CORRECTED

In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

Filed: March 31, 2021

KELLY RUPERT,	*	No. 15-841V
Petitioner,	*	Special Master Sanders
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Decision; Entitlement; Influenza ("Flu") Vaccine; Significant Aggravation; Kidney Failure; Glomerulonephritis
Respondent.	*	

William E. Cochran, Jr., Black McLaren et al., P.C., Memphis, TN, for Petitioner.
Sarah C. Duncan, United States Department of Justice, Washington, D.C., for Respondent.

DECISION[1]

On August 7, 2015, Kelly Rupert ("Petitioner") filed a petition for compensation pursuant to the National Vaccine Injury Compensation Program ("Program").[2] Pet. at 1, ECF No. 1; 42 U.S.C. §§ 300aa-1 to 34 (2012). Petitioner alleges that the influenza ("flu") vaccine she received on September 23, 2013, caused a significant aggravation of her kidney failure[3] and glomerulonephritis.[4] Am. Pet. at 1, ECF No. 36.

---

[1] This Decision shall be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 note (2012) (Federal Management and Promotion of Electronic Government Services). In accordance with Vaccine Rule 18(b), a party has 14 days to identify and move to delete medical or other information that satisfies the criteria in § 300aa-12(d)(4)(B). Further, consistent with the rule requirement, a motion for redaction must include a proposed redacted decision. If, upon review, I agree that the identified material fits within the requirements of that provision, such material will be deleted from public access.

[2] National Childhood Vaccine Injury Act of 1986, Pub L. No. 99-660, 100 Stat. 3755. Hereinafter, for ease of citation, all "§" references to the Vaccine Act will be to the pertinent subparagraph of 42 U.S.C. § 300aa (2012).

[3] Kidney failure, also called renal failure, is "the inability of a kidney to excrete metabolites at normal plasma levels under conditions of normal loading, or the inability to retain electrolytes under conditions of normal intake, so that waste products and metabolites accumulate in the blood." *Kidney Failure*, DORLAND'S MEDICAL DICTIONARY ONLINE [hereinafter "DORLAND'S"], https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Renal Failure*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[4] Glomerulonephritis is "nephritis accompanied by inflammation of the capillary loops in the renal glomeruli." *Glomerulonephritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). Nephritis is "inflammation of the kidney[.]" *Nephritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). Renal glomeruli are "globular tuft[s] formed by capillaries in the kidney, the

After carefully analyzing and weighing all the evidence and testimony presented in this case in accordance with the applicable legal standards, I find that Petitioner has not met her legal burden. Petitioner has failed to provide preponderant evidence that the flu vaccine she received on September 23, 2013, significantly aggravated her kidney failure or glomerulonephritis. Accordingly, Petitioner is not entitled to compensation.

I. Procedural History

Petitioner filed her petition for compensation on August 7, 2015. Pet. at 1. Shortly thereafter, on August 10, 2015, Petitioner filed proof of her vaccination, along with ten medical record exhibits. Pet'r's Exs. 1–11, ECF Nos. 6–7. The next day, Petitioner filed her first statement of completion. ECF No. 8. On November 5, 2015, Respondent filed his Rule 4(c) report, recommending that compensation be denied. ECF No. 13. A status conference was held on November 23, 2015, during which Petitioner was ordered to submit an amended petition (clarifying the date of vaccination) by December 4, 2015, and updated medical records by January 4, 2016. ECF No. 15. Petitioner was also ordered to file an expert report by no later than January 25, 2016. *Id*.

On December 3, 2015, Petitioner filed an amended petition. ECF No. 16. Following two extension requests, Petitioner submitted two additional sets of medical records on March 16, 2016, followed by one additional set on April 6, 2016. Pet'r's Exs. 14–16, ECF Nos. 21, 26. Petitioner filed her second statement of completion on April 6, 2016. ECF No. 27.

Petitioner submitted an expert report from Eric Gershwin, M.D., accompanied by supporting medical literature, on April 15, 2016. Pet'r's Exs. 19–46, ECF Nos. 28–31. On the same date, Petitioner filed an opinion letter from Wesam Ballouk, M.D. ECF No. 28. On July 21, 2016, Respondent filed two responsive expert reports, one from Arnold Levinson, M.D., and one from Derek Fine, M.D., along with fourteen pieces of supporting medical literature. Resp't's Exs. A–D, ECF Nos. 33-1, 34-2–34-3, 34-8; Resp't's Ex. A, Tabs 1–10, ECF Nos. 33-2–34-1; Resp't's Ex. C, Tabs 1–4, ECF Nos. 34-4–34-7.

The parties convened for a status conference on July 27, 2016, at which time Petitioner was ordered to file a second amended petition (to limit her claim to significant aggravation) and updated medical records. ECF No. 35. Petitioner filed a second amended petition and the requested medical records on August 30, 2016. ECF Nos. 36–37.

On January 3, 2017, Petitioner filed a supplemental expert report from Dr. Gershwin along with a supplemental opinion letter from Dr. Ballouk. Pet'r's Exs. 49–50, ECF No. 40-1–40-2. The case was reassigned to me on January 9, 2017. ECF No. 41. On February 17, 2017, Respondent filed a responsive supplemental expert report from Dr. Fine. Resp't's Ex. E, ECF No. 43-1.

On July 5, 2017, I issued an order directing the parties to file a status report with proposed dates for an entitlement hearing. Scheduling Order, docketed July 5, 2017. The matter was subsequently set for a hearing on December 5–6, 2018. ECF Nos. 51–52. The hearing date was

---

site of the filtration barrier between the blood and the kidney[.]" *Renal Glomerulus*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

subsequently rescheduled to October 29–30, 2019, due to the funeral of former President of the United States George H.W. Bush. ECF No. 71. The entitlement hearing was held as scheduled on these dates. *See* Min. Entry, docketed Oct. 31, 2019.

This matter is now ripe for consideration.

II. Factual Background

A. Medical Records

Petitioner was born on March 17, 1968. *E.g.*, Pet. at 1. Petitioner's pre-vaccination medical history is notable for hypertension,[5] edema,[6] obesity, smoking,[7] pain, and anxiety. *See generally* Pet'r's Ex. 1. Petitioner's first record from Raymond Nino, M.D., a primary care physician ("PCP"), is from August 10, 2010. *See id.* at 36. Petitioner's blood pressure readings were relatively stable and within or near normal range[8] until July 12, 2011, when her provider reported a spike at 138/90.[9] *Id.* at 28; *see also id.* at 29–36. Also on July 12, 2011, Petitioner's provider noted that she had edema. *Id.* at 28. Although Petitioner's blood pressure was sometimes normal after this occasion, it continued to spike at times between 2011 and 2013. *See id.* at 1–27. It reached a high of 176/124 on August 20, 2013. *Id.* at 4. On that date, Petitioner also complained of leg and back pain, which she rated as a two out of ten on a pain scale. *Id.* Dr. Nino assessed Petitioner with

[5] Hypertension is "high arterial blood pressure; various criteria for its threshold have been suggested, ranging from 140 mm Hg systolic and 90 mm Hg diastolic to as high as 200 mm Hg systolic and 110 mm Hg diastolic. Hypertension may have no known cause . . . or be associated with other primary diseases." *Hypertension*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 7, 2021).

[6] Edema, also called dropsy or hydrops, is "the presence of abnormally large amounts of fluid in the intercellular tissue spaces of the body, usually referring to subcutaneous tissues." *Edema*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 7, 2021).

[7] Petitioner testified that she quit smoking in the fall of 2013. Tr. 33:16–18.

[8] The Centers for Disease Control and Prevention ("CDC") states that "[a] normal blood pressure is less than 120/80 mmHg." *High Blood Pressure Symptoms and Causes*, CENTERS FOR DISEASE CONTROL AND PREVENTION, https://www.cdc.gov/bloodpressure/about.htm (last visited Feb. 19, 2021).

[9] As indicated in *Dorland's*, *supra* note 5, there is not a universal cutoff used to identify hypertension. *See High Blood Pressure Symptoms and Causes*, CENTERS FOR DISEASE CONTROL AND PREVENTION, https://www.cdc.gov/bloodpressure/about.htm (last visited Feb. 19, 2021). The CDC refers to two different guidelines, one from 2003 and another from 2017. *Id.* The 2003 guideline ("The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure") indicates that high blood pressure, or hypertension, is 140 mm Hg or higher systolic and 90 mm Hg or higher diastolic. *Id.* Said guideline also indicates that 120–139 mm Hg systolic and 80–89 mm Hg diastolic is "elevated" and qualifies as prehypertension. *Id.* The 2017 guideline ("The American College of Cardiology/American Heart Association Guideline for Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults") identifies hypertension as 130 mm Hg or higher systolic and 80 mm Hg or higher diastolic. *Id.* It indicates that 120–129 mm Hg systolic with less than 80 mm Hg diastolic is elevated. *Id.*

"[osteoarthritis[10] ("OA") of her lumbar] spine[11]" and gave her a 120-count refill for her Roxicodone[12] prescription. *Id.* The records from Dr. Nino indicate that Petitioner regularly took Roxicodone and sometimes took Xanax.[13] *See generally* Pet'r's Ex. 1. Petitioner's provider also noted that she had edema on May 24, 2012, June 26, 2012, and May 20, 2013. *Id.* at 6, 18–19.

Petitioner received the flu vaccination at issue at a Rite Aid on September 23, 2013. Pet'r's Ex. 2 at 1. On October 1, 2013, Petitioner attended a follow-up appointment with Dr. Nino. *Id.* at 3. Petitioner again complained of back and left leg pain, but she rated said pain, when she took her Roxicodone prescription as directed, as a zero on the pain scale. *Id.* Petitioner also complained of anxiety. *Id.* She further complained of one day of mild vaginal bleeding, which she reported had occurred the previous month. *Id.* Petitioner explained that her "last menstrual period was [in] September 2012." *Id.* She was assessed with "OA L[-]Spine," anxiety, and vaginal bleeding. *Id.* She was given another 120-count Roxicodone prescription refill, a 90-count Xanax prescription refill and instructed to follow up with a gynecologist. *Id.*

Petitioner attended another follow-up appointment with Dr. Nino on November 7, 2013. *Id.* at 2. Petitioner again complained of left leg and back pain. *Id.* Petitioner voiced no other complaints at this visit. *Id.* Dr. Nino assessed Petitioner with OA of her lumbar spine and gave Petitioner another 120-count refill of her Roxicodone prescription. *Id.*

On November 21, 2013, Petitioner presented to the emergency room at Monongahela Valley Hospital ("MVH") "with complaints of having abdominal pain, nausea, vomiting and diarrhea for the last two weeks." Pet'r's Ex. 3(b) at 289. Doctors noted that Petitioner's abdominal pain was "in the periumbilical[14] region[,]" and that Petitioner rated the pain as a five out of ten on the pain scale. *Id.* Petitioner stated that "once she vomits and passes diarrhea then her abdominal pain [is] relieve[d] to a certain extent." *Id.* Petitioner further explained that "[s]he feels nauseated

---

[10] Osteoarthritis is "a noninflammatory degenerative joint disease seen mainly in older persons, characterized by degeneration of the articular cartilage, hypertrophy of bone at the margins, and changes in the synovial membrane. It is accompanied by pain . . . and stiffness . . . ." *Osteoarthritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[11] The lumbar spine is "the part of the spine comprising the lumbar vertebrae[,]" which are "the five vertebrae[,]" labeled L1 through L5 "between the thoracic vertebrae and the sacrum." *Lumbar Spine*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Lumbar Vertebrae*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Vertebrae Lumbales*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[12] Roxicodone is a trademark for oxycodone hydrochloride, which is "the hydrochloride salt of oxycodone, used as an analgesic[.]" Oxycodone is an "opioid agonist analgesic . . . ." *Roxicodone*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Oxycodone Hydrochloride*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Oxycodone*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[13] Xanax is a trademark for alprazolam, which is "a short-acting benzodiazepine used as an antianxiety agent in the treatment of anxiety disorders and panic disorders and for short-term relief of anxiety symptoms . . . ." *Xanax*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Alprazolam*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[14] Periumbilical means "near or around the umbilicus[,]" which is the navel. *Periumbilical*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Umbilicus*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

and . . . vomits [one]-[two] times a day[,]" and that she has "diarrhea [three]-[four] times in a day." *Id.* CT scans of Petitioner's abdomen and pelvis conducted while she was in the emergency room "revealed no evidence of calculus[15] or hydronephrosis,[16]" and Petitioner's "appendix was . . . normal." *Id.* In addition, doctors wrote that "[t]here was no evidence of inflammatory bowel disease[17]" and that Petitioner's uterus and adnexa were also normal. *Id.* Lastly, doctors noted that Petitioner's "BUN[18] was . . . [thirty-three] with [her] creatinine[19] [at] 2.8." *Id.* Both results were classified as high. *See id.* at 283. Additionally, Petitioner's urinalysis revealed high protein levels at greater than 300 mg/dl as well as the presence of blood and red blood cells. *Id.* Doctors assessed Petitioner with, among other things, abdominal pain of a "not very clear" etiology, diarrhea with a "not very obvious" etiology, dehydration, and chronic back pain. *Id.* at 292. They determined that Petitioner would "continue with her pain medications." *Id.* In addition, doctors assessed Petitioner with "[r]enal insufficiency [that] appears to be acute renal insufficiency[20] because of dehydration." *Id.* They noted that they would continue to monitor Petitioner's BUN and creatinine and proceeded to schedule a nephrology consultation for the next day. *Id.* Petitioner was admitted for further observation. *Id.* However, the next day, Petitioner checked herself out of the hospital against medical advice. *Id.* at 288.

Petitioner presented to Dr. Nino for a follow-up appointment on December 10, 2013. Pet'r's Ex. 1 at 1. Petitioner complained of back and left leg pain but did not voice any additional complaints. *Id.* Dr. Nino did not make any notations or statements regarding Petitioner's recent hospitalization. *See id.* Dr. Nino's only assessment was OA of Petitioner's lumbar spine. *Id.* He provided Petitioner an additional 120-count refill of her Roxicodone prescription. *Id.*

On January 22, 2014, Petitioner presented to a new PCP, Joanna Swauger, D.O., to establish care. Pet'r's Ex. 12 at 30. Petitioner stated that "she went to the ER this fall, for abdominal pain. [She w]as told that she was severely dehydrated and given [three] liters of NSS." *Id.*

---

[15] Calculus, or stone, is "an abnormal concretion in the body, usually composed of mineral salts." *Calculus*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[16] Hydronephrosis is "distention of the pelvis and calices of the kidney with urine, as a result of obstruction of the ureter[,]" which is "the fibromuscular tube that conveys the urine from the kidney to the bladder." *Hydronephrosis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Ureter*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[17] Inflammatory bowel disease is "a general term for those inflammatory diseases of the intestines that have an unknown etiology . . . ." *Inflammatory Bowel Disease*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[18] BUN is "blood urea nitrogen[.]" *BUN*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[19] Creatinine is "the cyclic anhydride of creatine, produced as the final product of decomposition of phosphocreatine[]" and "is excreted in the urine." *Creatinine*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).
Creatine is "an amino acid formed by methylation of guanidinoacetic acid, found in vertebrate tissues, particularly in muscle." *Creatine*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[20] Renal insufficiency is "a state of disordered function of the kidneys verifiable by quantitative tests[]" that "may progress to renal failure." *Renal Insufficiency*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). "Acute" refers to "a short and relatively severe course." *Acute*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

Petitioner further stated that her nausea and vomiting "resolved." *Id.* Petitioner noted that "she has been having issues with her back," although she explained that her recent weight loss had "really helped to decrease her back pain." *Id*. Petitioner's blood pressure was elevated at 160/110. *Id.* at 31. At this visit, Petitioner underwent a urinalysis, which revealed high levels of potassium, BUN, and creatinine. Pet'r's Ex. 3(a) at 5. Dr. Swauger wrote that Petitioner had an "[o]verall normal exam, aside from [blood pressure] and [urinalysis]. Will obtain old records and [follow up] accordingly." Pet'r's Ex. 12 at 31. Regarding Petitioner's back pain, Dr. Swauger wrote that she "encourage[d Petitioner to] use her Oxycodone sparingly. Advised her that the [fifteen milligram] dose is rather high, and that if she will require frequent use, she may need to be referred to [a] pain clinic." *Id*. at 32. Dr. Swauger also wrote that she would "send [Petitioner's urinalysis] for eval[uation] at [the] lab . . . [to] rule out [infection]. If negative, will need to obtain [ultrasounds] of [her] kidneys for eval[uation] and possibly [obtain a] consultation by [a] nephrologist." *Id*. Dr. Swauger directed Petitioner to follow up in four weeks. *Id*.

Petitioner underwent ultrasounds of her kidneys on January 29, 2014. Pet'r's Ex. 3(a) at 16. The ultrasounds revealed "mild prominence of the renal pyramids[21] bilaterally. This may reflect papillary necrosis.[22]" *Id*. Petitioner also underwent a thyroid ultrasound on this date. *Id.* at 17. The impression of this test was a "[m]ultinodular thyroid." *Id*. Also, on this date, Dr. Swauger received the lab results of Petitioner's urinalysis, which showed that "the total protein was 11,365." Pet'r's Ex. 12 at 27. In response, Dr. Swauger wrote the following:

> I have not seen her old records, so not sure how long this has been going on with her kidneys. Her [blood work] from today shows that her creatinine is about the same as last week – abnormal at 3.5 (last week was 3.6) . . . . Please tell [Petitioner] that her kidneys are leaking too much protein, and that this needs to be addressed ASAP. . . . I see that she had [ultrasounds] of the kidneys. It looks like they are normal in size and shape, but the center of them looks like they may have something called "papillary necrosis." This can have various causes, but [it] is commonly caused by overuse of pain med[ications]. So [she should] try to avoid them at all cost for now and go see the kidney [doctors] for [an] eval[uation].

Id. Dr. Swauger also noted that Petitioner's thyroid ultrasound "showed . . . a couple nodules" that were concerning, and Dr. Swauger thought they "need[ed] to be biopsied." *Id*. Dr. Swauger's nurse wrote in the same note that she had spoken with Petitioner, and Petitioner had stated that "she has not taken any form of pain med[ication] since she received the news about her kidneys." *Id.* Petitioner also indicated that "she want[ed] to get to the bottom of [her] kidney problems before she does anything with [her] thyroid." *Id*.

---

[21] Renal pyramids are "the conical masses that make up the substance of the renal medulla[,]" which is "the inner part of the substance of the kidney . . . ." *Pyramides Renales,* DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Renal Medulla,* DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[22] Papillary "pertain[s] to or resembl[es] a papilla," which is "a small nipple-shaped projection, elevation, or structure." *Papillary,* DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). Necrosis is "the sum of morphologic changes indicative of cell death and caused by the progressive degradation action of enzymes[.]" *Necrosis,* DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

On January 30, 2014, Petitioner presented to Ronald Lutes, D.O., a nephrologist, for a consultation. Pet'r's Ex. 9 at 1. Dr. Lutes wrote that "[s]everal months ago[, Petitioner] had severe [vomiting/diarrhea,] which has since resolved. She has been feeling well." *Id.* at 3. Dr. Lutes reviewed Petitioner's prior lab work and conducted a physical examination, which was unremarkable. *Id.* at 3–4. Dr. Lutes assessed Petitioner with proteinuria,[23] chronic kidney disease ("CKD")[24] - stage IV, and hematuria.[25] *Id.* at 1. Dr. Lutes wrote that Petitioner had "[p]rogressive renal dysfunction with nephrotic range proteinuria and hematuria." *Id.* He also wrote that he "strongly suspect[ed] a glomerulonephritis[,]" and he believed that "[t]he most likely diagnosis at this time would be one of proliferative glomerulonephritis[26] and a concern towards a vasculitic process[,] i.e. lupus or a[n] Anca[-]associated process.[27]" *Id.* Dr. Lutes also noted that Petitioner may need to undergo a renal biopsy. *Id.*

Petitioner underwent a left renal biopsy on February 19, 2014. Pet'r's Ex. 3(a) at 62, 70–71, 102–03. Prior to the biopsy, Petitioner told doctors "that she had a flu shot sometime in October and . . . that she had not been feeling well since that time." *Id.* at 70. The biopsy revealed "a fibrillary glomerulonephritis [("FGN")][28][] that is associated with extensive chronic changes

---

[23] Proteinuria, also called albuminuria, is "excessive serum proteins in the urine, such as in renal disease, after strenuous exercise, and with dehydration. *Proteinuria*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[24] Chronic kidney disease, or chronic renal failure, is "gradual loss of kidney function, with progressively more severe renal insufficiency . . . ." *Chronic Kidney Disease*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 4, 2021).

[25] Hematuria, also called erythrocyturia, refers to "blood (erythrocytes) in the urine[.]" *Hematuria*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). Erythrocytes are "one of the elements found in peripheral blood." *Erythrocyte*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 4, 2021).

