V.S.R.'s death. Further, respondent has not met his own preponderant burden of proof with respect to establishing that a factor unrelated to vaccination led to V.S.R.'s death. This outcome is inextricably intertwined with the specific legal standards of this program and the presumption of vaccine causation allowed in certain circumstances. Nothing about this ruling purports to be critical of the autopsy performed by Dr. Davenport or to present a definitive explanation for V.S.R.'s death. Nor does anything in this ruling suggest that petitioners should have or could have done anything different in their care of V.S.R. Petitioners and their family have my deepest sympathy and condolences for their loss.

A separate damages order will be issued, setting forth the next steps in the case.

IT IS SO ORDERED.

s/Daniel T. Horner
Daniel T. Horner
Special Master