[26] Proliferative Glomerulonephritis refers to "any of various types accompanied by proliferation of endothelial or mesangial cells in the glomeruli . . . ." *Proliferative Glomerulonephritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). Endothelial refers to the endothelium, "the layer of epithelial cells that lines the interior structures such as the cavities of the heart, the lumina of blood and lymph vessels, and the serous cavities of the body[.]" *Endothelium*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).
Mesangial refers to the mesangium, "the thin membrane that helps support the capillary loops in the renal glomerulus." *Mesangium*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[27] ANCA-associated vasculitis is "a subgroup of small vessel vasculitis in which there are circulating antineutrophil cytoplasmic autoantibodies (ANCA) . . . ." *ANCA-Associated Vasculitis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). Vasculitis is "inflammation of a blood or lymph vessel[.]" *Vasculitis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).
ANCA, also called antineutrophil cytoplasmic autoantibody, is "an autoantibody to cytoplasmic constituents of monocytes and neutrophils, found in increased amounts in some types of vasculitis[]" which has "several different subtypes, each characterized serologically by reactivity against particular cellular antigens[.]" *ANCA*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Antineutrophil Cytoplasmic Autoantibody*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[28] Fibrillary glomerulonephritis is "a rare form of glomerulonephritis characterized by infiltration of the glomeruli with fibrils slightly larger than amyloid fibrils that do not stain with Congo red." *Fibrillary Glomerulonephritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). Fibrils are

involving all components of the parenchyma[29] including focal global glomerulosclerosis,[30] extensive tubular atrophy and interstitial fibrosis,[31] and moderately severe vascular sclerosis.[32]" *Id*. at 95. It also showed "extensive interstitial inflammation . . . ." *Id*. Petitioner's biopsy revealed that eighteen out of twenty-three of her present glomeruli were globally sclerosed. *Id*. Additionally:

> [T]hree glomeruli show segmental sclerosis, with segmental adhesion of the glomerular tufts to the Bowman's capsule.[33] The glomeruli do not show any

---

"minute filament[s], such as a component of fiber." *Fibril*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). Amyloid, deposits of which are primarily composed of fibrils, is "a waxy eosinophilic substance deposited in amyloidosis." *Amyloid*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). Amyloidosis refers to "a group of conditions of diverse etiologies characterized by the accumulation of insoluble amyloid in various organs and tissues of the body, which compromises vital function." *Amyloidosis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). Congo red refers to a powder used "as a diagnostic aid in amyloidosis." *Congo Red*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[29] Parenchyma refers to "the essential or functional elements of an organ, as distinguished from its framework (stroma)." *Parenchyma*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[30] Glomerulosclerosis is "fibrosis and scarring with senescence of the renal glomeruli." *Glomerulosclerosis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). Fibrosis refers to "the formation of fibrous tissue, as in repair or replacement of parenchymatous elements." *Fibrosis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[31] Interstitial fibrosis refers to idiopathic pulmonary fibrosis, a "chronic inflammation and progressive fibrosis of the pulmonary alveolar walls, with steadily progressive dyspnea, resulting finally in death from oxygen lack or right heart failure." *Interstitial Fibrosis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). Pulmonary "pertain[s] to the lungs." *Pulmonary*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). Dyspnea is "breathlessness or shortness of breath[.]" *Dyspnea*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[32] Vascular sclerosis refers to arteriosclerosis, which is "any of a group of diseases characterized by thickening and loss of elasticity of arterial walls[.]" *Arteriosclerosis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[33] The glomerular capsule, also known as the Bowman, malpighian, or müllerian capsule, is "the double-walled globular dilatation that forms the beginning of a renal tubule and surrounds the glomerulus; the inner wall is called the visceral layer and the outer wall is called the parietal layer." *Capsula Glomeruli*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

> evidence of crescent[34] formation, fibroid necrosis,[35] thrombosis,[36] or endocapillary proliferation. The glomerular basement membranes[37] appear thickened . . . . The interstitial infiltrates contain mostly mononuclear cells. In one area, there is formation of a small granuloma[38] with giant cells. There is also extensive tubular atrophy . . . .

Id. at 95–96.

On February 28, 2014, Petitioner presented to another nephrologist, Sudha M. Nayar, M.D.,[39] for a follow-up. Pet'r's Ex. 9 at 6. Dr. Nayar reviewed Petitioner's biopsy results with her, noting that it showed "[f]ibrillary [g]lomerulonephritis, that is associated with extensive chronic changes involving all components of the parenchyma . . . ." *Id*. Dr. Nayar further noted that the "light microscopic features do[] not show any evidence of [membranoproliferative glomerulonephritis ("MPGN")[40], crescents or proliferative GN." *Id*. However, Dr. Nayar wrote that the biopsy did "show[] extensive tubular atrophy and fibrosis[,] but some areas show interstitial inflammation and infiltration with mononuclear cells." *Id*. She then discussed treatment options, including an "immunosuppressive regimen," but noted that she was "not sure if immunosuppressive regimen would help delay the progression of the eventual [end-stage renal

---

[34] An epithelial crescent is "a more or less crescentic mass of cells found between the tuft of a glomerulus and the inside of Bowman capsule in rapidly progressive glomerulonephritis." *Epithelial Crescent*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 4, 2021). Rapidly progressive glomerulonephritis is "acute glomerulonephritis marked by a rapid progression to end-stage renal disease . . . ." *Rapidly Progressive Glomerulonephritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 4, 2021).

[35] Fibrinoid necrosis, also known as necrotizing arteriolitis, is "deposition of fibrin and other plasma proteins in the walls of afferent renal arterioles in malignant hypertension, often accompanied by an inflammatory infiltrate within the walls and thrombosis of the vessel lumen." *Fibrinoid Necrosis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). Fibrin is "the insoluble protein from fibrinogen by the proteolytic action of thrombin during normal clotting of blood; it forms the essential portion of the blood clot." *Fibrin*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). An arteriole, or arteriola, is "a minute arterial branch, especially one just proximal to a capillary." *Arteriola*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[36] Thrombosis is "the formation, development, or presence of a thrombus[,]" which is "a stationary blood clot along the wall of a blood vessel" that "frequently caus[es] vascular obstruction." *Thrombosis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021); *Thrombus*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[37] A basement membrane is "a thin sheet of amorphous extracellular material upon which the basal surfaces of epithelial cells rest[]" and "is interposed between the cellular elements and the underlying connective tissue." *Basement Membrane*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[38] Granuloma is "an imprecise term applied to either a small, nodular, delimited aggregation of mononuclear inflammatory cells or a similar collection of epithelioid cells[.] . . . Granuloma formation represents a chronic inflammatory response that can be initiated by infectious or noninfectious agents." *Granuloma*, DORLAND'S, https://www.dorlandsonline.com (last visited Mar. 30, 2021).

[39] Dr. Nayar worked in the same practice as Dr. Lutes. *See* Pet'r's Ex. 9 at 6.

[40] Membranoproliferative glomerulonephritis is "a chronic glomerulonephritis characterized by mesangial cell proliferation and irregular thickening of the glomerular capillary wall." *Membranoproliferative Glomerulonephritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

disease ("ESRD")[41]." *Id.* Dr. Nayar recommended "weekly bloodwork to closely monitor [Petitioner's] renal function." *Id.* at 7. Dr. Nayar further discussed with Petitioner the possibility of "renal replacement therapy including hemodialysis[42] and peritoneal dialysis[.][43]" *Id.* Petitioner expressed a desire to obtain a second opinion, and Dr. Nayar agreed that she should. *Id.*

Petitioner's medical records contain an undated note recounting a phone message Dr. Nayar left for Dr. Swauger. Pet'r's Ex. 12 at 26. Dr. Nayar stated that she "got [the] results of [Petitioner's kidney biopsy], which showed a lot of fibrosis." *Id.* Therefore, Dr. Nayar thought "that this may have been ongoing longer." *Id.* Dr. Nayar noted that the biopsy "revealed a type of proliferative GN, with fibrosis [that] can be assoc[iated] with malignancy or myeloproliferative disorder.[44]" *Id.* Dr. Nayar further noted that Petitioner's creatinine "seems to be worsening, [and was] now up to 3.9." *Id.* Dr. Nayar explained that Petitioner "may be a candidate for immunosuppressive/steroids for [treatment], but [Dr. Nayar was] not sure it will be effective . . . ." *Id.* After reviewing Petitioner's other results, Dr. Nayar concluded by recommending that Petitioner stop taking her Oxycodone immediately. *Id.*

On March 4, 2014, Petitioner presented to Dr. Swauger for a follow-up. *Id.* at 23. Petitioner stated that, despite extensive bloodwork and a kidney biopsy, her nephrologists "are not certain what the source of her kidney failure is from." *Id.* Petitioner told Dr. Swauger that "overall she feels well." *Id.* In addition, Petitioner told Dr. Swauger that "[s]he was told to have a cancer [workup], as underlying malignancy may be the source of [her] . . . problem[s]." *Id.* Dr. Swauger recommended that Petitioner undergo a chest x-ray and a biopsy of her thyroid nodule. *Id.* at 23–24. Petitioner underwent a chest x-ray on March 10, 2014, which was unremarkable. Pet'r's Ex. 3(a) at 158. Petitioner subsequently underwent a thyroid biopsy on March 21, 2014, which was "negative for malignant cells." Pet'r's Ex. 6(b) at 305, 311–13.

Petitioner had another follow-up appointment with Dr. Nayar on March 31, 2014. Pet'r's Ex. 9 at 12. Petitioner reported "feeling well" and having "good" urine output. *Id.* She did not report experiencing any nausea, vomiting, or diarrhea, and did not have any edema on examination. *Id.* Petitioner told Dr. Nayar that she had an appointment scheduled with transplant services the following month. *Id.* Petitioner also stated that she "talked with the [peritoneal dialysis ("PD")] nurse, and if needed[,] she would rather do PD." *Id.*

---

[41] End-stage renal disease is "chronic renal failure that is irreversible." *End-Stage Renal Disease*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 4, 2021).

[42] Hemodialysis is "the removal of certain elements from the blood by virtue of the difference in the rates of their diffusion through a semipermeable membrane." *Hemodialysis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[43] Peritoneal dialysis is "hemodialysis through the peritoneum[,]" which is "the serious membrane lining the walls of the abdominopelvic cavity . . . and investing the viscera . . . ." *Peritoneal Dialysis*, DORLAND'S, https://www.dorlandsonline.com/dorland/definition?id=33488&searchterm=nephritis (last visited Feb. 2, 2021); *Peritoneum*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[44] Myeloproliferative disorders are "a group of usually neoplastic diseases, which may be related histogenetically by a common multipotential stem cell . . . ." *Myeloproliferative Disorders*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

On May 31, 2014, Petitioner presented to Dr. Nayar for a follow-up. *Id.* at 16. Dr. Nayar wrote that Petitioner "has had worsening of her [r]enal functions, [with her] BUN [at ninety-five], creatinine [at] 5.4[, potassium] . . . at 5.4[, and] PO4 . . . [at] 6.6." *Id.* Dr. Nayar recommended that Petitioner "get the PD catheter[45] placed." *Id.*

Petitioner presented to Dr. Swauger on June 4, 2014, for a follow-up. Pet'r's Ex. 12 at 19. Petitioner did not complain of any "symptoms aside from continuous[,] unexplained weight loss." *Id.* Dr. Swauger noted that Petitioner's "[k]idney function has continue[d] to progressively decline, although she denies swelling, [shortness of breath], [and] fatigue." *Id.* Petitioner reported that she was scheduled to have a PD catheter placed later that month. *Id.* Dr. Nayar "[r]ecommended that [Petitioner] be vaccinated for [Hepatitis A and B], [measles, mumps, and rubella,] . . . Varicella[,] and obtain a [tetanus-diphtheria-acellar-pertussis] . . . particularly if she is anticipating a transplant, which will be followed by immune suppressive medications." *Id.* at 20. Petitioner agreed to consider getting these vaccinations but declined them on that date. *Id.*

On June 9, 2014, Petitioner presented to Dr. Nayar for a follow-up. Pet'r's Ex. 9 at 20. Dr. Nayar noted that Petitioner's "[r]enal function continues to worsen . . . ." *Id.* Petitioner's creatinine was 6.6. *Id.* Petitioner did not report any complaints and "denie[d] any uremic[46] symptoms." *Id.* Dr. Nayar wrote that Petitioner was "scheduled to . . . undergo PD cath[eter] placement on the 18th [of that month]." *Id.* Dr. Nayar continued, "[i]f [Petitioner's] labs worsen, then we will have [the surgeon] place an exposed catheter and begin [dialysis] in [two] weeks. Otherwise we will keep it buried until RRT is needed." *Id.* Dr. Nayar directed Petitioner to follow up again in three weeks. *Id.*

Petitioner had a PD catheter placed on June 18, 2014, and began PD the same day. Pet'r's Ex. 4 at 2–3. Both her pre-operative and post-operative diagnoses were listed as "[e]nd-stage renal failure." *Id.* at 2. On July 12, 2014, Petitioner presented to the emergency room "to get [her PD] catheter checked." *Id.* Petitioner explained that she "usually do[es her PD with] gravity[,]" but she had "used a circulator for the first time [that] morning and . . . [thought] it was too much . . . ." *Id.* at 25. Petitioner further explained that doctors had "increased [her dialysis] fluids to 1500 [milliliters six] days ago." *Id.* Petitioner was examined and released the same day. *See id.* at 25–41.

On August 22, 2014, Petitioner underwent a chest x-ray. Pet'r's Ex. 3 at 276. The results showed "mild emphysema[47] . . ." and "a [three millimeter,] possibly calcified pulmonary nodule laterally within the left upper lobe, likely benign but follow[-]up recommended." *Id.* at 277. They

---

[45] A catheter is "a tubular, flexible, surgical instrument that is inserted into a cavity of the body to withdraw or introduce fluid." *Catheter,* DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 4, 2021).

[46] Uremia refers to "the entire constellation of signs and symptoms of chronic renal failures, including nausea, vomiting, anorexia, a metallic taste in the mouth, a characteristic odor of the breath, pruritus, urea frost on the skin, neuromuscular disorders, pain and twitching in the muscles, hypertension, edema, mental confusion, and acid-base and electrolyte imbalances." *Uremia*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[47] Emphysema is "a pathologic accumulation of air in tissues or organs." *Emphysema*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

also showed "a 1.9 [by] 1.6 [centimeter] right thyroid nodule for which ultrasound correlation and likely biopsy [are] recommended." *Id.*

Petitioner was transported to the emergency room after suffering a seizure on August 26, 2014. Pet'r's Ex. 5 at 78. Petitioner's sister stated that Petitioner "ha[d] not been complaining of anything recently. She has not recently been sick, though the dialysis does make [her] vomit daily." *Id.* Petitioner's husband explained that Petitioner "was somewhat ill throughout the day with anorexia[,] which progressed to vomiting and some [altered mental status] . . . ." *Id.* at 76. He stated that Petitioner "then had [a] seizure [and] fell [and] hit her head." *Id.* While being treated by emergency medical services ("EMS"), Petitioner "was very combative and had a second seizure . . . ." *Id.* After her second seizure, Petitioner "was again very combative and was intubated for airway protection [and given rapid sequence intubation ("RSI")] drugs . . . ." *Id.* On arrival at the emergency room, Petitioner was "intubated, sedated on Propofol,[48] and paralyzed." *Id.* Petitioner's blood pressure on arrival was highly elevated, and her sister explained that Petitioner "ha[d] not taken any [blood pressure] med[ication] as she ran out last Friday." *Id.* at 78.

Petitioner underwent a head CT, which did not reveal "definite evidence of large acute intracranial hemorrhage,[49] territorial infarction,[50] midline shift or mass effect." *Id.* at 83. However, it did reveal some "minimal left frontal sulcal[51] hyperdensity[,] which could be artificial." *Id.* Petitioner also underwent a brain MRI, which revealed "areas of abnormal T2/FLAIR signa1 intensity seen predominantly in the subcortical white matter[52] in the left posterior temporal/occipital lobe region[,][53] as well as in the right occipital region, bilateral centrum

---

[48] Propofol is "a short-acting anesthetic and sedative used in induction and maintenance of general anesthesia and also for sedation . . . ." *Propofol*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[49] An intracranial hemorrhage is "bleeding within the cranium, which may be extradural, subdural, subarachnoid, or cerebral (parenchymatous)[.]" *Intracranial Hemorrhage*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[50] Infarction, or infarct, is "an area of coagulation necrosis in a tissue due to local ischemia resulting from obstruction of circulation to the area . . . ." *Infarct*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). Ischemia is "deficiency of blood in a part . . . of a blood vessel." *Ischemia*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[51] A sulcus is a "long groove or furrow, especially one of the cerebral sulci[,]" which are "the furrows on the surface of the brain between the cerebral gyri." *Sulcus*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021); *Cerebral Sulci*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). Cerebral gyri are "the tortuous convolutions of the surface of the cerebral hemispheres, caused by folding of the cortex and separated by sulci." *Cerebral Gyri*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[52] White matter, also known as white substance and substantia alba, is "the nervous tissue of the brain and spinal cord composed mostly of myelinated nerve fibers arranged in bundles (fasciculi)." *Substantia Alba*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[53] The temporal lobe is "the lower lateral lobe of the cerebral hemisphere . . . ." *Lobus Temporalis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). The occipital lobe is "the posterior portion of the cerebral hemisphere, on the medial surface extending from the posterior pole to the parietooccipital fissure but on the lateral surface continuous with the parietal lobe superiorly and with the temporal lobe inferiorly." *Lobus Occipitalis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). The cerebral hemisphere is "either half of the cerebrum, "which is "the main portion

semiovale, [and] left parietal region." Pet'r's Ex. 6(b) at 219. Doctors noted that, "[g]iven [Petitioner's] clinical history, these findings are concerning for an etiology such as posterior reversible encephalopathy [("PRES")].[54]" *Id*. Petitioner also underwent a psychiatric consultation on August 29, 2014. *Id*. at 216. The note reflects that Petitioner's medical history was "significant for self[-]home[-]dialysis for ESRD apparantly [sic] sustained after a flu shot a year ago." *Id.* Petitioner "acknowledged depression '[ten percent] of the time' and anxiety, related to her kidney malfunction requiring home dialysis and ultimately needing a . . . kidney transplant." *Id*. Petitioner ultimately expressed that she "does not want or require psychiatric treatment[,]" and she "decline[d] recommendation measures that include psychotherapy and potential medication . . . ." *Id*. at 220. Petitioner was discharged from the hospital that day with a final diagnosis of PRES and a prescription for Dilantin.[55] *Id*. at 222.

On September 4, 2014, Petitioner presented to Dr. Swauger to follow up regarding her recent hospitalization. Pet'r's Ex. 12 at 16. Petitioner reported "feeling okay" since discharge. *Id.* She also reported being "a little swollen, but [was not experiencing any] further headaches." *Id.* She noted that she has not experienced any nausea, vomiting, or blurred vision, but she "[a]dmit[ted] that she still d[id] not have much of an appetite . . . ." *Id*. Petitioner's examination was unremarkable, and Dr. Swauger directed her to follow up again in two months. *Id*.

Petitioner underwent a repeat brain MRI on October 2, 2014. Pet'r's Ex. 6(b) at 200. The impression was "[i]nterval resolution of areas . . . previously seen [as] parenchymal signal abnormality[] compatible with resolution of PRES." *Id*. In addition, there were "[n]o new lesions [seen] elsewhere in [Petitioner's] brain." *Id*.

On October 10, 2014, Petitioner presented to the emergency room for a malfunctioning PD catheter. Pet'r's Ex. 4 at 5. She was released the same day. *See id*. at 7. Petitioner presented to Dr. Nayar for a follow-up on October 13, 2014, and reported that "[s]he has not been able to drain [her PD catheter] since last Thursday and has not had a complete dialysis [treatment] in [five] days." *Id*. Dr. Nayar noted that Petitioner's "PD site is [clean/dry/intact,]" and a "[workup] was negative

---

of the brain, occupying the upper part of the cranial cavity." *Hemisphaerium Cerebri*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021);
Cerebrum, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[54] Posterior reversible encephalopathy syndrome, also known as reversible posterior leukoencephalopathy syndrome, posterior leukoencephalopathy syndrome, and posterior reversible leukoencephalopathy syndrome, is "a syndrome resulting from leukoencephalopathy with edema in posterior parts of the occipital and parietal lobes, characterized by headaches, confusion, seizures, and visual disturbances[.]" *Reversible Posterior Leukoencephalopathy Syndrome*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). Leukoencephalopathy refers to "any group of diseases affecting the white matter of the brain, especially of the cerebral hemispheres, and occurring as a rule in infants and children." *Leukoencephalopathy*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). The parietal lobe is "the upper central lobe of the cerebral hemisphere . . . ." *Lobus Parietalis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[55] Dilantin is a trademark for phenytoin, an anticonvulsant used to treat and prevent seizures and related disorders. *Dilantin*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021); *Phenytoin*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

for [p]eritonitis.[56]" *Id.* On exam, Dr. Nayar noted that Petitioner was "volume overloaded[,]" although she "state[d that] she is voiding a moderate [amount] on her current dose of Lasix[57] . . . ." *Id.* Therefore, Dr. Nayar "advised [Petitioner] to go to the hospital for [hemodialysis ("HD") cath[eter] placement so [they] could start [HD] . . . ." *Id.* However, Petitioner "refus[ed] to do so at [that] time[]" and noted that she had an appointment for an evaluation of her PD catheter the following day. *Id.*

Petitioner reported again to the emergency room on October 15, 2015, "with complaints of abdominal pain, generalized fatigue, malaise[,] and diaphoresis.[58]" Pet'r's Ex. 3(a) at 331. The note continues that, "[a]pparently, [Petitioner] ha[d] not received her scheduled [PD] due to malfunctioning of her [PD] catheter." *Id.* Petitioner indicated that she "had a laparoscopic removal of [her PD] catheter scheduled . . . ; however, owing to her condition becoming worse[,] she presented to the [emergency room]." *Id.* While at the emergency room, Petitioner had a consultation with Dr. Nayar. *Id.* at 334–36. Dr. Nayar reviewed Petitioner's medical history and noted that Petitioner was "on [the] active transplant list and [was] waiting for her sister to possibly donate a kidney." *Id.* at 334. Dr. Nayar was concerned that Petitioner was suffering from peritonitis, and she conducted a draining procedure to procure fluid to culture. *Id.* at 335. Dr. Nayar also wrote that Petitioner would undergo "[HD] until [doctors could] evaluate the PD catheter to see if this modality can be continued." *Id.* at 336. Petitioner underwent a successful HD catheter placement on that date. Pet'r's Ex. 3(b) at 97. Petitioner was ultimately diagnosed with peritonitis and prescribed Vancomycin[59] and Zosyn.[60] Pet'r's Ex. 3(a) at 339. She was discharged on October 17, 2014. *Id.* at 318.

On October 22, 2014, Petitioner presented to Dr. Swauger for a follow-up. Pet'r's Ex. 12 at 11. Petitioner reported that she was "currently receiving the antibiotics while on HD[]" and was "going to HD on [Monday/Wednesday/Friday]." *Id.* Petitioner further stated that "[s]he ha[d] not had any further seizures[] and [was] weaning off of the [seizure] medication." *Id.* Dr. Swauger recommended that Petitioner receive the Hepatitis A/B, flu, and pneumovax vaccines, but Petitioner declined. *Id.* at 12. Dr. Swauger noted that Petitioner was "tolerating HD much better than [PD]." *Id.*

---

[56] Peritonitis is "inflammation of the peritoneum, with exudations of serum, fibrin, cells, and pus . . . ." *Peritonitis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[57] Lasix is a trademark for furosemide, "a loop diuretic used in the treatment of edema associated with congestive heart failure or hepatic or renal disease, as an adjunct in the treatment of acute pulmonary edema, and in the treatment of hypertension . . . ." *Lasix*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[58] Diaphoresis is another word for sweating. *Diaphoresis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[59] Vancomycin hydrochloride is an antibiotic. *Vancomycin Hydrochloride*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[60] Zosyn is a trademark for a combination of piperacillin sodium and tazobactam sodium, which are used to treat infections. *Zosyn*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Piperacillin Sodium*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Nephritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Tazobactam Sodium*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

Petitioner had an AV fistula[61] placed in her left arm by Gene W. Manzetti, M.D., on November 20, 2014. Pet'r's Ex. 10 at 18. At follow-up appointments with Dr. Manzetti on January 12 and February 9, 2015, Dr. Manzetti noted that Petitioner's fistula was "showing some maturation" but also noted that Petitioner "does have a lot of venous tributaries over her forearm." *Id.* at 6–7. On March 9, 2015, Petitioner's fistula was declared "occluded[,]" and Dr. Manzetti wrote that "the plan will be to have [Petitioner] undergo creation of a higher AV fistula." *Id.* at 5. Petitioner underwent a successful placement of an AV fistula in her upper left arm on March 17, 2015. *Id.* at 2.

III. Experts

A. Expert Review

1. Petitioner's Expert, M. Eric Gershwin, M.D.

Dr. Gershwin received his medical degree from Stanford University in 1971. Pet'r's Ex. 20 at 1. He is licensed to practice in California and holds board-certifications in internal medicine, internal medicine with a subspecialty in rheumatology as well as allergy and clinical immunology. *Id.* at 2. Dr. Gershwin's clinical experience includes serving as the Chief of the Division of Rheumatology/Allergy and Clinical Immunology at the University of California School of Medicine, Davis since 1982. *Id.* He also has academic experience, including serving as the Jack and Donald Chia Professor of Medicine within the Division of Rheumatology/Allergy and Clinical Immunology at the University of California, Davis and as a Distinguished Professor of Medicine within the same division. *Id.* at 1. Dr. Gershwin's curriculum vitae includes numerous books, book chapters, and research papers of which he is a listed author. *See id.* at 8–125.

During his testimony, Dr. Gershwin stated that he has experience with treating patients with kidney diseases, but he also noted that he "do[es] not have significant experience" treating patients with FGN and estimated that he "perhaps [had] seen one or two [FGN] patients" during his entire career. *See* Tr. 54:23–55:12. In response to my questioning, Dr. Gershwin stated that neither his research nor his publications involved FGN, although he has conducted research on nephritis, which he described as being "mostly related to lupus[,]" and on "other autoimmune kidney diseases . . . ." Tr. 56:18–57:4.

Dr. Gershwin submitted two expert reports and testified at the entitlement hearing. *See* Pet'r's Exs. 19, 49; Tr. 51:1–106:23, 167:1–168:7. At Petitioner's request, and without objection from Respondent, I admitted Dr. Gershwin to testify as an expert in internal medicine, rheumatology, and immunology. Tr. 56:9–16.

2. Petitioner's Expert, Wesam F. Ballouk, M.D.

[61] AV fistula refers to a "passage[that] may be . . . created surgically for arteriovenous access . . . ." *Fistula*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *see also AV*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

Dr. Ballouk received his medical degree from Damascus University in 1996. Pet'r's Ex. 18 at 1. He completed an internship in psychiatry/internal medicine and a residency in internal medicine at the University of Tennessee Health Science Center in 2000 and 2002, respectively. *Id.* Dr. Ballouk also completed a post-residency fellowship in nephrology at the same institution in 2005. *Id.* He is licensed to practice medicine in both Tennessee and Arkansas, and he is board-certified in both internal medicine and nephrology. *Id.* at 2; Tr. 175:25–176:2. Dr. Ballouk's clinical experience includes serving as the Chairman of the Nephrology Division in the Internal Medicine Department at Saint Francis Hospital in Bartlett, Tennessee since 2006. *Id.* Also beginning in 2006, Dr. Ballouk has served as the Medical Director of multiple HD units in Tennessee, and in 2013, Dr. Ballouk began serving as the Medical Director of a home dialysis unit. *Id.* Dr. Ballouk also has academic experience, including serving as an Assistant Professor of Internal Medicine at the University of Tennessee Health Science Center from 2007 to 2015. *Id.*

Dr. Ballouk submitted two expert reports and testified at the entitlement hearing. *See* Pet'r's Exs. 18, 50; Tr. 174:20–283:25, 388:16–402:7. At Petitioner's request, and without objection from Respondent, I admitted Dr. Ballouk to testify as an expert in internal medicine and nephrology. Tr. 177:15–20.

3. Respondent's Expert, Arnold Levinson, M.D.

Dr. Levinson received his medical degree from the University of Maryland in 1969. Resp't's Ex. D at 1. He is licensed to practice medicine in Pennsylvania and is board-certified in internal medicine and allergy and clinical immunology. *Id.* at 2–3. Dr. Levison has extensive academic and practical experience, although he retired in 2014. He served as a Professor of Medicine and Neurology at the University of Pennsylvania School of Medicine from 1994 to 2009, and as an Associate Director of Undergraduate Medical Education at the same institution from 1997 to 1999. *Id.* at 2. His clinical experience includes serving as the Chief of the Allergy and Immunology Section within the Pulmonary, Allergy, and Critical Care Division at the University of Pennsylvania School of Medicine from 1998 to 2009. *Id.* He also served as the Chief of Allergy and Immunology at the Philadelphia Veterans Administration Medical Center from 1999–2007. *Id.* His curriculum vitae includes numerous publications and editorials of which he is a listed author. *See id.* at 10–21.

Since his retirement in 2014, Dr. Levinson explained that he, among other responsibilities, "still maintain[s] a significant amount of activity . . . at [the University of Pennsylvania] . . . in the teaching arena, particularly teaching and mentoring fellows, and to some extent residents . . . ." Tr. 109:17–24. Prior to his retirement, Dr. Levinson estimated that "about [twenty] percent[]" of his time was devoted to patient care, mainly those "who suffered from complex allergic autoimmune . . . and/or immunodeficiency disorders." Tr. 110:12–21.

Dr. Levinson submitted one expert report and testified at the entitlement hearing. *See* Resp't's Ex. C; Tr. 107:23–163:6. At Respondent's request, and without objection from Petitioner, I admitted Dr. Levinson to testify as an expert in immunology and clinical immunology. Tr. 113:19–23.

4. Respondent's Expert, Derek M. Fine, M.D.

Dr. Fine received his medical degree from the Johns Hopkins University School of Medicine in 1994. Resp't's Ex. B at 1. He completed his internship and residency at the Johns Hopkins Hospital/University School of Medicine from 1994 to 1997, and a fellowship in nephrology at the same institution from 1997 to 1999. *Id.* at 2. He currently holds both academic and clinical positions. *Id.* at 1. Beginning in 2008, he has served as an Associate Professor of Medicine at the Johns Hopkins University School of Medicine, and since 2009, he has served as the Fellowship Director within the Division of Nephrology at the same institution. *Id.* Beginning in 2014, Dr. Fine has served as the Medical Director at Johns Hopkins Davita – Bond Street Dialysis Unit. *Id.* His curriculum vitae includes numerous publications of which he is a listed author. *See id.* at 2–10. Dr. Fine estimated that he spends five to fifteen percent of his time on research, depending on the year. Tr. 289:19–22.

Dr. Fine explained during his testimony that his work involves diagnosing patients at all stages of various renal diseases, and that he has seen "probably around four or five[]" patients with FGN throughout his career. Tr. 290:25–291:10. Dr. Fine also noted that he has experience in pathology, which he described as "sort of [an] ongoing education in pathology [whereby he] frequently look[s] at pathology with [the] pathologists [at Johns Hopkins] and discuss[es] the findings and the implications [of biopsies and pathology reports,] and [therefore he has] a fairly solid base of . . . nephropathology." Tr. 291:11–292:5.

Dr. Fine submitted two expert reports and testified at the entitlement hearing. *See* Resp't's Exs. A, E; Tr. 284:19–387:23. At Respondent's request, and without objection from Petitioner, I admitted Dr. Fine to testify as an expert in nephrology. Tr. 292:6–9.

B. Expert Reports and Testimony

1. Petitioner's Expert, Dr. Gershwin

Dr. Gershwin stated that his theory was that the flu vaccine "exacerbated [Petitioner's] ongoing FGN." Tr. 58:3–4. Specifically, Dr. Gershwin wrote that his theory was "that the cytokine response following the [flu] vaccination would have accelerated [Petitioner's] [GN] and made it worse. In other words, she went from the onset of a renal disease to requiring dialysis at a more rapid rate than one would anticipate." Pet'r's Ex. 19 at 1. He explained that he built his theory on two assumptions. First, Dr. Gershwin assumed "that the time of onset of [Petitioner's] FGN was about the same time, [or] certainly preceded the [flu] vaccination." Tr. 58:6–8. He noted that "if the time of [FGN] onset was distant from the vaccination, then [he] would not hold" the opinion that the flu vaccine exacerbated Petitioner's FGN. Tr. 58:8–9. Dr. Gershwin stated that "[i]f this disease started six months before the vaccination[,]" he would not hold his opinion or offer it. Tr. 83:2–4. He indicated that his opinion was based on onset "certainly within a window of six weeks before the vaccine." Tr. 83:9–10. Second, Dr. Gershwin "assumed that [Petitioner's] FGN was worse than what one would expect in an individual of her age with FGN." Tr. 58:10–12. Again, Dr. Gershwin noted that "if there's evidence and the Court is convinced that the natural history of her FGN was the same as you would expect of another cohort of patients with FGN, then [he] would not be here." Tr. 58:12–15.

During his testimony, Dr. Gershwin discussed cytokines in detail. He explained that "a cytokine is a low molecular weight material produced by a whole variety of cells in the body." Tr. 61:6–7. He noted that "[v]irtually any cell can produce some form of cytokine, or a chemokine or what's often called its cognizant receptor," and explained that they are "a way to signal or activate cells. [Cytokines] allow[] cells to talk to each other." Tr. 61:8–11. He stated that cytokines "facilitate[] the immune response, amplif[y the] immune response." Tr. 62:19–20. He further stated that cytokine signaling can affect cell behavior in a multitude of ways, the effectiveness of which "will depend on the health of the cell . . . ." Tr. 64:2–7. He provided the following example of how cytokines can affect cell behavior: "a very simple example is [a cytokine] can make cells divide. It can make cells go through autophagy, which is a form of how cells die . . . ." Tr. 64:5–11. Dr. Gershwin further testified that cytokines are involved in both the innate and adaptive immune systems, and that doctors "classically . . . divided cytokines into what are called Th1 and Th2 responses, [or] those that promote inflammation and those that inhibit inflammation." Tr. 62:24–63:7.

Dr. Gershwin also opined that cytokines can act both locally and systemically. Tr. 66:8–16. He cited to an article by Ortega and Fornoni to support this proposition. Tr. 65:3–66:7; Pet'r's Ex. 57.[62] The authors of this article conducted a literature review to "provide a general comprehensive overview of the role of the main cytokine families in the setting of [acute kidney injury], CKD, [end stage kidney disease], [GN], and transplantation, and to explore their relationship to clinical outcomes, mortality, and recovery of renal function." Pet'r's Ex. 57 at 2. They noted that "cytokines may act in a systemic, paracrine, or an autocrine fashion." *Id*. at 1. Dr. Gershwin provided further explanation of these terms. He explained that "systemic" means that "cytokines that are produced elsewhere [in the body] . . . can act at a distant site [elsewhere in the body]." Tr. 65:16–17. He further explained that "paracrine" refers to "a cell-to-cell interaction," whereas "autocrine" refers to "an individual cell [that] secretes cytokines and then the cytokines will feed back and impact its own cell." Tr. 65:19–66:1. Dr. Gershwin affirmed that the "key takeaway" from this article is the discussion of the different ways that cytokines can act on a cell. Tr. 66:8–11. During his testimony, he noted that "in this case, we're really referring to systemic." Tr. 66:11–12. Dr. Gershwin testified, however, that "these [types of action] overlap." Tr. 66:12–13. The article concludes by noting that currently available studies on cytokines "do not provide any evidence for a causative role of a given cytokines in disease pathogenesis or progression." Pet'r's Ex. 57 at 12.

In his first expert report, Dr. Gershwin wrote that "[t]he role of cytokines in the activity of the immune mediated/inflammatory renal disease has been the subject of intense study for more than [twenty] years." Pet'r's Ex. 19 at 2. He cited to a study by Niemer et al., the data of which Dr. Gershwin described as "confirmatory of earlier work that there is a contribution of both pro-inflammatory and anti-inflammatory cytokines[63] by renal cells that contribute to the natural history

---

[62] Luis M. Ortega & Alessia Fornoni, *Role of Cytokines in the Pathogenesis of Acute and Chronic Kidney Disease, Glomerulonephritis, and End-stage Kidney Disease*, 2 INTERN. J. OF INTERFERON, CYTOKINE AND MEDIATOR RESEARCH 49 (2010).

[63] Cytokine is "a generic term for nonantibody proteins released by one cell population . . . on contact with a specific antigen, which act as intercellular mediators, as in the generation of an immune response." *Cytokine*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

of disease." *Id.*; Pet'r's Ex. 52.[64] In this study, the authors "examined the in situ expression of [interleukin ("IL")]-10[65] and [tumor necrosis factor ("TNF")[66]]-α in renal biopsy specimens from patients with different forms of GN and variable clinical presentations." *Id.* at 2. They found "that resident renal cells are the major source of TNF-α and IL-10." *Id.* at 12. They "propose[d] that TNF-α is involved in the pathogenesis of interstitial fibrosis, . . . [whereas the] excessive production [of IL-10] seems to be associated with active and/or progressing glomerular lesions." *Id.* The authors concluded that their study "confirm[s] previous suggestions that pro[-]inflammatory and anti[-]inflammatory cytokines are produced in situ by resident renal cells and contribute to the natural course of human GN." *Id.* at 1.

Dr. Gershwin opined that "[a] vaccine would not work unless it produced cytokines." Tr. 61:13–14. Dr. Gershwin cited to a paper by Morel and Turner to support this proposition. Tr. 61:17–62:9; Pet'r's Ex. 56.[67] The authors conducted a "review [that] focus[es] on recent advances in the ways [dendritic cells][68] and cytokines can be used to develop the most appropriate and effective vaccines." Pet'r's Ex. 56 at 1. When discussing cytokines, the authors wrote that "[c]ytokine production . . . plays an important role in defining the type of T cell effector response that is induced." *Id.* at 2. They concluded that "[dendritic cells] and the cytokines they produce play a key role in driving . . . immune responses and can be harnessed to induce an effective immune response against the pathogen or disease of choice." *Id.* at 7–8. Dr. Gershwin testified that this article "emphasiz[es] that in producing vaccines, the measurement of cytokines is basically the gold standard, meaning when you're trying to design a vaccine, one way to predict how optimal it is [by] how good of a cytokine response it produces." Tr. 62:10–16.

When discussing the flu vaccine generally, Dr. Gershwin testified that it triggers the production of cytokines. Tr. 67:14–16. He explained that the types of cytokines produced by the flu vaccine in "individuals will be different, and they'll be different by age, but some of the key [cytokines produced by the flu vaccine] are interferon family, IL-2, IL-5, IL-10, IL-17, IL-21.

---

[64] Zofia I. Niemir et al., *In Situ Upregulation of IL-10 Reflects the Activity of Human Glomerulonephritides*, 32:1 AM. J. OF KIDNEY DISEASES 80 (1998).

[65] Interleukin-10 is "a cytokine produced by activated macrophages, certain lymphocytes, and other cells that decreases both innate and T cell-mediated immune inflammation[.]" *Interleukin-10*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[66] Tumor necrosis factor refers to "either of two lymphokines that are capable of causing in vivo hemorrhagic necrosis of certain tumor cells but not affecting normal cells[.]" *Tumor Necrosis Factor*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). Lymphokines are "soluble cytokine[s] that mediate[] immune responses[]" that are "released by sensitized lymphocytes on contact with antigen." *Lymphokine*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). Lymphocytes are "any of the mononuclear, nonphagocytic leukocytes, found in blood, lymph, and lymphoid tissues, that are the body's immunologically competence cells and their precursors." *Lymphocyte*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). Leukocytes are white blood cells, "colorless blood cell[s] capable of ameboid movement[.]" *Leukocyte*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[67] Penelope A. Morel & Michael S. Turner, *Designing the Optimal Vaccine: The Importance of Cytokines and Dendritic Cells*, 3 OPEN VACCINE J. 7 (2010).

[68] Dendritic refers to dendrites, which are "threadlike extensions of the cytoplasm of a neuron . . . ." *Dendritic*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021); *Dendrite*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

Lots of other ones as well." Tr. 67:17–23. Dr. Gershwin stated that cytokines produced by the flu vaccine "help facilitate the immune response, they will act on cells, they will amplify them, so in effect cell differentiation, [and] would promote inflammation." Tr. 68:20–24. He continued, "[t]hey will make an ongoing inflammation get worse," depending on "the window of opportunity" of when the vaccine is administered. Tr. 68:25–69:2. When asked whether "cytokines that are produced in a host following a vaccine[] . . . travel around the body," Dr. Gershwin responded that "they do get in the sera, and they do have a sera half[-]life. And the antigen [in the vaccine] will be systemic as well, but it's really in the sera cytokines that will affect, in a systemic way, peripheral cells as well." Tr. 69:3–10. He further explained that the cytokines "get around the body because you can measure them in circulation." Tr. 69:11–12. Dr. Gershwin also opined that these cytokines would interact with the kidneys, "[p]articularly . . . if . . . [the vaccination occurs in] the early phase of [Petitioner's kidney] disease." Tr. 70:1–5.

Dr. Gershwin also discussed FGN during his testimony, although he noted that he "will defer to [the] nephrologists" on FGN-specific topics. Tr. 70:8–9. He described FGN as "an enigmatic form of [GN]. [It is an e]nigmatic form of kidney inflammation, and there are these . . . filaments that are deposited, they're very small, they stain. We don't know that much about it." Tr. 70:9–13. Dr. Gershwin referred to FGN as an immunological disease, and he cited to an article by Rosenstock and Markowitz for support. Tr. 70:24–72:6; Pet'r's Ex. 55.[69] The authors of this paper wrote that "[t]he fibrils that characterize FGN are predominantly confined to the glomeruli and stain intensely by IF for IgG, C3, κ, and λ, strongly suggesting that the fibrils are composed of a complex of antibodies and antigens." Pet'r's Ex. 55 at 1. They continue, "[t]he absence of staining for Congo red (with rare exception) and the composition of the fibrils help to differentiate FGN from amyloidosis,[70] while the diameter of the fibrils and the absence of a microtubular appearance with a hollow core help differentiate FGN from immunotactoid glomerulopathy.[71]" *Id.* Dr. Gershwin testified that this passage suggests that FGN is an immunological disease, as the authors "even use the word immunotactoid, in the next to last word of that [passage]. But there is still a wide gap in knowledge." Tr. 71:24–72:6.

When asked whether cytokines played a role in pathogenesis of FGN, Dr. Gershwin stated that "cytokines play a role in [GN]. As far as [he] know[s] . . . there is nobody who has studied cytokine biology in FGN." Tr. 72:7–11. He explained that this lack of a definitive answer stems from FGN being "uncommon, [and he] suspect[s] people don't have enough patients in one series to be able to do those sorts of intensive studies . . . . There haven't been evidence-based, double-blind studies, as there have been in lupus nephritis[72][, for example.] So[,] there is this gap." Tr. 72:14–24. However, Dr. Gershwin stated he "would still argue that proof of principle analogy that

---

[69] Jordan L. Rosenstock & Glen S. Markowitz, *Fibrillary Glomerulonephritis: An Update*, 4 KIDNEY INT. REP. 917 (2019).

[70] *Id.*

[71] Immunotactoid glomerulopathy is "a type of fibrillary glomerulonephritis having particularly large fibrils (immunotactoids). *Immunotactoid Glomerulopathy*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[72] Lupus nephritis is "glomerulonephritis (diffuse, focal, or membranous) associated with systemic lupus erythematosus, marked by deposition of antigen-antibody complexes in the mesangium and basement membrane." *Lupus nephritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

cytokine biology, as with any other form of inflammation, would play a critical role." Tr. 72:25–73:2.

Dr. Gershwin testified that he "[a]bsolutely" recommends the flu vaccine to his patients. Tr. 75:16–18. Dr. Gershwin further testified that he would recommend the flu vaccine to his patients that have kidney disease "if they aren't in the early phase" of the disease. Tr. 75:19–20. He explained that "some of the best studies that have been done on vaccination are done in people with established disease." Tr. 76:3–5. He further explained this distinction by comparing patients with "ongoing" disease, like lupus and rheumatoid arthritis [("RA")],[73] with patients that have an acute onset of kidney disease. Tr. 75:22–77:2. Dr. Gershwin testified that lupus and rheumatoid arthritis have "latency time[s] . . . measured in years. So[,] if [he] see[s] a patient in [his] clinic and [he's] about to start the biologics, [he] will vaccinate them, but . . . their disease . . . probably began [five] or [ten] years earlier." Tr. 76:2–10. He further explained that doctors "can find evidence of antibodies in the blood in rheumatoid arthritis and even lupus patients many, many years before they ever get clinical symptomatology." Tr. 76:10–13. Therefore, he would vaccinate these types of patients. Tr. 76:2.

However, Dr. Gershwin stated that that is "a different scenario than comparing the safety of vaccines in somebody . . . just beginning the throws of an acute renal process[,] which involves inflammation." Tr. 76:21–24. He wrote that "[t]he basis for concern regarding administration of [the flu] vaccine in an active inflammatory response is the altered immune profile and, in particular, the cytokine response that is produced following vaccination." Pet'r's Ex. 19 at 3. He explained that the "[flu] vaccine elicits a rigorous cytokine response and this response begins within hours of the vaccination." *Id*. He further explained that "[t]his [inflammatory response] would have significantly aggravated any underlying inflammation, including and, in particular, [Petitioner's] pre[-]existing [FGN]." Pet'r's Ex. 49 at 1.

Dr. Gershwin explained that the flu vaccination "accelerated [Petitioner's] kidney disease." Tr. 79:18. He affirmed that Petitioner would have been at risk for exacerbation by the flu vaccine "[i]f . . . [Petitioner] was in the early phases of [her] disease[]" when she was vaccinated. Tr. 78:2–6. If this was the case, then Dr. Gershwin believes that Petitioner "was a susceptible host because she was in the initial phases of her active kidney disease." Tr. 79:15–16. In this scenario, he explained that:

> [the flu vaccine] would have led to upregulation of multiple cytokines, including pro-inflammatory cytokines, which . . . would exacerbate an ongoing inflammatory process in the kidney, both from a systemic perspective, . . . cytokines coming in affecting cells, which might affect those cells both in a paracrine and in an autocrine fashion.

Tr. 78:16–22.

[73] Rheumatoid arthritis is "a chronic systemic disease primarily of the joints, usually polyarticular, marked by inflammatory changes in the synovial membranes and articular structures and by muscle atrophy and rarefaction of the bones." *Rheumatoid Arthritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

Prior to receiving the flu vaccine at issue, Dr. Gershwin stated that Petitioner had not been diagnosed with or treated for nephritis. Tr. 73:13–16. Dr. Gershwin nonetheless opined that Petitioner "was suffering from it at the time of her vaccin[ation]," although he was "really bas[ing] that on the nephrologist." Tr. 73:20–23. He continued that nephrologists "have an opinion about that . . . , which helps [them] to come to that [opinion], and that is that the nausea that people experience from renal failure often is more dependent on the rate of rise of BUN in the absolute amount." Tr. 73:22–74:1. He further explained that "somebody with acute renal failure in which there's a . . . rise in BUN[] is more likely to experience nausea." Tr. 74:5–8. However, Dr. Gershwin again stated that he would defer to a nephrologist" when asked whether he had an opinion as to the onset date of Petitioner's FGN. Tr. 74:15–18.

Dr. Gershwin discussed the harm caused by Petitioner's flu vaccine by citing to Petitioner's biopsy results. Dr. Gershwin identified the "extensive inflammation" present, which he noted was "critical to [his] opinion because inflammation is never helpful, even in most infectious diseases. It can be harmful." Tr. 80:21–24. He also identified the following line in the biopsy report as significant to his opinions: "The interstitial infiltrates contain mostly mononuclear cells." Tr. 81:11–12 (quoting Pet'r's Ex. 3 at 96). Dr. Gershwin described "mononuclear cells, or monocytes," as "professional antigen-presenting cells[]" that "would be particularly susceptible to cytokines." Tr. 81:14–15. He also referenced "the one giant cell," which he described as "consistent with an immune inflammatory response." Tr. 81:22–82:2.

Although Dr. Gershwin wrote, "it is unknown what the actual date of onset of [Petitioner's GN] is," he noted that, "it is clear that there was significant exacerbation in the beginning of November 2013, which culminated in the hospitalization on November 21, 2013." Pet'r's Ex. 19 at 3. Dr. Gershwin disagreed that Petitioner's symptoms during this hospitalization were caused by a gastrointestinal illness, as suggested by Respondent, because "[t]here wasn't anyone else who was sick at the time, there wasn't any blood, there wasn't a history of food poisoning . . . ." Tr. 83:24–84:4. Dr. Gershwin also noted that none of Petitioner's treaters diagnosed her with a gastrointestinal illness during this time. Tr. 84:11–14. In addition, Dr. Gershwin thought that Petitioner's "symptoms [during her hospitalization] would be consistent with acute renal failure. The nausea, the vomiting, the abdominal pain on exam was said to be mild, but it would be consistent with someone who's vomiting." Tr. 84:2–6. Dr. Gershwin further opined that diarrhea, which Petitioner also experienced, "can be present with acute renal failure." Tr. 84:7–8.

In addition, Dr. Gershwin testified that he "couldn't find any[]" other aggravating factor for Petitioner's FGN other than the flu vaccine. Tr. 84:14–18. He disagreed that Petitioner's use of prescription pain medication played a role in her disease course, noting that "there was no concurrent evidence of liver disease[, which] one would have expected such a feature in many patients." Pet'r's Ex. 19 at 3. He testified that Petitioner "showed no signs of liver toxicity[]" despite being "on [the pain medication] for a long time." Tr. 82:13–14. Dr. Gershwin also wrote that "there is no literature to support the induction of [FGN] with pain medication." Pet'r's Ex. 19 at 3.

Dr. Gershwin concluded his first expert report by writing that he "would not have recommended vaccination on September 23, 2013," because Petitioner was in the acute process of

her FGN. *Id*. However, Dr. Gershwin further wrote that he does "not have any concern about vaccinating her now. In other words, her kidney disease is essentially burned out and she is dependent on dialysis." *Id*. Therefore, he does "not envision a problem for further vaccination in people with stable renal failure." *Id*. However, on cross-examination, Dr. Gershwin testified that he "would ask . . . a nephrologist" as to when Petitioner's disease burned out. Tr. 93:23–94:1. Dr. Gershwin clarified that he made his statement regarding vaccinating Petitioner now "only to explain . . . that [he] had no problem about vaccinating people with [ESRD] or longstanding autoimmune disease." Tr. 94:4–7.

In response to my questioning, Dr. Gershwin explained that the inflammation stays in Petitioner's kidneys because there's "already . . . an early ongoing inflammatory process going on, which is immunologic, and then the cytokines would work there, produce harm . . . . It's like a wound that [the cytokines are] exacerbating." Tr. 100:3–7. He disagreed that Petitioner had inflammation in other parts of her body, namely her intestine and arm, noting that "the intestine was just the symptom of the elevated BUN and the nausea from renal failure." Tr. 100:8–14. He opined that "if you do a biopsy, there was no colitis, no ulcerative colitis, no inflammatory gastroenteritis . . . . [A]t the [vaccination] site, there was some marker inflammation, and yes, that is part of the immune response to the vaccine . . . . [B]ut [he doesn't] think it played any role in systemic disease." Tr. 100:16–22. He continued, "[a]nd because there wasn't already an ongoing disease going on there, there's nothing for [the vaccine] to exacerbate." Tr. 100:22–24.

2. Petitioner's Expert, Dr. Ballouk

Dr. Ballouk submitted two expert reports in this case. In his first report, Dr. Ballouk wrote that he "agree[s] that [Petitioner] has rapidly progressing [FGN,]" which he described as an "inflammatory disease." Pet'r's Ex. 17 at 2. He opined that Petitioner "was likely suffering from nephritis at the time of her vaccination . . . , but she did not have any clinical manifestations of nephritis at that time." *Id*. Dr. Ballouk wrote that "[i]t is possible that vaccination accelerated and made [Petitioner's] nephritis worse[,]" and if it did, he argued that "the timing was appropriate given her hospitalization in November 2013 with renal insufficiency, which was likely the first clinical manifestation of her nephritis." *Id*. Dr. Ballouk noted that "[i]t is [his] opinion that [the] flu vaccin[e] can produce an immune response[,] which includes cytokine production[;]" however, Dr. Ballouk also wrote that "the opinions of an immunologist would be helpful[]" in determining "whether it is more likely than not that [Petitioner's] vaccination did aggravate her nephritis . . . ." *Id*. Aside from a brief factual background on Petitioner's clinical course, Dr. Ballouk did not provide any additional information in his first expert report. *See id*. at 1–2.

During his testimony, Dr. Ballouk expanded upon the points he discussed in his first expert report. Dr. Ballouk described GN as "inflammation of the glomeruli, which is the filtering part of the nephron[74] in the kidneys. Each kidney has millions of nephrons, and if there's any

[74] The nephron is "the anatomical and functional unit of the kidney, consisting of the renal corpuscle, the proximal convoluted tubule, the descending and ascending limbs of the loop of Henle . . . and the collecting tubule." *Nephron*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). The renal corpuscle is "a body that forms in the beginning of a nephron, consisting of a glomerulus surrounded by the glomerular capsule (an expanded portion of the renal tubule). *Renal Corpuscle*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). The proximal convoluted tubule

inflammation of the glomeruli, that will affect the function of the kidney." Tr. 183:1–7. He stated that there are multiple causes of GN, including immune diseases, vasculitis, or nephrotic syndrome. Tr. 183:8–12. He also stated that GN "can cause renal failure." *Id*.

Dr. Ballouk described FGN as "one rare kind of [GN]." *Id*. He noted that "the exact cause is not yet known[,]" although he explained that "there are some coexisting factors found in the literature, like . . . [ten] to [twelve] percent [of FGN patients] have [an] autoimmune disease, like lupus." Tr. 184:17–21. He also listed "[H]epatitis C" and "malignancy" as other coexisting factors. Tr. 184:20–21. Dr. Ballouk stated that FGN is a "little bit closer to an immune disease, so [it is] treat[ed] with immunosuppressants . . . [and] Prednisone.[75]" Tr. 184:22–185:1. He explained that FGN is thought of as an immune disease because "[t]here are new research studies showing that [FGN] is more like an inflammation with antibodies presented in the kidneys, . . . called DNAJB. That will tell me that there is acute inflammation of the kidneys. . . . [I]t's kind of similar to autoimmune disease, like we see in lupus, and that will make me feel that . . . immunosuppressant medications will help in this kind of disease." Tr. 185:2–13.

Dr. Ballouk testified that FGN is "usually diagnosed by biopsy." Tr. 183:24–25. He explained that "[f]irst . . . , the nephrologist will suspect [that] the patient [has GN] from the symptoms[,]" which he described as "swelling, sometimes feeling bad like nausea. All the symptoms of renal insufficiency and proteinuria." Tr. 185:15–21. In addition, Dr. Ballouk explained that many patients will complain of "foamy urine, . . . and a urine test . . . [will] find that they have a lot of protein or blood in the urine." Tr. 185:21–22. He continued, "[t]hen [doctors will] do . . . blood work[,] which shows . . . BUN and creatinine . . . rising, so [doctors] will send [the patient] for a kidney biopsy . . . ." Tr. 185:23–25. Dr. Ballouk noted that FGN is "very hard to diagnose . . . without a biopsy." Tr. 183:25–184:1.

During his testimony, Dr. Ballouk discussed the results of Petitioner's kidney biopsy. Tr. 196:10–199:16. Dr. Ballouk stated that the biopsy results showed that Petitioner "had [FGN] for sure, with interstitial nephritis and focal global glomerulosclerosis and some extensive fibular atrophy." Tr. 199:21–24. He continued, "looking at live microscope, that will also tell [a doctor] that [Petitioner] has some meningeal infiltrations with few nuclear cells." Tr. 196:24–197:1. Dr. Ballouk explained that "in the live microscopy, [one] will find some changes consistent with [GN], there will be an infiltration and inflammation in the mesangial and the glomerular basement membrane . . . ." Tr. 197:2–5. In addition, Dr. Ballouk wrote "the lack of crescents on [Petitioner's] biopsy does not mean that [Petitioner's] vaccination did not aggravate her disease. [The b]iopsy

---

is "the most proximate part of the renal tubule, extending from the glomerular capsule to the proximate straight tubule[.]" *Tubulus Contortus Proximalis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). The loop of Henle, or nephron loop, is "a long, U-shaped part of the renal tubule, extending through the medulla from the end of the proximal convoluted tubule to the beginning of the distal convoluted tubule." The loop "begins with a descending limb having a thick-walled segment called the proximal straight tubule, followed by a thin-walled segment called the thin or attenuated tubule; this is followed by the ascending limb, which sometimes includes the distal end of the attenuated tubule and always ends with a long thick-walled segment called the distal straight tube." *Ansa Nephroni*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[75] Prednisone is "a synthetic glucocorticoid derived from cortisone, administered orally as an antiinflammatory and immunosuppressant in a wide variety of disorders." *Prednisone*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

was performed approximately [five] months post vaccination and [four] months after her first recorded elevated creatinine. Therefore, active disease could have ceased prior to biopsy." Pet'r's Ex. 50 at 2. When asked about the lack of crescents in Petitioner's biopsy, Dr. Ballouk espoused that "[a]ctually, reviewing the literature about [crescents], [they don't] exist [in] probably more than like [thirteen] percent [of patients] in this kind of [this] disease. So[,] this is not the disease where you will have crescents all the time." Tr. 198:2–7. He also stated that "the timing also means [you] probably . . . will not see the crescents even if presented at – you know, so just to make it simple, you don't have to see crescents to diagnose [FGN]." Tr. 198:9–12. When asked whether "the lack of crescents rule out . . . the probability that [Petitioner's] vaccination may have accelerated her disease course[,]" Dr. Ballouk responded, "[n]o[,] . . . the literature say[s] that most of the time [doctors] will not see crescents at all." Tr. 198:13–18.

In his second expert report and corresponding testimony, Dr. Ballouk discussed "the manner in which [Petitioner's] condition progressed differently as a result of vaccination than it would have otherwise." Pet'r's Ex. 50 at 1. He cited to and referenced multiple articles outlining the general FGN disease course. The first is an article by Nasr et al., which Dr. Ballouk described as "the largest, longest, single-center study of [FGN] patients . . . ." Pet'r's Ex. 50 at 1; Resp't's Ex. A, Tab 5.[76] The authors of this study wrote that the objective of the study was "[t]o better define the clinical-pathologic spectrum and prognosis [of FGN] . . . ." Resp't's Ex. A, Tab 5, at 1. The study included "[sixty-six] patients with FGN that were followed for a mean time of [fifty-two] months." *Id*. at 2. The sixty-six patients included sixty-three Caucasian patients, two Hispanic patients, and one Black patient, with a mean age of fifty-three at the time of biopsy. *Id*. at 2–3. At biopsy, seventy-one percent of patients had hypertension and fifty-nine percent had edema. *Id.* at 4. All patients had proteinuria at the time of biopsy, with fifty-five percent of patients in the nephrotic range and thirty-eight percent of patients with full nephrotic syndrome. *Id*. at 3. The authors followed these patients for an average of 52.3 months, with a range of two to 209. *Id.* at 6. During this period, "[three] patients ([five percent]) had [complete remission], [five] patients ([eight percent]) had [partial remission], [twenty-six] patients ([forty-three percent]) had [persistent renal disease], and [twenty-seven] patients (forty-four percent]) progressed to ESRD." *Id*. The authors noted that "[g]ender, type of therapy, . . . presence of underlying malignancy, and presence of underlying autoimmune disease did not correlate significantly with outcome." *Id.* The authors concluded that FGN "[p]rognosis is poor, with nearly one half of patients progressing to ESRD within [four] years." *Id*. at 9. They also concluded that the clinical "[f]eatures associated with poor renal outcome include older age, higher creatinine at biopsy, higher 24-hour urine protein at biopsy, and higher percentage of globally sclerotic[77] glomeruli." *Id*.

Dr. Ballouk also discussed a paper by Javaugue et al. in which the authors conducted a retrospective study of "[twenty-seven] adults with [FGN] referred to [fifteen] nephrology departments in France between 1990 and 2011 . . . ." Tr. 201:19–202:19; Resp't's Ex. A, Tab 7, at 1.[78] Of these twenty-seven patients, there were sixteen men and eleven women, with a median age

---

[76] Samih H. Nasr et al., *Fibrillary Glomerulonephritis: A Report of 66 Cases from a Single Institution*, 6 CLIN. J. AM. SOC. NEPHROL. 775 (2011).

[77] Sclerotic means "hard, or hardening[.]" *Sclerotic*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[78] Vincent Javaugue et al., *Long-term Kidney Disease Outcomes in Fibrillary Glomerulonephritis: A Case Series of 27 Patients*, 62(4) AM. J. KIDNEY DIS. 679 (2016).

of fifty-nine. Resp't's Ex. A, Tab 7, at 2. The authors wrote that, "[a]t the time of diagnosis, most patients presented with hypertension ([seventy percent]) and lower-limb edema ([fifty-six percent]). All patients had proteinuria . . . with nephrotic syndrome in [eleven] patients ([forty-one percent] and microhematuria[79] in [nineteen] patients ([seventy-three percent])." *Id.* at 2–3. In terms of patient outcomes, the authors wrote that "[r]enal prognosis in [FGN] is poor and most previously reported patients progressed to ESRD." *Id.* at 9 (citing *id.* at 10, Table 4). They continued, "[w]ith a median follow-up of [forty-six] months, [forty-eight percent] of patients from the present series developed ESRD after a median of [forty-four] months after diagnosis." *Id.* at 9.

During his testimony, Dr. Ballouk also stated that he relied on an article by Rosenstock et al. as a basis for his opinions. Tr. 202:20–203:1; Resp't's Ex. C, Tab 1; Resp't's Ex. A, Tab 8; Pet'r's Ex. 23.[80] The authors of this article wrote that "[c]ontroversy surrounds the relatedness of . . . FGN and immunotactoid glomerulonephritis ("IT")[,]" and they therefore set out "[t]o better define their clinicopathologic features and outcome[s by] . . . report[ing] the largest single center series of [sixty-seven] cases biopsied from 1980 to 2001, including [sixty-nine] FGN and [six] IT [cases]." Resp't's Ex. C, Tab 1, at 1. The FGN patients in this study included "[twenty-four] males and [thirty-seven] females . . . age [twenty-eight] to [eighty-one] years old . . . . These included [fifty-six] Caucasian, [three] African American, and [two] Hispanic patients." *Id.* at 3. The authors also noted that, "at the time of biopsy," forty-four of the sixty-one FGN patients had renal insufficiency, thirty-six of the patients had hypertension, and "[a]ll patients presented with proteinuria . . . ." *Id.* In terms of outcomes, the authors wrote that follow-up was conducted on fifty-six FGN patients. *Id.* at 6. These patients "were followed for a mean of [twenty-three] months[,]" and "[twenty-five] patients developed ESRD." *Id.* The authors continued, "[w]hile only [eighteen percent] of patients who presented without renal insufficiency progressed to ESRD, [seventy-two percent] . . . of patients who presented with a creatinine [greater than] 2.0mg/dL reached ESRD." *Id.* The authors found that "[t]he median time to ESRD was 24.4 [plus/minus] 15.2 months (mean, 57.6 [months plus/minus] 9.49 months)." *Id.* The authors concluded that this study "confirm[s] the high risk of ESRD in FGN, with a median renal survival . . . of only [twenty-four] months from the time of biopsy." *Id.* at 8.

Based on these articles, Dr. Ballouk argued that Petitioner's "[GN] advanced to ESRD much more rapidly than would be expected." Pet'r's Ex. 50 at 2. Dr. Ballouk opined that "[o]nly [forty-four] percent of . . . patients . . . will end up on dialysis with a median of [twenty-four] months." Tr. 186:25–187:1. He relied on the Rosenstock et al. article to argue that Petitioner progressed to ESRD quicker than what is normally associated with an FGN patient. Tr. 204:21–205:4. He stated:

> If [one] look[s] at the literature, [one] would expect [Petitioner] to have – if she's from the bad patients who end up on dialysis, . . . [they] usually [reach ESRD requiring dialysis in] two years . . . . [Petitioner] [reached ESRD requiring dialysis]

---

[79] Microhematuria, or microscopic hematuria, is "blood in the urine visible only with a microscope, defined as at least two to three red blood cells per high-power field." *Microscopic Hematuria*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[80] Jordan L. Rosenstock et al., *Fibrillary and Immunotactoid Glomerulonephritis: Distinct Entities with Different Clinical and Pathologic Features*, 63 KIDNEY INTER. 1450 (2003).

> in four months. So . . . [Petitioner progressed to ESRD requiring dialysis] at least a year and a half faster than the average.

Tr. 205:6–11. Regarding the Nasr et al. study, Dr. Ballouk wrote:

> Applying the results of this study to [Petitioner's] situation, . . . she advanced from biopsy to ESRD much more rapidly than expected. The average time from biopsy to ESRD was [fifty-two] months. [Petitioner], however, reached ESRD in only [four] months from the date of biopsy and only [seven] months from her first recorded elevated serum creatinine. This is a significant difference.

Pet'r's Ex. 50 at 2. Dr. Ballouk continued, "[w]hile it can be argued that [P]etitioner would likely have still reached ESRD at some point, she reached it much faster than the majority of other similarly situated [FGN] patients." *Id*.

On cross-examination, Dr. Ballouk was asked about Petitioner's onset date, which he argued was "seven to eight weeks before [her] symptoms start[ed,]" or the "early part of September [2013]." Tr. 209:11–20. He explained that this estimation "has nothing to do with [Petitioner's] vaccination[,]" but rather was based on "when [Petitioner's] symptoms started, like the nausea, vomiting . . . ." Tr. 210:4–13. Dr. Ballouk agreed that kidney disease can be present without symptoms, but he stated that a person "may have some vague symptoms, but [the person] will not be aware" that she has a kidney disease. Tr. 210:14–211:1. Dr. Ballouk testified that Petitioner had "silent" kidney disease for "at least" a couple of months. Tr. 211:4–6.

Dr. Ballouk also discussed Petitioner's hypertension and edema on cross-examination. Dr. Ballouk agreed that hypertension was a clinical manifestation of kidney disease, but he stated that "hypertension is very, very common in overweight patients, so if [a person has] hypertension, it doesn't mean [that person has a] kidney disease." Tr. 211:12–17. However, after reviewing Petitioner's medical records, Dr. Ballouk conceded that Petitioner had normal blood pressure readings in 2010 even though she was overweight and smoking at that time. Tr. 212:17–215:11. Dr. Ballouk also agreed that edema is a clinical manifestation of kidney disease. Tr. 216:2–5. He conceded that Petitioner's primary care physician began documenting Petitioner's edema approximately two years prior to her vaccination, although he again noted that "[o]bese patients like [Petitioner] . . . will have edema . . . but it doesn't [mean] that [Petitioner] has kidney disease at that time . . . ." Tr. 216:8–15. However, Dr. Ballouk did acknowledge that Petitioner began having high blood pressure and edema findings at around the same time, in July 2011. Tr. 216:16–217:2.

Rather, Dr. Ballouk asserted that Petitioner's first clinical manifestation of her FGN occurred on November 21, 2013, when she presented to the hospital with complaints of abdominal pain, vomiting, nausea, and diarrhea. Tr. 217:7–218:1. Dr. Ballouk opined that these symptoms were all "clinical manifestations" of "renal insufficiency." Tr. 218:5–9. However, upon questioning during cross-examination, Dr. Ballouk acknowledged that he did not refer to these symptoms as manifestations of renal insufficiency or kidney disease in his expert reports because he "indirectly [did as much when he] said that [Petitioner] had [GN] when she presented to the hospital. This is how [he] came to this conclusion, from [Petitioner's] symptoms and labs." Tr.

218:10–18. Dr. Ballouk also conceded that he did not file any medical literature listing these symptoms as "clinical manifestations" of kidney disease, although he argued that "it's well known that patients with renal insufficiency . . . will have nausea, . . . vomiting, . . . and sometimes . . . abdominal pain." Tr. 218:19–219:1. When asked about the Clinical Practice Guidelines published by the National Kidney Foundation, which do not list these symptoms as manifestations of kidney disease or renal insufficiency, Dr. Ballouk responded that he "[did not] think [that] they mention every single manifestation, . . . but . . . any nephrologist will know that if [someone has] a rapid rise in BUN, [they] will feel bad and [they] may have nausea and vomiting." Tr. 219:7–15. Dr. Ballouk disagreed that these symptoms were likely a manifestation of a gastrointestinal illness ("GI") because Petitioner had been complaining of these symptoms for two weeks, was also suffering from proteinuria, and had increased creatinine that did not improve with hydration. Tr. 219:24–220:16.

Dr. Ballouk also discussed Petitioner's potential dehydration during her November 2013 hospitalization and its effect on her creatinine levels. He testified that "it's hard to say" exactly "how severe" her dehydration was. Tr. 229:7–8. However, he explained that "[t]he worse [Petitioner's dehydration was,] the higher the creatinine [would be]." Tr. 229:13. When pressed, Dr. Ballouk stated that Petitioner was "moderately dehydrated[,]" and that her actual creatinine level, if she had not been dehydrated, would have been "around 1.5 to 1.7." Tr. 229:15–18, 21–25. Dr. Ballouk explained that this estimation was based on his "personal experience[,]" although he later conceded that he did not cite to any medical literature as support. Tr. 230:3, 5–8. In addition, Dr. Ballouk stated that he would "expect to [see] some tachycardia[81] and low blood pressure[]" in a person who is moderately dehydrated. Tr. 252:19–22. When asked whether Petitioner exhibited these symptoms during her hospitalization, Dr. Ballouk asserted that Petitioner had an initial normal pulse reading and high blood pressure when she presented to the hospital. Tr. 250:24–252:4. Dr. Ballouk explained, however, that whether a person is exhibiting these symptoms "depends on the severity [of the dehydration] and it depends on the [patient's] baseline [blood pressure and pulse levels]." Tr. 252:23–24.

Under my questioning, Dr. Ballouk stated that vomiting and diarrhea are caused by renal failure when there is a "[rise] of the BUN and the creatinine . . . ." Tr. 256:2–8. He also explained that, "[o]n the other hand, . . . if you [are] vomiting and dehydrated, that will worsen your renal failure. It's . . . a vicious cycle." Tr. 256:17–19. When asked "how long it would take the effects of renal failure to lead to GI symptoms[]" in Petitioner's case, Dr. Ballouk responded "a couple of months." Tr. 256:24–257:4.

Also, under my questioning, Dr. Ballouk estimated that Petitioner's FGN began "around early September [2013]." Tr. 267:2–4. He agreed that the progression of Petitioner's FGN up to the date of vaccination was "natural . . . because there [hadn't] been any . . . catalyst to exacerbate her condition." Tr. 268:7–10. However, he stated that Petitioner's increase in creatinine between her November 2013 reading and January 2014 reading indicated that Petitioner's disease was rapidly progressing during that time. *See* Tr. 267:11–12. He clarified that he meant that Petitioner's disease was "progressive [because of the rise in Petitioner's creatinine and proteinuria between

[81] Tachycardia is "excessive rapidity in the action of the heart[.]" *Tachycardia*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

November and January], and it is aggressive because she ended up on dialysis [in] four months." Tr. 280:12–281:1.

During re-direct examination, Dr. Ballouk opined that the presence of mesangial involvement, as well as the fact that Petitioner did not have one hundred percent sclerosed glomeruli, indicated that she was in the MES subgroup, which showed "exclusively mesangial proliferation or sclerosis" Tr. 274:20–275:1; Resp't's Ex. A, Tab 6, at 4. Citing the Rosenstock et al. study, Dr. Ballouk stated that a patient in the MES subgroup would take eighty months to reach ESRD. Tr. 275:2–5.

3. Respondent's Expert, Dr. Levinson

Dr. Levinson submitted an expert report in which he wrote that he "disagree[s] with the claim that the [flu] vaccination accelerated the progression of [Petitioner's] FGN to [ESRD]." Resp't's Ex. C at 3. He noted that while he "concur[s] with [Petitioner's] diagnosis of FGN[,]" he "leave[s] detailed discussion of [the disease] to . . . [R]espondent's expert in renal disease, and will focus on aspects of this disease that influenced formulation of [his] dissenting opinion." *Id.*

In his expert report, Dr. Levinson wrote that "[i]t is widely accepted that vaccines elicit the production of cytokines as a prerequisite for the induction of desired adaptive immune (antibody and cell-mediated) responses." *Id.* at 5. He explained that the cytokine production "provides a favorable milieu in the lymph nodes that drain injection sites for promoting the activation of lymphocytes (B and T cells), which respond to the vaccine's antigenic constituents." *Id.* Therefore, Dr. Levinson wrote that the "production of cytokines, even proinflammatory cytokines, is an expected and desired outcome in vaccination strategy." *Id.*

However, Dr. Levinson further wrote that "[i]t is not immediately clear to [him]" what Dr. Gershwin was referring to when he wrote in his expert report that the "[flu] vaccine elicits a rigorous cytokine response . . . ." *Id.* (quoting Pet'r's Ex. 19 at 3). Dr. Levinson opined that "it is highly unlikely that the cytokine response to the inactivated seasonal [flu] vaccine [received] by [Petitioner] reached a level of magnitude to deleteriously impact organs distant to the injection site." *Id.* While Dr. Levinson wrote that the "[flu] virus . . . may induce intense lung inflammation and additional organ dysfunction due to the release of extremely large amounts of pro-inflammatory cytokines," a phenomenon he described as a "cytokine storm," he explained that "there is no credible scientific evidence . . . that vaccines otherwise elicit such dangerous levels of cytokines." *Id.* He testified that "[m]any of [the] people [who receive the flu vaccine] have underlying autoimmune diseases. Some of them are stable, some of them are not so stable." Tr. 119:11–13. He therefore concluded that "if Dr. Gershwin's . . . theory[] is correct, . . . [then] we would see a lot more reports of flu vaccine-induced exacerbations of autoimmune disease, and we just don't see that." Tr. 120:12–19.

Dr. Levinson wrote that "[t]he bottom line of the extant scientific literature is that inactivated vaccines, including seasonal [flu] vaccines, have not been shown to induce flares of disease activity in patients with stable autoimmune disease or augment disease expression in patients with active autoimmune disorders." *Id.* Dr. Levinson testified that, while these studies do not directly address vaccination and FGN, he nonetheless explained that they are important

because the Court "heard . . . from Dr. Gershwin that FGN may . . . represent an autoimmune disease, and to the extent that that may be true, then . . . what the studies that dealt with the effect of flu vaccine on autoimmune disease probably are relevant to FGN." Tr. 115:25–116:11. He cited two articles as support. The first is by Westra et al. Resp't's Ex. C, Tab 2.[82] The authors of this article "provide an analysis of data on vaccination of patients with an [autoimmune inflammatory rheumatic diseases ("AIRD")[83]]." *Id.* at 1. The authors note that "[s]afe vaccination is particularly important for patients with an AIRD, as vaccine-induced antigenic stimulation might exacerbate the underlying autoimmune disease." *Id.* at 6. In terms of the flu vaccine specifically, the authors wrote that "several studies have found that autoantibody titers[84] increase in some patients with an AIRD after [flu] vaccination," although they note that "other studies could not confirm these findings, and in the majority of cases this increase . . . was not associated with clinical disease activity." *Id.* Regarding RA, the authors noted that "[i]n most of the latest studies[,] . . . no significant influence of vaccination on disease activity has been reported." *Id.* In addition, they noted that "in pre–post studies after [flu] vaccination, patients with RA did not experience increased disease activity." *Id.* For patients with systemic lupus erythematosus ("SLE"),[85] the authors wrote that "a number of studies" showed that "patients with SLE . . . did not develop more disease flares than unvaccinated patients with SLE." *Id.* The authors did, however, further note that "[o]ther studies of patients with SLE found either no flares or mild flares . . . ." *Id.* They also noted that "[o]nly one severe disease manifestation[] (renal flares with [GN]) occurred in [one] of [twenty-nine] patients with SLE." *Id.* at 6–7. However, the authors go on to note that "this study did not include a control of unvaccinated patients with SLE, and these data should therefore be interpreted with caution." *Id.* at 7. The authors concluded that, "[i]n general, [flu] vaccination is safe for patients with SLE and inactive disease." *Id.* The authors also found that "no increase in disease flares was found[]" in patients with granulomatosis with polyangiitis ("GPA")[86] when compared with non-vaccinated GPA patients. *Id.* Lastly, the authors wrote that "the inactivated [flu] vaccine seemed to be safe[]" after administration "[i]n a population of patients with diverse

---

[82] Johanna Westra et al., *Vaccination of Patients with Autoimmune Inflammatory Rheumatic Diseases*, 11 NAT. REV. RHEUMATOL. 135 (2015).

[83] An autoimmune disease, generally, is "a disorder caused by an immune response directed against self antigens" that is typically characterized by "demonstrable circulating autoantibodies or cell-mediated immunity against autoantigen, inflammatory lesions caused by immunologically competent cells or immune complexes in tissues containing the autoantigens . . . ." Although autoimmune diseases generally involve evidence of pathogenic process, "some diseases, such as systemic lupus erythematosus and rheumatoid arthritis[,] are often classified as autoimmune diseases even though their pathogenesis is unclear." *Autoimmune Disease*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[84] A titer is "the quantity of a substance required to produce a reaction with a given volume of another substance, or the amount of one substance required to correspond with a given amount of another substance. *Titer*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[85] Systemic lupus erythematosus is "a chronic, inflammatory, often febrile, multisystemic disorder of connective tissue that proceeds through remissions and relapses[]" that "is characterized principally by involvement of the skin . . . , joints, kidneys , and serosal membranes." *Systemic Lupus Erythematosus*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[86] Granulomatosis with polyangiitis is "a multisystem disease chiefly affecting males, characterized by necrotizing granulomatous vasculitis involving the upper and lower respiratory tracts, glomerulonephritis, and variable degrees of the ANCA-associated type of small vessel vasculitis. Most authorities consider this condition to be an aberrant hypersensitivity reaction to an unknown antigen." *Granulomatosis with Polyangiitis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

AIRDs . . . ." *Id.* In addition, "[f]lares of SLE occurred as often after vaccination . . . in an unvaccinated control group . . . , and disease activity scores did not increase after vaccination." *Id.* The authors concluded that "[s]tudies comparing adverse effects between vaccinated and unvaccinated patients, and from pre–post vaccination studies, do not seem to indicate that vaccination exacerbates underlying AIRDs." *Id.* at 8. They do note, "[h]owever, [that] serious vaccine-attributable conditions are rare; therefore, the clinical studies that have been done are too small to yield sufficient safety data." *Id.*

The second article is by van Assen et al. Resp't's Ex. C, Tab 3.[87] The authors of this article sought "to develop evidence-based European League Against Rheumatism ("EULAR") recommendations for vaccination in patients with [AIRDs]." *Id.* at 1. The authors included "experts representing [eleven] European countries, consisting of eight rheumatologists, four clinical immunologists, one rheumatologist/clinical immunologist, one infectious disease physician, one nephrologist, one paediatrician[sic]/rheumatologist, and one clinical epidemiologist." *Id.* They note that "[n]o studies have been performed comparing efficacy and harms between patients with AIRD with stable and unstable disease[]" and that "almost all vaccination studies in [AIRD] patients . . . addressed patients with quiescent disease." *Id.* They further note that "[s]tudies that also included patients with moderate or severe disease activity did not show more frequent side effects or disease flares, or decreased efficacy in patients with [AIRD] compared with healthy controls." *Id.* However, they nonetheless note that "the numbers of patients in these studies were too small to conclude that vaccination during active disease is safe and efficacious." *Id.* Therefore, the authors recommended that "vaccination in patients with [AIRD] should ideally be administered during stable disease . . . ." *Id.* Regarding the inactivated flu vaccine, the authors wrote that "[a]dverse events of [flu] vaccination in patients with [AIRD] seem comparable to those in healthy controls, although there are no studies that are sufficiently powered with regard to safety." *Id.* at 4. They recommend that "[i]nactivated [flu] vaccination should be strongly considered for patients with [AIRD]." *Id.* The authors conclude by writing that, "[a]lthough many case reports have been published demonstrating flares of AIRD or new-onset autoimmune diseases following vaccination, these adverse events remain rare and a causal relationship has not been proved." *Id.* at 6. They continue, "several controlled studies show no difference in the occurrence of flares of AIRD after vaccination, although these studies have not been powered to address specific adverse events, but efficacy. Because of the lack of sufficiently powered studies focusing on harms, these issues remain an important item on the research agenda." *Id.*

Dr. Levinson took issue with the studies that Dr. Gershwin cited "[t]o link the alleged vaccine-induced cytokines to [Petitioner's] FGN," which included "several studies that deal with 1) the interaction of pro[-] and anti-inflammatory cytokines during the course of host immune responses . . . , and 2) the potential of pro-inflammatory cytokines to inflict renal tissue injury." Resp't's Ex. C at 6 (citing Pet'r's Exs. 24–42). Dr. Levinson wrote that the first group of studies "are of general interest and importance and have been appreciated for many years. However, they are not relevant to considerations in this case, as there is no credible evidence that any of the cytokines discussed are involved in the pathogenesis of FGN." *Id.* In terms of the second group of studies, Dr. Levinson noted that, "although there is good evidence that pro-inflammatory cytokines

[87] S. van Assen et al., *EULAR Recommendations for Vaccination in Adult Patients with Autoimmune Inflammatory Rheumatic Diseases*, 70 ANN. RHEUM. DIS. 414 (2011).

can cause renal tissue injury in other autoimmune diseases," these studies concern "experimental animal models of autoimmune glomerulopathies and human autoimmune glomerulopathies in which tissue injury is initiated by antibodies that target renal tissue for destruction . . . ." *Id*. (citing Pet'r's Exs. 27–31, 38, 40, 42). Dr. Levinson opined that he is "not aware of any credible evidence that such adaptive immune precipitants lead to the characteristic pathologic fibrillary changes seen in FGN and none of these factors were detected during the course of [Petitioner's] diagnostic evaluation." *Id*. He wrote that these articles "deal with studies in which renal tissue injury is attributed to pro-inflammatory cytokines that are **produced locally, i.e., in the kidneys,** by cells that are either renal tissue constituents or inflammatory cellular immigrants." *Id*. (citing Pet'r's Exs. 26–30, 38–42) (emphasis in original). Dr. Levinson contrasted that with Dr. Gershwin's theory, which "proposed that cytokines produced at sites remote from the kidneys in response to the [flu] vaccine promoted damage to [Petitioner's] kidneys." *Id*. Dr. Levinson opined that "[t]here is no basis for such a claim unless [Dr. Gershwin] is invoking a vaccine-induced cytokine storm. And surely there is no evidence that this catastrophic event occurred." *Id*.

Regarding the onset of Petitioner's FGN, Dr. Levinson wrote that "Dr. Gershwin is on shaky grounds when he makes claims about the vaccination aggravating a disease process whose time of onset relative to the vaccination is unclear to him." Resp't's Ex. C at 4. Dr. Levinson took issue with Dr. Gershwin's opinion that Petitioner's "persistent nausea, emesis, diarrhea and abdominal pain . . . in the two weeks leading up to her [November 21, 2013] hospital visit were the by-products of an exacerbation of [her] FGN." *Id*. Dr. Levinson described this conclusion as "a giant leap of faith[,]" and he instead opined that "those symptoms represented an unrelated gastrointestinal illness." *Id*. He continued that "it is extremely likely that this illness, which was associated with intravascular volume depletion and resultant dehydration . . . contributed to the renal insufficiency that was first noted at that time." *Id*. Dr. Levinson testified that Petitioner's CT scan of her intestines showed "signs of acute diverticulitis.[88]" Tr. 121:25–122:2. Dr. Levinson explained that "acute diverticulitis . . . is a pretty significant disorder[, which] . . . is associated with inflammation . . . ." Tr. 122:3–6. In addition, Dr. Levinson discussed Petitioner's blood tests conducted during her brief hospitalization, which showed "leukocytosis, [or] an elevated white cell count, which would go along with underlying inflammation, particularly an infection." Tr. 122:17–19.

Dr. Levinson also took issue with Dr. Gershwin's assertion that the flu vaccine exacerbated Petitioner's FGN, resulting in Petitioner reaching ESRD faster than what is normally expected with this disease. Resp't's Ex. C at 4. In doing so, Dr. Levinson cited to the Rosenstock et al. article. *See id.*; *see also* Resp't's Ex. C, Tab 1.[89] While Dr. Levinson agreed that "the median time of progression to [ESRD] in this . . . study . . . was reported to be 24.4 [plus/minus] 15.2 months," he noted that, "clearly, the length of progression time is influenced by the pathology seen on renal biopsy." Resp't's Ex. C at 4. In the article, the authors wrote that, of the sixty-one patients

[88] Diverticulitis is "inflammation of a diverticulum, especially inflammation related to colonic diverticula, which may undergo perforation with abscess formation." *Diverticulitis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021). The diverticulum is "a circumscribed pouch or sac of variable size occurring normally or created by herniation of the lining mucous membrane through a defect in the muscular coat of a tubular organ. *Diverticulum*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[89] Rosenstock et al., *supra* note 80.

with FGN included, forty-four percent of biopsies showed MPGN defined by mesangial expansion with foci of mesangial interposition and replication of glomerular basement membrane[90] . . . ." Resp't's Ex. C, Tab 1, at 4. In addition, "[t]wenty-one percent of biopsies had exclusively mesangial proliferation or sclerosis ("MES") [,]" while "[f]ifteen percent of patients had a diffuse proliferative ("DPGN")[91] pattern characterized by endocapillary proliferation including focal infiltrating leukocytes . . . ." *Id.* The authors further noted that seven percent of biopsies revealed a "membranous [pattern],[92] featuring predominantly subepithelial[93] fibrillar deposits separated by well-formed basement membrane spikes, with little or no mesangial hypercellularity[,][94]" and another "[t]hirteen percent of biopsies had a nondescript diffuse[95] sclerosing[96] pattern ("DS"), defined as glomerular sclerosis[97] obliterating [greater than seventy percent] of glomeruli . . . ." *Id.* While the authors did note that "[t]he median time to ESRD was 24.4 [plus/minus] 15.2 months[, with a] mean [of] 57.6 [plus/minus] 9.49 months[,]" they explained further that the "[m]ean time to ESRD varied according to histologic subgroups." *Id.* at 6. They wrote that "[t]he histologic subgroups of DS, DPGN, and MPGN progressed more rapidly to ESRD[, with a] mean [of seven] . . . , [twenty] . . . , and [forty-four] months[] respectively[,] compared to MES and MGN [subgroups, with a] mean [of eighty] . . . and [eighty-seven] months[] respectively[]." *Id.*

Based on this study, Dr. Levinson wrote that "patients with the chronic irreversible change of [DS] demonstrated a shorter time of progression from the time of diagnosis to [ESRD], compared to patients with other histopathological subtypes." Resp't's Ex. C at 4. He further noted that Petitioner's "renal biopsy demonstrated extensive histopathological signs of chronic and irreversible disease including [DS]. Therefore, her rate of progression to [ESRD] would be expected to be commensurate with the time period reported for such FGN patients studied in" the Rosenstock et al. article. *Id.* Dr. Levinson wrote that Petitioner exhibited "[i]mpaired renal function (creatinine of 2.8), proteinuria and hematuria . . . when she presented to [MVH] on November 21,

---

[90] Glomerular membrane refers to "the fenestrated basement membrane of the visceral layer of the glomerular capsule, lying adjacent to glomerular capillaries . . . ." *Glomerular Membrane*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[91] Diffuse glomerulonephritis is "a severe form in which there are proliferative changes in more than half the glomeruli, frequently with epithelial crescent formation and necrosis[. I]t is often seen in cases of advanced [SLE]." *Diffuse Glomerulonephritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 2, 2021).

[92] This refers to membranous glomerulonephritis, which is "glomerulonephritis characterized histologically by proteinaceous deposits on the glomerular basement membrane or by thickening of the membrane, with circulating antigen-antibody complexes, indicating immune complex disease." *Membranous Glomerulonephritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[93] Subepithelial means "beneath the epithelium." *Subepithelial*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[94] Hypercellularity is "a state characterized by an abnormal increase in the number of cells present . . . ." *Hypercellularity*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[95] Diffuse means "not definitely limited or localized; widely distributed." *Diffuse*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[96] Sclerosing is "causing or undergoing sclerosis." *Sclerosing*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[97] Glomerular sclerosis, or glomerulosclerosis, is "fibrosis and scarring with senescence of the renal glomeruli." *Glomerularsclerosis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

2013." *Id*. He explained that Petitioner began "[PD] . . . in June[] 2013 [sic].[98]" *Id*. Therefore, he calculated that "the approximate time of her progression to [ESRD] from the time of her diagnosis of a glomerulopathy was seven months and is totally consistent with the time period observed in" the Rosenstock et al. article. *Id*.

During cross-examination, Dr. Levinson opined that the time period measured in the Rosenstock et al. article "was . . . the time of diagnosis to the time of entering [ESRD]." Tr. 151:23–152:3. After further questioning, Dr. Levinson conceded that "it's not particularly clear[]" whether this article was measuring from the time of diagnosis to ESRD or the time of biopsy to ESRD. Tr. 153:5–10. Dr. Levinson explained "that based on the reading [he] did, . . . [he] assumed that that was from the time of diagnosis with a clinical disease of nephritis." Tr. 154:24–155:2.

4. Respondent's Expert, Dr. Fine

Dr. Fine wrote that FGN "is a poorly understood entity with limited treatment options." Resp't's Ex. A at 7. While he acknowledged that the causes of FGN are "unknown," Dr. Fine explained that FGN "has been associated with hematologic and nonhematologic malignancies, plasma cell dyscrasias,[99] autoimmune disease and [H]epatitis C." *Id*. Dr. Fine found it "notable that [FGN] has never been associated with the [flu] vaccine or any other vaccine." *Id*. He then discussed an association between FGN and Oxycodone use. *See id*. However, during his testimony, Dr. Fine clarified that he did not believe that Petitioner's Oxycodone use caused her FGN. Tr. 300:22–24. He explained that he included this discussion in his expert reports "because if someone is going to claim that a flu vaccine did it and there's never been a publication and she's on a substance that has been described as causing . . . [FGN], then at least there's a paper on something else that she is exposed to." Tr. 301:1–6. He continued, "[s]o if one is going to speculate that a vaccine did it and there's no data and you've got something that she is taking and there is data, it makes [Oxycodone use] more likely than at least the flu shot." Tr. 301:6–9. Dr. Fine concluded this discussion by stating that, "as of now, [he does not] have any reason to believe that Oxycodone was certainly not more likely than not [the cause of Petitioner's FGN]." Tr. 301:13–14. In fact, Dr. Fine believed that it was "much less likely than not that Oxycodone was the culprit." Tr. 301:15–16.

Regarding Petitioner's health pre-vaccination, Dr. Fine opined that she exhibited two symptoms that are considered manifestations of kidney disease. The first is hypertension. Resp't's Ex. A at 4–5. Dr. Fine wrote that "[h]ypertension is a well[-]described feature of chronic kidney disease." *Id*. at 5. He cited to the National Kidney Foundation's Clinical Practice Guidelines for

[98] Petitioner had her PD catheter placed in June 2014, which would be seven months from November 2013. *See* Pet'r's Ex. 4 at 2–3. It is clear based on context that Dr. Levinson's reference to June 2013 is a typographical error.

[99] Plasma cell dyscrasias are "a diverse group of neoplastic diseases involving proliferation of a single clone of cells producing a serum M component (a monoclonal immunoglobulin or immunoglobulin fragment)." *Plasma Cell Dyscrasias*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). An M component is "an abnormal monoclonal immunoglobulin with a characteristic electrophoretic pattern, occurring in the serum of patients with plasma cell dyscrasias and formed by the proliferating concentrations of immunoglobulin-producing cells." *M Component*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

Chronic Kidney Disease: Evaluation, Classification and Stratification as support. *Id*.; Resp't's Ex. A, Tab 1.[100] The guidelines state that "[h]igh blood pressure is both a cause and a complication of chronic kidney disease." Resp't's Ex. A, Tab 1, at 45. When hypertension arises "[a]s a complication, [it] may develop early during the course of chronic kidney disease and is associated with adverse outcomes – in particular, faster loss of kidney function and development of cardiovascular disease." *Id*. Dr. Fine also cited to an article by Coresh et al. as support. Resp't's Ex. A at 5; Resp't's Ex. A, Tab 3.[101] In this study, the authors conducted "[a] cross-sectional study of a representative sample of the US population . . . using 16,589 adult participants aged [seventeen] years and older . . . ." Resp't's Ex. A, Tab 3, at 1. They defined elevated serum creatinine as 141 μmol/L or higher (~1.6 mg/dL) for men and 124 μmol/L or higher (~1.4 mg/dL) for women (>99th percentile for healthy young adults) . . . ." *Id*. The authors found that, among others, "[h]igher systolic and diastolic blood pressures, presence of hypertension, [and] antihypertensive medication use . . . were all associated with higher serum creatinine levels." *Id.* They further noted that "[a]n estimated [three percent] (5.6 million) of the civilian, noninstitutionalized US population had elevated serum creatinine levels, [seventy percent] of whom were hypertensive." *Id*.

Furthermore, Dr. Fine testified that he submitted two additional articles "that document[] the prevalence of hypertension in patients with FGN[,]" which show that "around [seventy] percent" of FGN patients have hypertension. Tr. 194:2–12. The first of these articles is by Nasr et al., which was also discussed by Dr. Ballouk and described in more detail in section III.B.2 above. The authors of this article wrote that, of the sixty-six FGN patients studied, seventy-one percent presented with hypertension. Resp't's Ex. A, Tab 5, at 1. The second article, by Javaugue et al., was also discussed by Dr. Ballouk and described in section III.B.2 above. Resp't's Ex. A, Tab 7. The authors of this article wrote that, "at the time of diagnosis," seventy percent of the patients they studied "presented with hypertension . . . ." *Id*. at 2.

Dr. Fine stated these four studies are relevant because "when [hypertension] appears when you're not expecting it, it suggests the possibility of kidney disease . . . ." Tr. 294:19–21. He explained that "hypertension . . . is often the first sign of kidney disease," and that "in the presence of [CKD], whatever [the] cause, hypertension is very frequent, maybe even [occurring] the majority of the time as . . . one's disease progresses." Tr. 294:23–295:11. He further explained that "in the context of what happened to [Petitioner], it makes sense that [hypertension] was the onset of her kidney disease." Tr. 294:21–22. Regarding Petitioner, Dr. Fine explained that "her blood pressure measurements from August 2010 to May 2011 were very stable and ranged from 112–122/62–80 . . . . This appears to be her stable baseline blood pressure." Resp't's Ex. A at 2. He noted that Petitioner's "blood pressure [was] first noted to be elevated in July and August of 2011, long before her vaccine exposure." *Id*. at 4. Dr. Fine stated that Petitioner's heart rate was also higher than her baseline when she had her initial high blood pressure readings. *Id*. Dr. Fine acknowledged that her higher heart rate on these initial occasions might indicate that her high blood pressure readings were due to pain or anxiety. *Id*. at 2–3. He noted, however, that she had blood pressure and heart rate readings within her baseline range in May 2011, when she also had

[100] National Kidney Foundation, *K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification and Stratification*, 39 (Supp. 1) AM. J. KIDNEY DIS. S1 (2002).
[101] Josef Coresh et al., *Prevalence of High Blood Pressure and Elevated Serum Creatinine Level in the United States*, 161 ARCH. INTERN. MED. 1207 (2001).

a pain score of 7/10. *Id*. at 3. Regarding Petitioner's blood pressure readings, Dr. Fine continued, "[a]fter [July and August 2011], while they intermittently returned to baseline levels, [Petitioner's] blood pressures were generally higher than the prior baseline, fluctuated more[,] and were interspersed with spikes in blood pressure . . . ." *Id*. at 4–5. Dr. Fine also noted that, "[m]ost importantly, [Petitioner's] highest blood pressure of 176/124 . . . occurred on August 20, 2013, approximately a month prior to administration of the influenza vaccine on September 23, 2013 . . . ." *Id*. at 5. Dr. Fine concluded that "[t]hese blood pressure changes suggest that [Petitioner's] kidney disease was present for some time prior to diagnosis, and the very severe elevation in August 2013[,] certainly suggests that the disease was already flaring prior to the September 2013 vaccination." *Id*.

In addition to hypertension, Dr. Fine also stated that Petitioner's "lower extremity edema," noted on at least three separate visits prior to her vaccination, were manifestations of her FGN. Tr. 298:14–20. Dr. Fine noted that "edema is quite common[]" in kidney disease patients. Tr. 298:24–299:1. He explained that edema is "really a reflex of the ability of the kidney to get rid of fluid, although ultimately it's more related to salt than fluid. . . . [T]he two go hand[-]in[-]hand." Tr. 299:1–4. He further explained that:

> if you have either a declining kidney function, you could get fluid, or if you have excessive wasting of protein in the urine, people tend to retain sodium and get swollen as well. It's not specific for kidney disease, but in someone who has no other explanation, one has to consider kidney disease as being one of the possibilities.

Tr. 299:5–11. In the Javaugue et al. study discussed above, the authors wrote that fifty-six percent of the patients studied had "lower-limb edema" at the time of FGN diagnosis. Resp't's Ex. A, Tab 7, at 2.

Dr. Fine, however, stated that he did not believe that the Petitioner's symptoms of abdominal pain, nausea, vomiting, and diarrhea when she presented to the hospital on November 21, 2013, were the manifestation of her FGN. Tr. 302:24–303:8. He explained that "kidney disease does not usually present with these symptoms." Tr. 303:10–11. While he noted that "nausea and vomiting are well established symptoms of advanced kidney disease[,]" Dr. Fine explained that they are "just generally not symptoms [he's] going to see until . . . [a] very advanced [glomerular filtration rate ("GFR")[102] . . . ." Tr. 303:11–12, 17–18. Dr. Fine also stated that "[d]iarrhea is not a symptom of kidney disease that he's ever heard of." Tr. 303:20–21. Dr. Fine noted that "patients with kidney disease [may] present with diarrhea for some other reason[,]" but stated that, "in general, as a manifestation of either acute or [CKD], diarrhea is not something that would make [him] think . . . [someone has a] kidney disease." Tr. 303:24–304:2. Rather, Dr. Fine opined that

[102] The glomerular filtration rate is "the quantity of glomerular filtrate formed per unit time in all nephrons of both kidneys, equal to the inulin clearance; usually measured clinically by the endogenous creatinine clearance." *Glomerular Filtration Rate*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021). Glomerular filtrate is "the ultrafiltrate of plasma that passes across the membranes of the renal corpuscles into the urinary space." *Glomerular Filtrate*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

Petitioner's symptoms would have "immediately [put] the focus . . . on abdominal issues." Tr. 304:5–7.

In addition, Dr. Fine argued that three diagnostic findings show that Petitioner likely was suffering from a gastrointestinal illness at the time of her November 21, 2013 hospitalization. First, Dr. Fine noted that Petitioner had "a high white blood cell count" during her brief hospitalization. Tr. 304:7–8. He further stated that "Dr. Ballouk made an allusion to [Petitioner's] volume depletion, . . . the idea [being] as you lose water in the blood, the white [cell] count concentration goes up. That is not an accepted teaching. Hemoglobins[103] can go up when you get volume depleted, white [cell] counts generally don't." Tr. 306:11–15. Dr. Fine explained that "white cell counts don't go up just because of kidney failure. Generally[,] a high white blood cell count suggests an inflammatory or an infectious condition." Tr. 306:8–10. Furthermore, Dr. Fine explained that "if the white count went up because of hemodilution,[104] all the subtypes of white cells would go up together, but in her case, the one that indicates infection was actually higher than all the rest." Tr. 306:1–19. Therefore, he concluded "that the higher white cell count was not a feature of volume depletion[] but was truly a high white blood cell count." Tr. 306:21–23.

Second, Dr. Fine stated that, "on [Petitioner's] white count, there was what [is] . . . call[ed] a left shift." Tr. 304:13–14. He explained a "left shift" is "a high number of neutrophils,[105] which generally suggests an infection." Tr. 304:14–15. Third, Dr. Fine noted that Petitioner's abdominal "CT did show something that suggested a mild diverticulitis." Tr. 304:18–19. He explained that diverticulitis "is little appendices on the other side of the bowel." Tr. 305:2–3. He disagreed with Dr. Ballouk that diverticulitis cannot last "for [only] two weeks," as "there are cases of diverticulitis that spontaneously resolve." Tr. 304:20–23. In addition, Dr. Fine testified that "[t]he other feature that suggests . . . that this was gastrointestinal is [that] it resolved, and . . . [Petitioner] specifically [stated] that after this, she had intolerance of milk products . . . ." Tr. 305:3–8. He explained that "one of the most common causes of [lactose intolerance] is a gastroenteritis[106] type of presentation." Tr. 305:15–16. Dr. Fine opined that, taken together, "it's sort of added evidence that this was just a GI complaint." Tr. 306:20–21.

Dr. Fine also discussed the renal function testing performed during Petitioner's brief hospitalization and her estimated GFR ("EGFR"). In terms of testing renal function, Dr. Fine explained that "the standard test that [doctors] use, the most . . . reliable test [doctors] have is the creatinine [test]." Tr. 307:5–6. Dr. Fine further explained that creatinine levels differ person to person, where "creatinine in a very muscular person tends to be higher because it's made by [the]

---

[103] Hemoglobin is "the red oxygen-carrying pigment of the erythrocytes, formed by developing erythrocytes in bone marrow." *Hemoglobin*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 4, 2021).

[104] Hemodilution is an "increase of the fluid content of the blood with resulting decrease in concentration of its erythrocytes." *Hemodilution*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 4, 2021).

[105] Neutrophils are "mature granular leukocytes that [are] polymorphonuclear (its nucleus having three to five lobes connected by slender threads of chromatin, and cytoplasm containing fine granules)." *Neutrophil*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 3, 2021).

[106] Gastroenteritis is "inflammation of the lining of the stomach and intestines . . . ." *Gastroenteritis*, DORLAND'S, https://www.dorlandsonline.com (last visited Feb. 4, 2021).

muscle[s], and in someone who is less muscular, it will be lower." Tr. 307:22–25. Because "age, race and gender all affect muscle mass indirectly[,]" Dr. Fine testified that there is a "calculation, or . . . formula that's used[]" to "measure . . . the ability of the kidney to clear toxins." Tr. 307:25–308:2, 9–10. Dr. Fine explained that the formula "includes the creatinine [level], but then it tries to normalize that to the other features by looking at age, race[,] and gender[,]" and the number calculated by this formula is called the GFR. Tr. 308:2–8. He noted that "[t]he lower your GFR, the less well you clear toxins." Tr. 308:10–11. Dr. Fine testified that a "normal" GFR is "more than [ninety]." Tr. 308:17. He further testified that the GFR "more or less reflects percent of kidney function. So[,] if [GFR is] at [twenty], [then that person] has [twenty] percent of the normal kidney function." Tr. 308:18–20.

Dr. Fine explained that there are five stages of kidney disease and that "the staging of kidney disease is specifically based on [EGFR]." Tr. 308:23–309:1. Dr. Fine testified that the stages of kidney disease are as follows:

> Stage one is when the EGFR is more than [ninety]; stage two is [sixty] to [eighty-nine]; stage three [is thirty] to [fifty-nine]; and then stage four is [fifteen] to [thirty] . . . Stage five is less than [fifteen] and that's usually considered sort of near [ESRD], or [ESRD].

Tr. 309:1–6.[107] Dr. Fine explained that an EGFR of "below [fifteen is] . . . when [doctors] really start to monitor patients very closely for dialysis needs[,]" which usually begins once the patient exhibits "symptoms like nausea and vomiting, poor appetite." Tr. 309:6–9.

During Petitioner's November 21, 2013 hospitalization, Dr. Fine noted that her creatinine level was 2.8, which equated to an EGFR of "20 ml/min/1.73m2[,] representing approximately [twenty percent] of kidney function." Resp't's Ex. E at 3–4. Dr. Fine testified that this meant that Petitioner was already in stage four of her kidney disease by her November 21, 2013 hospitalization. Tr. 309:10–14. Dr. Fine disagreed with Dr. Ballouk's contention that Petitioner's creatinine was as high as it was because she was dehydrated. Tr. 309:15–19. While he agreed that "if [Petitioner] had gotten fluids and [doctors] rechecked her creatinine, it would probably have been a little lower[,]" Dr. Fine opined that he did not "think that it would be less than two . . . ." Tr. 309:19–22. He estimated that Petitioner's creatinine after receiving fluids was "probably somewhere around 2.5, but certainly it wouldn't have been a dramatic reduction in her creatinine and hence [not a drastic] increase in that GFR number . . . . [Y]ou can have a creatinine of 2.4, 2.5, [and] her GFR is still in the low [twenties]." Tr. 310:9–14. Further, Dr. Fine addressed the difference between Petitioner's creatinine readings in November 2013 and January 2014. He explained that, as kidney function worsens, "the creatinine rises way faster than the amount of kidney function you lose." Tr. 311:11–15. He continued that this did not result in a "massive change" in Petitioner's EGFR. Tr.311:19–12. Dr. Fine stated that the rise in Petitioner's creatinine

[107] Dr. Fine's testimony on the stages of kidney disease by EGFR closely tracks with the Kidney Disease Improving Global Outcomes' *2012 Clinical Practice Guidelines for the Evaluation and Management of Chronic Kidney Disease* that Dr. Fine submitted with his supplemental report. *See* Resp't's Ex. E, Tab 4, at 21; Kidney Disease Improving Global Outcomes, *2012 Clinical Practice Guidelines for the Evaluation and Management of Chronic Kidney Disease*, 3(1) KIDNEY INTERN. SUPP. 1, 21 (2013).

levels did not signal rapid progression because "[r]apidly progressive patients lose . . . half their kidney function in weeks." Tr. 311:22–24.

Dr. Fine took issue with how Petitioner characterized the Nasr et al. study and applied it to her disease progression. He testified that this study was "a case series, which is just a number of patients . . . [where researchers] look at what happens to [the patients] and how they presented . . . ." Tr. 313:11–13. He wrote that this "study is a retrospective one which is not designed to predict 'expected' progression." Resp't's Ex. E at 3. Rather, Dr. Fine opined that "[i]t is a descriptive study that presents a series of patients and how their disease behaved in order to give the reader insights into the disease." *Id*.

Nevertheless, Dr. Fine explained that "the features of [Petitioner's] disease, both clinical and histopathologic, are entirely consistent with those presented in this study of a relatively small patient population with a rare disease." *Id*. Specifically, Dr. Fine referred to a chart on page seven of the article, which "shows . . . the four factors that would predict, in their group of patients, at the time of biopsy, which [patient] is going to do the worst." Tr. 314:14–19. In the article, the authors "identified several independent predictors of ESRD by multivariate analysis . . . ." Resp't's Ex. A, Tab 5, at 9. They listed "older age, higher creatinine at biopsy, higher 24-hour urine protein at biopsy, and higher percentage of globally sclerotic glomeruli" as "predictors of renal survival in [FGN]." *Id*. Dr. Fine explained each predictor in greater detail during his testimony. He explained that, for the old age factor, "the older you are, your hazard ratio is one more, for each year in age, you have 0.12 percent, or [twelve] percent increased risk [of reaching ESRD]." Tr. 314:21–23. For the urine protein factor, Dr. Fine stated that "the higher the urine protein, the more likely [the patient is] going to be on dialysis." Tr. 314:25–315:2. Regarding serum creatinine at biopsy, Dr. Fine explained that "the higher that is, the greater risk of meeting [ESRD, which] . . . make[s] sense[] because . . . if you have higher creatinine, [then] you have more damage to your kidneys and are more likely to end up on dialysis." Tr. 315:3–8. Lastly, he explained that "globally sclerotic glomerulus is a dead glomerulus, [and] the more you have, the more likely you're going to be on dialysis." Tr. 315:9–12.

Looking at these factors, Dr. Fine opined that Petitioner "had high levels of proteinuria and creatinine at [the] time of biopsy and very high percent of sclerosed glomeruli." Resp't's Ex. A at 7. The only factor Dr. Fine did not believe applied to Petitioner was age. Tr. 316:2–3. Therefore, Dr. Fine concluded that "[i]t is not surprising . . . that she went on to develop ESRD." Resp't's Ex. A at 7.

Dr. Fine also discussed Petitioner's renal biopsy results in detail in both his written reports and testimony. Dr. Fine testified that he believed that "there are significant clues as to how long [Petitioner's FGN] was there based on [her] biopsy [results]." Tr. 312:12–14. He discussed three articles as support. The first was the Nasr et al. article. In this article, which studied sixty-six FGN patients, the authors noted that only one of the patients had a form of FGN called "diffuse sclerosing glomerulonephritis" ("DSGN"), which they defined as "[one hundred percent] of glomeruli showing global sclerosis." Resp't's Ex. A, Tab 5, at 3–4. They also noted that "fifty-five cases ([eighty-three percent]) showed interstitial inflammation, which was predominantly focal." *Id*. at 4. In addition, they found that "[t]he degree of tubular atrophy and interstitial fibrosis ranged from absent ([six percent] of cases) to mild ([fifty-one percent]) to moderate ([thirty-three

percent]) to severe ([nine percent]).” *Id.* The authors also found that the “[m]ean percentage of globally sclerotic glomeruli” was twenty-five percent. *Id.* at 5.

In addition to the Nasr et al. study, Dr. Fine also referenced the Rosenstock et al. study in support of his discussion of Petitioner’s biopsy results. Dr. Fine testified that this study “actually break[s FGN] down . . . based on pathology findings . . . .” Tr. 318:22–319:2. The authors of this study wrote that “[t]hirteen percent of biopsies had a nondescript diffuse sclerosing pattern . . . , defined as glomerular sclerosis obliterating [greater than seventy percent] of glomeruli . . . .” Resp’t’s Ex. C, Tab 1, at 4. They also wrote that “[i]nterstitial disease was most severe in the [diffuse sclerosing] subgroup, in which all biopsies . . . displayed moderate to severe interstitial fibrosis . . . .” *Id.* While the authors found that “[t]he [overall] median time to ESRD was 24.4 [plus/minus] 15.2 months,” with an overall “mean [time to ESRD] of 57.6 [plus/minus] 9.49 months[,]” they further noted that the “[m]ean time to ESRD varied according to histologic subtype . . . .” *Id.* at 6. They found that the diffuse sclerosing “subgroup[] . . . progressed more rapidly to ESRD” than other subgroups, noting that patients of this group reached ESRD in a mean of seven months. *Id.* A chart created by the authors showed that more than seventy percent of the diffuse sclerosing subgroup of patients reached ESRD within two months from the date of biopsy. *Id.* at 10.

During his testimony, Dr. Fine also discussed the Rosenstock and Markowitz article, which he described as a “more of a review type paper.” Tr. 326:16–17; Pet’r’s Ex. 55. On page two of this article, the authors provide a chart in which they list the clinical characteristics of patients with FGN included in the three studies reviewed by the authors. Pet’r’s Ex. 55 at 2. The authors found that, “[a]t the time of presentation, [seventy percent] of patients had renal insufficiency, and the mean serum creatinine was 2.9 . . . .” *Id.* at 1. They further noted that “[t]he mean [twenty-four]-hour urine protein was 5.7 . . . , and [thirty-six percent] of patients met criteria for full nephrotic syndrome.” *Id.* Dr. Fine stated that this study demonstrates that Petitioner’s FGN was a “classic” presentation. Tr. 327:20.

Regarding Petitioner’s renal biopsy, Dr. Fine wrote that the “biopsy findings are typical of an advanced [FGN] as described in the literature.” Resp’t’s Ex. A at 5. He noted that the biopsy revealed “extensive interstitial inflammation.” Tr. 340:23–24. He further noted that “[eighteen] out of [twenty-three] of [Petitioner’s glomeruli] . . . were dead glomeruli[,]” and “three other glomeruli that show segmental sclerosis, so it's starting to scar off, but it's probably an earlier stage scarring, with a significant lesion, glomerular tufts, and [the pathologists] say, ‘glomeruli show marginal increase in mesangial matrix . . . .” Tr. 339:10–12, 342:2–7. The results also revealed a “mild increase in cellularity due to few mononuclear cells. So[,] the few mononuclear cells say [there’s] maybe a little bit of inflammation, but this mesangial matrix increases the mesangial type lesion.” Tr. 342:9–12. He continued, “in the three glomeruli that [he] ha[s] that [he] can actually get real information out of, there isn't any evidence of something that's highly active.” Tr. 342:12–15. He further testified that the pathologists wrote “[t]he glomeruli do not show evidence of crescent formation, fibrinoid necrosis, thrombosis, or endocapillary proliferation.” Tr. 343:2–4. Dr. Fine opined that they wrote this “because they want [the nephrologist reading the results] to know that, because it's actually important in determining how active is the lesion.” Tr. 343:5–8. Dr. Fine argued that Petitioner’s theory that she “had a rapid loss of kidney function” fails because that type of deterioration doesn’t happen “without crescentic GN or some really aggressive

inflammation[,] which almost always results in crescentic formation." Tr. 344:9, 16–18. Dr. Fine opined that "[i]f there was ongoing active disease that was bad enough to cause renal failure from September through to the time of the biopsy," then "you would see evidence of whatever that process was that would do that." Tr. 345:3–5, 9–11. Dr. Fine noted that the "proliferative types [of FGN act in that manner], but there's no evidence [on Petitioner's biopsy] of proliferation." Tr. 345:13–14. However, he further noted that "the mesangial process doesn't behave that way." Tr. 345:12–13.

Dr. Fine disagreed with Dr. Ballouk that the lack of crescent formations on Petitioner's biopsy would be expected because the literature only notes that a small percentage of patients have crescents. Tr. 347:9–17. He submitted an article by Pusey, which provides more information on crescentic formations in renal injury. Resp't's Ex. A, Tab 6. The author wrote that crescents are a "hallmark of inflammatory [GN] and a histologic marker of severe glomerular injury." *Id.* at 1. He further wrote that "[c]rescentic [GN] is typically associated with the syndrome of rapidly progressive [GN] . . . ." *Id.* He explained that "[g]lomerular crescent formation appears to represent a nonspecific response to severe injury to the glomerular capillary wall[,]" and therefore "crescent formation appears to be a consequence, not a cause, of severe glomerular injury." *Id.* at 1, 9. Dr. Fine wrote that "a currently active glomerular disease would be expected to present with cellular crescents on biopsy, and one that was previously active but now 'burnt out' will have fibrous crescents (or sclerosed crescents)." Resp't's Ex. E at 4. He explained that "crescents evolve over time from cellular to fibrous, and later the entire glomerulus may sclerose or scar . . . ." *Id.* He further explained that "fibrous crescents will be present for months after the initial crescent formation and remain as evidence of a recent active lesion . . . ." *Id.* Dr. Fine stated that "the hallmark of [rapidly progressive] . . . renal lesions is the presence of a crescent." Tr. 349:14–15. Dr. Fine noted that Petitioner's biopsy did not show crescents, but rather "[o]nly [showed] sclerosed glomeruli," and he therefore concluded that Petitioner's "disease was present for a very long time." Resp't's Ex. E at 4.

During his testimony, Dr. Fine opined that Petitioner's FGN course was "typical." Tr. 354:7–9. He argued that Petitioner's "course is . . . what you see in someone who has had longstanding [FGN] . . . ." Tr. 354:21–22. He explained that "the reason it's longstanding is it is asymptomatic. You don't get symptoms. [A patient] might get hypertension, but . . . physicians are saying, . . . a lot of people get hypertension, and so [the physicians] ignore it or just expect [hypertension] for that particular patient." Tr. 354:23–355:2.

Regarding onset of Petitioner's FGN, Dr. Fine testified that he "sort of work[ed] backwards." Tr. 355:8–11. He explained that Petitioner had "a very advanced lesion[,]" which he stated "usually takes years to develop." Tr. 355:11–12. In addition, Dr. Fine testified that "based on pathology alone, [he] would . . . [estimate that] it's been there for years." Tr. 355:23–24. He wrote that "there were no cellular crescents [present on Petitioner's biopsy] suggesting no ongoing severe disease activity, and no fibrous crescents, suggesting no recent activity." Resp't's Ex. E at 4. Rather, Dr. Fine explained that Petitioner's biopsy only revealed "sclerosed glomeruli . . . , which indicates that the disease was present for a very long time." *Id.* He estimated that, although "an exact [onset] date is hard to determine, based on [his] clinical practice and experience . . . , the presence of global sclerosis of the diffuse nature seen on this kidney biopsy suggest that the damage had occurred more than [five] months before the biopsy." *Id.* He expounded on this belief

during his testimony. He noted that "the first signs [he] see[s] of something that would go with the kidney disease is the hypertension, the edema, and they both occur actually very similarly around the middle July, August of 2011 . . . ." Tr. 355:14–17. He further stated that "the fact that the glomerulus that's actually visible, that isn't dead yet, that mesangial form of fibrillary supports that this is the way that it would have progressed, would have been over a very long period of time." Tr. 356:8–13. Therefore, Dr. Fine estimated that the onset of Petitioner's FGN occurred in 2011. Tr. 356:14–15.

On cross-examination, Dr. Fine explained that Dr. Lutes' assessment that Petitioner had "renal insufficiency with nephrotic syndrome, [which] again, . . . has developed acutely over the past few months[]" did not change his opinion that Petitioner's FGN developed over a period of years. Tr. 367:15–21. He opined that Dr. Lutes "was wrong[]" in his opinion because Dr. Lutes "can't say it's acute or chronic at [that] point." Tr. 368:21–22. He continued, "at the time that Dr. Lutes" made that assessment, "all he has is one creatinine, and one creatinine doesn't tell you where [Petitioner is] in the course of [her] disease." Tr. 367:25–368:2.

Under my questioning, Dr. Fine stated that he had seen "triggers" in patients with "otherwise asymptomatic kidney disease" but not in FGN patients because he's "seen too few of them." Tr. 377:25–378:5. In kidney diseases other than FGN, Dr. Fine listed infection, medication, and stress as "triggers . . . for kidney diseases that can make them flare or get worse." Tr. 378:6–9. However, Dr. Fine opined that, if Petitioner's FGN "flared" because of an infection, for example, he "would have seen it on the biopsy three months later." Tr. 379:9–12.

I also asked Dr. Fine what he thought of Petitioner's PCP's statement that Petitioner's biopsy "results . . . showed a lot of fibrosis, so she thinks that this may have been ongoing longer." Tr. 384:5–7, 9–10 (quoting Pet'r's Ex. 12 at 26). Dr. Fine responded that he "think[s] that's the whole premise of [his] argument . . . ." Tr. 384:11–12. He explained that this "[t]ells [him Petitioner's FGN] . . . wasn't acute. This . . . was a longstanding lesion that was present for certainly more than five months . . . . This is years of lesion, before you get that level of fibrosis." Tr. 384:15–20.

IV. Applicable Legal Standards

A petitioner in the Program is entitled to compensation if a special master determines "on the record as a whole" that the petitioner "has demonstrated by a preponderance of the evidence the matters required in the petition by [§ 300aa-11(c)(1)], and that there is not a preponderance of evidence that the illness, disability, [etc.] described in the petition is due to factors unrelated to the [vaccination]." § 300aa-13(a)(1)(A)–(B). A special master cannot award compensation "based on the claims of a petitioner alone, unsubstantiated by medical records or by medical opinion." § 300(a)(1). Although a special master must consider all "diagnos[e]s, conclusion[s], [and] medical judgment[s] . . . regarding the nature, causation, and aggravation of the petitioner's [condition]," as well as diagnostic or evaluative tests, such are not binding on the court. § 300(b)(1). When considering the weight to be afforded to such medical evidence, the special master must "consider the entire record and the course of" the petitioner's condition. *Id.*

A. Petitioner's Overall Burden in Program Cases

To receive compensation under the Vaccine Act, a petitioner must demonstrate either that: (1) her condition is a "Table Injury," and therefore resulted from the receipt of a covered vaccine or vaccines within the time frame prescribed by the Vaccine Injury Table set forth at § 14, as amended by 42 C.F.R. § 100.3; or (2) her condition is an "off-Table Injury," one not listed on the Table, that resulted from her receipt of a covered vaccine. *See* § 11(c)(1)(C); *Moberly v. Sec'y of Health & Hum. Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Hum. Servs.*, 440 F.3d 1317, 1319–20 (Fed. Cir. 2006). Petitioner's claim that the flu vaccination significantly aggravated her kidney failure and glomerulonephritis does not fall within the Vaccine Table. Thus, Petitioner must prove that her flu vaccination was the cause-in-fact of the aggravation of her condition.

To establish causation-in-fact, a petitioner must demonstrate by a preponderance of the evidence that her vaccine was the cause of injury. § 13(a)(1)(A). A petitioner need not show that the vaccination was the sole cause, or even the predominant cause, of the alleged injury; showing that the vaccination was a "substantial factor" and a "but for" cause of the injury is enough for recovery. *Pafford v. Sec'y of Health & Hum. Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006); *Shyface v. Sec'y of Health & Hum. Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999).[108]

In *Althen v. Sec'y of Health & Hum. Servs.*, the Federal Circuit set forth a three-pronged test used to determine whether a petitioner has established a causal link between a vaccine and the claimed injury. *See* 418 F.3d 1274, 1278 (Fed. Cir. 2005). The *Althen* test requires a petitioner to set forth: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id*. To establish entitlement to compensation under the Program, a petitioner is required to establish each of the three prongs of *Althen* by a preponderance of the evidence. *See id*. (internal citations omitted).

Specifically, under the first prong of *Althen*, a petitioner must offer a scientific or medical theory that answers in the affirmative the question "can [the] vaccine(s) at issue cause the type of injury alleged?" *See Pafford v. Sec'y of Health & Hum. Servs.*, No. 01-0165V, 2004 WL 1717359, at *4 (Fed. Cl. Spec. Mstr. July 16, 2004), *aff'd*, 64 Fed. Cl. 19 (2005), *aff'd*, 451 F.3d 1352 (Fed. Cir. 2006), *cert. denied*, 551 U.S. 1102 (2007). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Hum. Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994); *see also Andreu v. Sec'y of Health & Hum. Servs.*, 569 F. 3d 1367, 1375, 1379 (2009) (ruling that the petitioners had satisfied *Althen* prong one where their expert witness had "presented a 'biologically plausible' theory"). Such a theory must only be "legally probable, not medically or scientifically certain." *Knudsen*, 35 F.3d at 548–49.

A petitioner may satisfy this prong in a number of ways. "Reliability and plausibility of . . . pathogenesis can be bolstered by providing evidence that at least a sufficient minority in the medical community has accepted the theory, so as to render it credible." *Pafford*, 2004 WL 1717359, at *4. Additionally, "epidemiological studies and an expert's experience, while not

[108] The Vaccine Act also requires petitioners to show by preponderant evidence that the "residual effects or complications" of the alleged vaccine-related injury lasted for more than six months. § 11(c)(1)(D)(i). It is undisputed that this six-month requirement is satisfied in this case.

dispositive, lend significant credence to the claim of plausibility." *Id*. Medical literature published in respected medical journals is also persuasive. *Id*. "However, publication 'does *not* necessarily correlate with reliability', because 'in some instances well-grounded but innovative theories will not have been published.'" *Id*. (quoting *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 593–94 (1993) (emphasis in original)). However, "a petitioner can satisfy her burden to prove a plausible medical theory without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory[.]" *Sharpe*, 964 F.3d 1072, 1085 (Fed. Cir. 2020) (citing *Andreu*, 569 F.3d at 1378–79).

In addition to showing that the vaccine at issue can cause a particular injury, a petitioner must also, under *Althen's* second prong, prove that the vaccine actually did cause the alleged injury in a particular case. *See Pafford*, 2004 WL 1717359, at *4; *Althen*, 418 F.3d at 1278. A petitioner does not meet this obligation by showing only a temporal association between the vaccination and the injury; the petitioner "must explain *how* and *why* the injury occurred." *Pafford*, 2004 WL 1717359, at *4 (emphasis in original) (internal citations omitted).

Although a temporal association alone is insufficient to establish causation, under the third prong of *Althen*, a petitioner must show that the timing of the injury fits with the causal theory. *See Althen*, 418 F.3d at 1278. The special master cannot infer causation from temporal proximity alone. *See Thibaudeau v. Sec'y of Health & Hum. Servs.*, 24 Cl. Ct. 400, 403–04 (1991); *see also Grant v. Sec'y of Health & Hum. Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992) ("[T]he inoculation is not the cause of every event that occurs within the ten[-]day period. . . . Without more, this proximate temporal relationship will not support a finding of causation." (quoting *Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983))).

B. Standards Applicable to Significant Aggravation Claims

Petitioners must establish causation in all off-Table cases; however, petitioners may establish they are entitled to compensation based on a claim that vaccination significantly aggravated a pre-existing condition. Here, Petitioner asserts that the flu vaccine significantly aggravated her pre-exiting FGN. The Vaccine Act defines significant aggravation as "any change for the worse in a pre[-]existing condition which results in markedly greater disability, pain, or illness accompanied by substantial deterioration of health." § 300aa-33(4). When a petitioner makes this argument, the evidentiary burden is expanded. *See Loving v. Sec'y of Health and Hum. Servs.*, 86 Fed. Cl. 135, 144 (2009). In *Loving*, the Court set forth a six-factor test, which requires establishing the following:

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

Loving, 86 Fed. Cl. at 144.

The *Loving* analysis requires the special master to "evaluat[e] whether the vaccine made the person worse than the person would have been but for the vaccination. In doing so, the natural course of the disease must be considered." *Locane v. Sec'y of Health & Hum. Servs.*, No. 99-589V, 2011 WL 3855486 at *10 (Fed. Cl. Spec. Mstr. Feb. 17, 2011), *mot. for review den'd*, 99 Fed. Cl. 715 (2011), *aff'd*, 685 F.3d 1375 (Fed. Cir. 2012); *see also Hennessey v. Sec'y of Health & Hum. Serv.*, No. 01-190V, 2009 WL 1709053, at *41–42 (Fed. Cl. Spec. Mstr. May 29, 2009), *mot. for review den'd*, 91 Fed. Cl. 126 (2010). However, a petitioner is not required "to demonstrate an expected outcome and that her current-post vaccination condition was worse than such expected outcome." *Sharpe*, 964 F.3d at 1081.

V. Analysis

A. *Loving* Prong One – Condition Prior to Vaccination

The parties agree that Petitioner's FGN predated her vaccination. However, they dispute how long her disease had been progressing before her vaccination and whether she was symptomatic before her vaccination. Regarding the onset of Petitioner's FGN, neither party proffers a precise date. Respondent's experts opine that Petitioner was experiencing two classic symptoms of renal disease, hypertension and edema, beginning in July and August 2011, more than two years before her September 23, 2013 vaccination. Petitioner's experts, in contrast, claim that her disease began, asymptomatically, shortly before her vaccination. Petitioner's experts maintain that Petitioner did not experience symptoms of her FGN until after her vaccination. The evidence in the record demonstrates that, by a preponderant standard, Petitioner was symptomatic as of July 2011. Thus, by Petitioner's September 23, 2013 vaccination, it is more likely than not that she had been suffering from FGN for more than two years.

The articles submitted by Respondent, and cited by Petitioner's expert, show that hypertension and edema are associated with renal disease generally, and FGN specifically. The Rosenstock et al. paper found that seventy-seven percent of FGN patients presented with hypertension and sixty-seven percent of patients presented with edema. Resp't's Ex. C, Tab 1, at 4. The Nasr et al. study found that seventy-one percent of FGN patients had hypertension and fifty-nine percent of patients had edema at biopsy. Resp't's Ex. A, Tab 5, at 4; *see also* Pet'r's Ex. 50 at 1–2, 2 n.1. The Javaugue et al. article found that seventy percent of patients at biopsy exhibited hypertension while fifty-six percent of patients exhibited edema. Resp't's Ex. A, Tab 7, at 2. These articles demonstrate that a substantial majority of FGN patients exhibit hypertension and/or edema during the course of their disease.

Furthermore, expert opinions in the record indicate that hypertension is often the first symptom, and sometimes the only symptom in the early stages of renal disease. Dr. Fine stated that "hypertension . . . is often the first sign of kidney disease . . . ." Tr. 294:23–295:11. Dr. Fine asserted that a person with longstanding FGN may have longstanding FGN precisely because she is asymptomatic. Tr. 354:21–23. Dr. Fine indicated that an FGN patient might be asymptomatic except for hypertension, which doctors commonly attribute to other causes. *See* Tr. 354:23–355:2.

The medical records first indicate that Petitioner suffered from hypertension and edema during a July 12, 2011 visit with Dr. Nino. *See* Pet'r's Ex. 1 at 28. Petitioner again presented with edema on May 24, 2012, June 26, 2012, and May 30, 2013. Pet'r's Ex. 1 at 6, 18–19. During her July 12, 2011 visit, Petitioner's blood pressure reading was 138/90. *Id.* at 28. Her blood pressure during her next appointment, on August 17, 2011, was 140/86. *Id.* at 27. These readings were above Petitioner's baseline from previous visits. *See* Resp't's Ex. A at 2. During previous visits with Dr. Nino on January 22, March 7, April 18, and May 31, 2011, her blood pressure readings were all within normal range at 118/62, 122/80, 112/66, and 118/80, respectively. *Id.* According to the more recent of the two guidelines cited by the CDC, high blood pressure is 130 mm Hg or higher systolic and 80 mm Hg or higher diastolic.[109] Petitioner's readings from July up to her September 23, 2013 vaccination fluctuated, but were generally higher than her baseline. Petitioner's highest blood pressure reading during that time occurred on August 24, 2013, approximately one month before her vaccination. Her blood pressure on August 24, 2013, was 176/124. *Id.* at 4.

While hypertension, even when accompanied by edema, may be too common to be used as a basis for diagnosis of any specific disease, neither symptom can be discounted once a disease associated with both symptoms is diagnosed. There are no other readily identified conditions or injuries in Petitioner's medical history that would cause edema and high blood pressure to appear in such close proximity to each other. Furthermore, there is no evidence that Petitioner's physicians attributed her high blood pressure or edema to any other cause. *See generally* Pet'r's Ex. 1. While Petitioner does have a history of smoking and obesity, these are unlikely causes of her edema or hypertension. Petitioner had a long history of obesity and smoking, but no history of hypertension or edema prior to 2011. Notably, Petitioner testified that she quit smoking in the fall of 2013. Tr. 33:16–18. On January 22, 2014, she reported weight loss that had helped remedy her back pain. Pet'r's Ex. 12 at 30. Yet, even after she quit smoking and reported at least some weight loss, Petitioner's blood pressure was still significantly elevated at 160/110 on January 22, 2014. *Id.* at 31. Dr. Fine briefly considered whether pain or anxiety could have contributed to her high blood pressure, but these too are unlikely. Petitioner had a history of both pain and anxiety, including longstanding treatment with medication. Yet, Petitioner's blood pressure did not begin to spike until July 2011. Further, even if a different condition did explain Petitioner's high blood pressure on one or a few occasions, that would not account for why it was consistently high in years leading up to her flu vaccination. Based on the expert testimony and the temporal relationships, I find it more likely than not that Petitioner's hypertension and edema were early indicators of Petitioner's FGN.

That Petitioner's FGN began years before her vaccination is further supported by her biopsy results. Dr. Fine testified that Petitioner's biopsy showed "a very advanced lesion[,]" which "usually takes years to develop." Tr. 355:11–12. He continued that "based on pathology alone, [he] would . . . [estimate that] it's been there for years." Tr. 355:23–24. Dr. Fine stated that the presence of sclerosed glomeruli on biopsy "indicates that the disease was present for a very long time." Resp't's Ex. E at 4.

[109] *See supra* note 9. Petitioner's readings are also close to qualifying as high blood pressure according to the older set of guidelines mentioned by the CDC. *See id.*

Based on the foregoing, I find it more likely than not that Petitioner was suffering from and exhibiting symptoms of FGN, in the form of hypertension and edema, for more than two years prior to her vaccination.

B. *Loving* Prong Two – Current, or Post-Vaccination, Condition

Petitioner's condition post vaccination is not disputed by either party. Nearly two months post vaccination, Petitioner presented to the emergency room with complaints of abdominal pain, nausea, vomiting, and diarrhea. *See* Pet'r's Ex. 3(b) at 289. During her brief hospitalization, Petitioner had her first high creatinine reading. *See id.* at 283. She was biopsied and definitively diagnosed with FGN on February 19, 2014. *See* Pet'r's Ex. 3(a) at 62, 95. She progressed to ESRD requiring dialysis by June 2014. *See* Pet'r's Ex. 4 at 2. At the time of the hearing, Petitioner was undergoing regular HD and was awaiting kidney transplantation. Tr. 28:1–3, 29:5–6. I find it more likely than not that Petitioner was still suffering from FGN, which later progressed to ESRD, post vaccination.

C. *Loving* Prong Three – Significant Aggravation

The parties' most significant dispute is whether the course of Petitioner's disease after her vaccination constituted a significant aggravation of her FGN. Petitioner alleges that she progressed to ESRD faster than what is normally expected for FGN patients. Respondent, however, argues that Petitioner's FGN was more chronic in nature and that her clinical course aligned with the expected progression of her particular iteration of FGN. After considering the entire record, particularly the literature filed by the parties[110] and Petitioner's biopsy results, I find that it is more likely than not that the flu vaccine did not significantly aggravate the course of Petitioner's disease.

The articles discussed by both parties indicate various time frames in which a FGN patient would likely reach ESRD. Petitioner points to some of these time frames to demonstrate that Petitioner progressed to ESRD at an accelerated rate. Dr. Ballouk cited the Nasr et al. study, which found "nearly one half of patients [studied] progressing to ESRD within [four] years." Resp't's Ex. A, Tab 5, at 9. Dr. Ballouk discussed the Jauvague et al. paper, which showed forty-eight percent of patients developing ESRD a median of forty-four months following diagnosis. Resp't's Ex. A, Tab 7, at 9. Dr. Ballouk further discussed the Rosenstock et al. study, which showed that forty-five percent of patients (including seventy-two percent of patients presenting with a creatinine level above 2.0) reached ESRD after a median of about two years. Resp't's Ex. C, Tab 1, at 6. Asserting that he relied on the Rosenstock et al. article to form the basis of his opinions, Dr. Ballouk testified that forty-four percent of FGN patients "will end up on dialysis with a median of [twenty-four] months." Tr. 186:24–187:1, 202:24–203:1. Dr. Ballouk later opined that the

[110] Neither party is required to file medical literature, however, it can be effective support for expert opinions, particularly when the opposing party does not provide rebuttal. While the undersigned has reviewed all of the information filed in this case, only those filings and records that are most relevant to the decision will be discussed. *Moriarty v. Sec'y of Health & Hum. Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision.") (citation omitted); *see also Paterek v. Sec'y of Health & Hum. Servs.*, 527 F. App'x 875, 884 (Fed. Cir. 2013) ("Finding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered.").

presence of mesangial involvement, as well as the fact that Petitioner did not have one hundred percent sclerosed glomeruli, indicated that she was in the MES subgroup. Tr. 274:20–275:1. Citing the Rosenstock et al. study, Dr. Ballouk stated that a patient in the MES subgroup would take eighty months to reach ESRD. Tr. 275:2–5. Dr. Ballouk, however, neglected that Petitioner falls into the clearly stated definition of the DS subgroup articulated in that study, which is seventy percent of sclerosed glomeruli. *See* Resp't's Ex. C, Tab 1, at 4. Overall, the time frames presented by Petitioner do not take account of the percentage of Petitioner's glomeruli that were already sclerosed by the time of biopsy.

Respondent's use of the Rosenstock et al. article to demonstrate that Petitioner's disease progressed at a normal rate is very compelling. As Dr. Ballouk acknowledged, this article showed that the time frame to ESRD varies by histologic FGN-subgroup based on biopsy. Resp't's Ex. C, Tab 1, at 6. Specifically, as stated above, the authors of this study noted that the DS subgroup of FGN reached ESRD an average of seven months post biopsy. *Id.* at 4, 6. Furthermore, a chart included in the article indicates that over seventy percent of patients in the DS subgroup reached ESRD within two months post biopsy.[111] *See id.* at 10.

Petitioner's biopsy results revealed eighteen of twenty-three glomeruli were sclerosed, which equates to seventy-eight percent. Petitioner, therefore, falls within the DS subgroup as defined in the Rosenstock et al. article. She progressed from her first high creatinine finding in November 2013 to ESRD by June 2014. Dr. Levinson indicated that Petitioner's creatinine, proteinuria, and hematuria findings on November 21, 2013, constitute "her diagnosis of a glomerulopathy." *See* Resp't's Ex. C at 4. Dr. Levinson stated that counting from November 2013, Petitioner's diagnosis occurred approximately seven months before she reached ESRD, which was consistent with the DS subgroup. *Id.* Even if the appropriate date to count from is that of Petitioner's February 19, 2014 biopsy, that time frame of more than three months between Petitioner's biopsy and ESRD is well within the range appropriate for her subgroup.

Beside her FGN subgroup, Petitioner's November 21, 2013 hospitalization revealed that she had other risk factors for reaching ESRD. The Nasr el al. article discussed by both parties identified "older age, higher creatinine at biopsy, higher 24-hour urine protein at biopsy, and higher percentage of globally sclerotic glomeruli" as "predictors of renal survival in [FGN]." Resp't's Ex. A, Tab 5, at 9. Dr. Fine concluded that it was unsurprising that Petitioner reached ESRD at the time she did, because age was the only risk factor that Petitioner did not have. Tr. 316:2–3; Resp't's Ex. A at 7.

I did consider that the damage to seventy-eight percent of Petitioner's glomeruli, as well as the rise to high creatinine and urine protein levels, could also be evidence of an accelerated course following Petitioner's vaccination. Petitioner, however, did not persuasively explain how Petitioner's medical history illustrates this potential argument. Dr. Ballouk also did not persuasively distinguish how these indicators, present in Petitioner's case, can be distinguished from a more commonly seen, slower development of FGN. He indicated during my questioning that Petitioner's increase in creatinine between her November 2013 reading and January 2014

[111] The average was seven months, however, because the remaining DS patients did not reach ESRD until twenty-four months or more post biopsy, as shown in the referenced chart. *See* Resp't's Ex. C, Tab 1, at 10.

reading indicated that Petitioner's disease was rapidly progressing. *See* Tr. 267:11–12. However, Dr. Fine persuasively rebutted this by noting that this did not dramatically impact Petitioner's EGFR and explaining that, as kidney function worsens, "the creatinine rises way faster than the amount of kidney function you lose." Tr. 311:11–21. Dr. Fine concluded that this did not signal rapid progression because "[r]apidly progressive patients lose . . . half their kidney function in weeks." Tr. 311:22–24. Furthermore, Dr. Ballouk clarified that he meant that Petitioner's disease was "progressive [because of the rise in Petitioner's creatinine and proteinuria between November and January], and it is aggressive because she ended up on dialysis [in] four months." Tr. 280:12–281:1. However, the issue in this matter is whether Petitioner's disease progressed abnormally quickly, not whether it progressed at all. Overall, the evidence in the record does not demonstrate abnormal progression.

Furthermore, Petitioner's argument fails because her biopsy did not show any evidence that her FGN had progressed at an abnormal rate following her vaccination. Dr. Fine noted that "[eighteen] out of [twenty-three of [Petitioner's glomeruli] . . . were dead glomeruli[,]" and that an additional three of Petitioner's glomeruli displayed segmental sclerosis. Tr. 339:10–12. Dr. Fine stated that such sclerosis indicates that the glomeruli were "starting to scar off, but it's probably an earlier stage scarring . . . ." Tr. 342:2–5. Dr. Fine continued, "in the three glomeruli that . . . he can actually get real information out of, there isn't any evidence of anything that's highly active." Tr. 342:12–15. Dr. Fine noted that the pathologists indicated that the glomeruli did not evince "crescent formation, fibrinoid necrosis, thrombosis, or endocapillary proliferation." Tr. 342:2–4. Dr. Fine argued that this meant Petitioner did not suffer "rapid loss of kidney function" beginning in September 2013, because such rapid loss does not occur "without crescentic GN or some really aggressive inflammation which almost always results in crescentic formation." Tr. 344:8–19. Dr. Fine stated that if Petitioner's disease activity was bad enough to cause renal failure between September 2013, and Petitioner's biopsy, the biopsy would show "evidence of whatever that process was that would do that." Tr. 345:3–5, 9–11. Dr. Fine indicated that a lack of evidence could occur with "proliferative types, but there's no evidence [on Petitioner's biopsy] of proliferation." Tr. 345:13–14. Dr. Fine opined that the lack of cellular crescents or fibrous crescents on Petitioner's biopsy, respectively, "suggest[ed] no ongoing severe disease activity[] and . . . no recent activity." Resp't's Ex. E at 4.

In contrast, Dr. Ballouk opined that "the lack of crescents on [Petitioner's] biopsy does not mean that [Petitioner's] vaccination did not aggravate her disease." Pet'r's Ex. 50 at 2. Dr. Ballouk indicated that only around thirteen percent of biopsies of patients with Petitioner's disease reveal crescents. Tr. 198:2–7. He stated that Petitioner's "active disease could have ceased prior to biopsy." Pet'r's Ex. 50 at 2.

Overall, I find Dr. Fine's explanation of Petitioner's disease progression more compelling than Dr. Ballouk's. Dr. Ballouk estimated that Petitioner's disease began around September 2013 and was aggravated by her vaccination that same month. Dr. Ballouk argued that Petitioner manifested symptoms of her disease by November 2013, about two months after his proposed onset. In contrast to the acute progression suggested by Dr. Ballouk, Dr. Fine, argued that Petitioner's disease progression was more chronic in nature. He estimated that Petitioner's disease began in 2011 because Petitioner was experiencing symptoms, in the form of hypertension and edema, at that time.

Dr. Ballouk estimated the onset of Petitioner's FGN based on the notion that her November 2013 gastrointestinal issues were sequela of her FGN. Dr. Ballouk then concluded that Petitioner reached ESRD at an accelerated rate from September 2013, but he did not point to any medical literature to explain how this can occur. The lack of literature is not fatal, however. Due to the rare nature of vaccine-caused injuries, Petitioner is not required to submit medical literature in support of her medical theory. Dr. Ballouk also did not persuasively support his theory regarding onset by using Petitioner's medical record or other corroborative evidence. As previously discussed, Dr. Ballouk noted the difference between Petitioner's creatinine levels in November 2013 and January 2014, but he did not present persuasive evidence that this represented abnormal progression. In this case, with respect to FGN symptomatology, I must consider Dr. Ballouk's opinion that is substantially unsupported, versus Dr. Fine's theory that effectively relies on supporting literature and explains Petitioner's medical record.

Dr. Fine's reliance on medical literature to link edema and hypertension to kidney disease is persuasive. The literature helped to explain that hypertension and edema are often the first symptoms in an otherwise asymptomatic early phase of disease. Dr. Fine then related this information to Petitioner's medical records and explained the progression of Petitioner's disease. Dr. Fine explained that he believed Petitioner was already in stage four of her disease by her November 21, 2013 hospitalization, based on her elevated creatinine levels on that date. *See* Tr. 309:10–22. Dr. Fine maintained this assertion even when accounting for Dr. Ballouk's suggestion that Petitioner's creatinine levels were elevated on that date due to dehydration. *See* Tr. 310:9–14.

Dr. Ballouk explained that active disease could have ceased prior to biopsy, Pet'r's Ex. 50 at 2, but he did not explain how crescents could have appeared and subsequently disappeared all within a few months of the rapid acceleration of her disease. Furthermore, Dr. Ballouk failed to explain how rapid progression of Petitioner's disease before biopsy would not result in crescents or any other indicators of disease activity. Dr. Ballouk noted that the majority of FGN biopsies do not reveal crescents. *See* Tr. 198:2–18. However, he did not explain under what circumstances they would appear or distinguish those cases from Petitioner's. Dr. Fine did, however, explain that the three segmentally sclerosed glomeruli he identified would have revealed crescent formation if Petitioner's disease had been recently active. *See* Resp't's Ex. E at 4. Dr. Fine asserted that the biopsy would have revealed recent activity, in the form of fibrous crescents, even if her disease had "burnt out" prior to her February 19, 2014 biopsy. *Id*. Petitioner did not rebut this.

I am not persuaded by Dr. Ballouk's assertion that Petitioner's clinical course was significantly aggravated by the flu vaccine, largely because he did not effectively use her medical record to identify indicators of disease exacerbation. Dr. Fine provided strong support for his assertions in the record and through medical literature that were not rebutted by Dr. Ballouk. I conclude that Petitioner did not establish it is more likely than not that her disease was highly active following her September 23, 2013 vaccination, or because of it. Further, Petitioner's biopsy did not reveal persuasive evidence to support Petitioner's claim of an accelerated course. Without additional support, I cannot conclude that, by a preponderant standard, Petitioner's vaccination significantly aggravated her injury.

D. *Loving* Prong Four/*Althen* Prong One – Medical Theory

Dr. Gershwin presented a theory whereby "the cytokine response following the [flu] vaccination would have accelerated [Petitioner's] [FGN] and made it worse." Pet'r's Ex. 19 at 1. For the reasons discussed below, Petitioner's theory fails to meet her burden under *Loving* prong four/*Althen* prong one.

Dr. Gershwin testified that the flu vaccine produces cytokines. Tr. 67:14–23. He went on to identify some of these cytokines and explained that cytokines can act locally or systemically. *See* Tr. 62:23, 66:8–16. Dr. Gershwin continued that cytokines produced in response to a vaccination travel through the body. Tr. 69:3–12. He opined that cytokines produced in response to a vaccination that travel throughout the body could then interact with the kidneys, especially if the vaccination occurred "in the early phase of disease." Tr. 70:1–5. Dr. Gershwin stated that cytokines produced following a vaccination travel around the body because they "get in the sera . . . ." Tr. 69:3–9. He explained that someone in the early phases of disease "was a susceptible host" because the pro-inflammatory cytokines "would exacerbate an ongoing inflammatory process in the kidney . . . ." Tr. 78:16–22, 79:15–16.

Petitioner's discussion of vaccine-induced cytokines and her attempt to link them to her disease do not constitute a sufficient medical theory. Petitioner fails to account for the fact that many different types of cytokines are typically present in the body and stem from a variety of causes. Although Dr. Gershwin stated that some of the "key" cytokines produced in response to the flu vaccine are from the interferon family, *see* Tr. 67:17–23, he did not clarify the role of interferons in his theory. In particular, he did not explain whether interferons were the only types of cytokines involved in the reaction he alleged. Ultimately, Dr. Gershwin's assertions that different people will produce different cytokines in response to the flu vaccine and that there are many different cytokines that can be produced in such a response equivocate his attempt to identify a "key" family of cytokines. An assertion that vaccine-induced cytokines caused the significant aggravation of a disease, without a specific or even general explanation of the types of cytokines involved and how they could aggravate the condition, is too general to constitute a sufficient medical theory. *See Jaafar v. Sec'y of Health & Hum. Servs.*, No. 15-267V, 2018 WL 4519066 at *5 (Fed. Cl. Spec. Mstr. Aug. 10, 2018) (determining that a petitioner did not establish an adequate medical theory that vaccine-induced cytokines triggered a condition when the "cytokine theory [was] conclusory and not persuasively supported[]"); *Cf. Doe/11 v. Sec'y of Health & Hum. Servs.*, No. 99-212V, 2008 WL 4899356 at *9 (Fed. Cl. Spec. Mstr. Oct. 29, 2008) (decision on remand) (concluding that the petitioners satisfied the first prong of *Althen* when they explained the two particular cytokines involved and explained how their release resulted in the injury in question), *mot. for review den'd*, 87 Fed, Cl. 1 (2009), *aff'd*, 601 F.3d 1349 (Fed. Cir. 2012), *cert. den'd*, 562 U.S. 1029 (2010).

Dr. Levinson opined that "it is highly unlikely that the cytokine response to the inactivated seasonal [flu] vaccine [received] by [Petitioner] reached a level of magnitude to deleteriously impact organs distant to the injection site." Resp't's Ex. C at 5. Dr. Levinson stated that the flu virus may induce a "cytokine storm" causing lung inflammation and other organ dysfunction. *Id.* However, he maintained that "there is not credible scientific evidence" that vaccines are capable of inducing a cytokine storm. *Id.* Petitioner does not allege that she suffered from a cytokine storm

as a result of her vaccine. Cytokine storm is a catastrophic autoimmune response, and there is not evidence of that occurring in Petitioner's case.

Petitioners are not required to submit the exact biological mechanism for a vaccine-caused injury. However, any theory that is asserted should be applicable to the vaccination given and the disease Petitioner suffers from. Petitioner's purported mechanism amounts to little more than a vague declaration that there are proteins (cytokines) that appear post-vaccination (produced as result of an immune response triggered by the vaccine), travel to the kidneys (because the kidneys are already diseased), and tell the kidney to attack itself (for reasons unknown). Petitioner has not asserted that the flu vaccination elicited any specific cytokines in her case. In fact, Dr. Gershwin stated that the types of cytokines triggered by the flu vaccine vary from person to person. Tr. 67:17–23. Furthermore, there is no explanation of why this vaccine would produce cytokines triggered by pre-existing kidney disease. Dr. Gershwin submitted numerous articles to illustrate the role pro-inflammatory cytokines play in renal injury. However, none of these articles were specific to FGN. And, as Dr. Levinson explained, the articles submitted all discuss pro-inflammatory cytokines that are produced in the kidneys rather than elsewhere in the body. The fact that these cytokines are produced in the kidneys provides a logical explanation for why they would target an already diseased kidney. Dr. Gershwin did not link any of these cytokines to FGN or explain why they are instructive to Petitioner's case. Therefore, the articles are unhelpful in explaining how cytokines produced locally in response to a vaccination would travel to Petitioner's kidneys and lead to organ damage.

Again, I must note that Petitioner is not required to provide a specific biological mechanism. However, given the ubiquitous nature of cytokines in the body, it cannot be enough to simply say "cytokines did it." Petitioner has not provided sufficient evidence that cytokines of any kind impact FGN. Importantly, Petitioner has not provided reliable medical evidence that vaccine-induced cytokines can cause or aggravate inflammation or injury at a distant site.

Furthermore, Dr. Gershwin opined during his testimony that FGN is an immunological disease but conceded that there has not been a definitive characterization found in the literature. *See* Tr. 70:24–72:6. In addition, Dr. Gershwin submitted numerous studies that discuss the immunological components of the disease. Taken together, these articles do support the contention that FGN is an immunologic disease. Neither of Respondent's experts rebutted this contention, and Dr. Levinson even testified under the assumption that FGN may be an immunological disease in order to rebut other parts of Petitioner's theory. *See* Tr. 115:25–116:11. Therefore, I find that FGN is an immunological disease.

However, Petitioner has failed to establish by a preponderant standard that inactivated vaccines can cause exacerbation of underlying autoimmune diseases, regardless of whether they are active or stable. Dr. Levinson provided two articles that supported that such vaccines are considered safe for people with AIRDs. *See* Resp't's Ex. C, Tabs 2–3. The authors of both of those articles acknowledged that research into the issue is incomplete. However, both articles show that existing studies have not established a link or causal relationship between vaccines and disease flares in AIRD patients. Furthermore, Dr. Levinson stated during his testimony that, if Petitioner's theory was correct, then based on the amount of people who are vaccinated each year with the inactivated flu vaccine, who have underlying autoimmune diseases, there should be more

documented cases and studies showing the aggravating effects of the vaccine. *See* Tr. 119:11–13, 120:12–19. I conclude that although FGN is an immunologic disease, this does not clarify Petitioner's purported theory.

Based on the foregoing, I find that Petitioner has not presented preponderant evidence that the flu vaccine can significantly aggravate FGN.

E. *Loving* Prong Five/*Althen* Prong Two – Actual Causation

Petitioner has failed to present preponderant evidence that the flu vaccine she received significantly aggravated her FGN. As I have already discussed, Petitioner did not meet her burden under *Loving* prong three.

Furthermore, although Petitioner's purported theory is that her FGN was aggravated by a vaccine-induced cytokine response, Dr. Gershwin does not point to evidence in Petitioner's medical record to support his contention that she suffered from a vaccine-induced cytokine response. Dr. Gershwin stated that the "[flu] vaccine elicits a rigorous cytokine response and this response begins within hours of the vaccination." Pet'r's Ex. 19 at 3. Dr. Gershwin, however, did not explain what "a rigorous cytokine response" would look like or how it would have manifested in Petitioner's case. As Dr. Levinson noted, the medical records do not indicate cytokine testing or any evidence that Petitioner suffered from a cytokine storm.

Based on the foregoing, I find that Petitioner has failed to meet her burden under *Loving* prong five/*Althen* prong two.

F. *Loving* Prong Six/*Althen* Prong Three – Temporal Relationship

Dr. Gershwin specified that "if the time of [FGN] onset was distant from the vaccination, then [he] would not hold" the opinion that the flu vaccine exacerbated Petitioner's FGN. Tr. 58:8–9. He indicated that his position would be inappropriate if the onset of Petitioner's FGN was more than six weeks before her vaccination. *See* Tr. 83:9–10. I have already concluded by a preponderant standard that Petitioner's FGN predated her vaccination by more than two years. Therefore, relying on Petitioner's own expert, Petitioner's course exhibits an inappropriate time frame for the flu vaccine to significantly aggravate her FGN. Accordingly, Petitioner has failed to meet her burden under *Loving* prong six/*Althen* prong three.

VI. Conclusion

Based on the foregoing, I find that Petitioner has failed to show by preponderant evidence that the flu vaccine she received on September 23, 2013, significantly aggravated her FGN. Therefore, her petition is hereby **DISMISSED**.

In the absence of a motion for review filed pursuant to RCFC Appendix B, the clerk of the court SHALL ENTER JUDGMENT in accordance with the terms of the above decision.[112]

[112] Pursuant to Vaccine Rule 11(a), entry of judgment is expedited by the parties' joint filing of a notice renouncing the right to seek review.

IT IS SO ORDERED.

s/Herbrina D. Sanders
Herbrina D. Sanders
Special Master