In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

LAWRENCE ROMINE,	*	
	*	No. 19-468V
Petitioner,	*	Special Master Christian J. Moran
v.	*	
	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Filed: March 13, 2026
	*	
Respondent.	*	

Jeffrey S. Pop, Jeffrey S. Pop & Associates, Beverly Hills, CA, for petitioner;
Irene Angelica Firippis, United States Dep't of Justice, Washington, DC, for respondent.

PUBLISHED DECISION DENYING ENTITLEMENT TO COMPENSATION[1]

Lawrence Romine alleges that a vaccine called Prevnar, which prevents invasive diseases caused by certain *Streptococcus pneumoniae* serotypes, caused him to suffer a neurologic disease, Guillain-Barre syndrome ("GBS"). Mr. Romine supported his claim with opinions from two doctors, Steven Sykes and Lawrence Steinman. The Secretary opposes the claim and relies upon opinions from two experts, David Alexander and Lindsay Whitton.

Both parties argued their positions through briefs submitted before a hearing. All four experts and Mr. Romine testified at a hearing. Following the hearing, the parties renewed their arguments in another set of briefs.

Mr. Romine has not established that he is entitled to compensation. Mr. Romine has not shown a persuasive and reliable theory by which the Prevnar vaccine can cause GBS.

The beginning portion of this decision follows a relatively traditional path of opinions from special masters regarding entitlement. Basic information about Mr. Romine's health, relevant vaccines, and GBS are set out in Section I. The procedural history, which is relatively

[1] Because this decision contains a reasoned explanation for the action taken in this case, it must be made publicly accessible and will be posted on the United States Court of Federal Claims' website, and/or at https://www.govinfo.gov/app/collection/uscourts/national/cofc, in accordance with the E-Government Act of 2002. 44 U.S.C. § 3501 note (2018) (Federal Management and Promotion of Electronic Government Services). This means the decision will be available to anyone with access to the internet. In accordance with Vaccine Rule 18(b), the parties have 14 days to identify and move to redact medical or other information, the disclosure of which would constitute an unwarranted invasion of privacy. Any changes will appear in the document posted on the website.

straightforward, is presented in Section II. Section III states the well-established standards for adjudication. The analysis begins in Section IV with an exploration of epidemiology. Section V turns to the theories that Dr. Steinman presented, molecular mimicry based upon proteins and molecular mimicry theory based upon phospholipids.

The next three sections expand beyond the traditional structure of adjudication. Section VI evaluates whether Dr. Steinman's opinions are reliable as measured against the factors for reliability set out in Daubert. Section VII presents additional comments in a summary. Finally, Section VIII compares the result in this case to the different outcomes in many other cases involving Prevnar and GBS. An appendix containing the bibliographic information for the medical literature cited throughout this Decision is attached.

I. Background: Petitioner's Health, Vaccines, and GBS

Mr. Romine was born in 1951. Exhibit 1 (declaration) ¶ 1. He was married with two daughters. For employment, he managed a factory that multiple generations in his family had owned. For recreation, he enjoyed golfing, and his handicap was in the single digits.

Before March 15, 2018, Mr. Romine's health seemed ordinary. See Exhibit 1 ¶¶ 3-4. The Secretary did not assert any pre-existing problems contributed to his GBS. See Resp't's Rep., filed pursuant to Vaccine Rule 4, on April 20, 2020, at 5-7.

On March 15, 2018, Mr. Romine received a vaccine against pneumococcus. Pneumococcus is a type of bacteria. Scientists sometimes classify bacteria by how they respond to a stain called Gram staining. For an explanation of Gram staining, see Exhibit C (Dr. Whitton's report) at 10. Pneumococcus is Gram positive.

Pneumococcus has different strains. Different strains of pneumococcus are reflected in the different vaccines against pneumococcus. One pneumococcal vaccine is known as Pneumovax 23, a polysaccharide-type vaccine which is typically given to adults. The Vaccine Program does not compensate claims based upon Pneumovax 23. See National Vaccine Injury Compensation Program: Addition of Pneumococcal Conjugate Vaccines to the Vaccine Injury Table, 66 Fed. Reg. 28166 (May 22, 2001) ("Through this notice, pneumococcal conjugate vaccines are now included as covered vaccines under Category XIII of the Table. Because the CDC only recommended pneumococcal conjugate vaccines to the Secretary for routine administration to children, polysaccharide-type pneumococcal vaccines are not covered under the VICP or included on the Table.").

Mr. Romine can bring his claim in the Vaccine Program because he received a pneumococcal vaccine that was not Pneumovax 23. The pneumococcal vaccine Mr. Romine received on March 15, 2018 is known as Prevnar 13. This vaccine is recommended for children, which explains why the Vaccine Program covers Prevnar. Prevnar 13 differs from Pneumovax 23 because the strains of pneumococcus are conjugated. "Conjugate," in this context, refers to two substances being paired. Dorlands Illus. Med. Dictionary 399 (33rd ed.). According to an article by Tseng et al., "unconjugated polysaccharide vaccines likely do not confer long-lasting protection," whereas conjugated vaccines such as Prevnar 13 have "vaccine serotypes after vaccination and the ability to prolong the duration of protection in elderly adults, with no apparent increase in safety concerns." Tseng at 7. In conjugated pneumococcal vaccines, the

strains of the pneumococcus bacteria are conjugated onto a protein called CRM. The CRM protein is a basis for Dr. Steinman's theory, and more information about CRM is provided in that context.

As stated earlier, Mr. Romine alleges his vaccination with Prevnar on March 15, 2018 caused his ill health. The first deterioration in his health occurred around March 28, 2018. See Exhibit 3 at 35-45 (medical record created April 3, 2018, reporting development of problems six days ago). This date is about 13 days after the vaccination. Dr. Whitton accepts the latency as one for which an inference of causation is appropriate.

While hospitalized, Mr. Romine was diagnosed with GBS. Exhibit 4 at 1-16 (discharge summary), 42 (evaluation on April 10, 2018). GBS is a disease of the peripheral nervous system. "Peripheral" refers to nerves that extend outside of the spinal cord. By contrast, the central nervous system refers to the brain and spinal cord. In the peripheral nervous system, the part that transmits electrical signals (like a wire) is an axon. In the peripheral nervous system, most nerves are myelinated. Myelin is a substance similar to the insulation for an electrical wire. Myelin itself is composed of lipids. Dorland's at 1201; see also Yuki at 2298.

The portion of the nerve primarily attacked is a basis for dividing GBS into different variants. For example, when the axon is damaged, a person may develop a subtype of GBS known as acute motor axonal neuropathy (AMAN), which primarily affects the motor nerves and lacks features of demyelination. See 42 C.F.R. § 100.3(c)(15)(ii). However, this form is rare in the United States and Mr. Romine did not have this form. Rather, Mr. Romine suffered from the more common form of GBS, acute inflammatory demyelinating polyneuropathy (AIDP).

The causes of AIDP are not known. A medical term for not knowing the cause is "idiopathic." Dorland's at 901. Although doctors have not discovered the cause(s) of AIDP, they have observed that in roughly two-thirds of the cases, the person suffered from an infection before developing GBS. Jasti at 1176.

A well-known example of an infectious organism that precedes GBS is *campylobacter jejuni* ("*C. jejuni*"). *C. jejuni* is a Gram-negative bacterium that causes gastrointestinal problems such as diarrhea. See Dorland's at 271. Reliable evidence supports the idea that when the body's immune system responds to a *C. jejuni* infection, the immune system produces antibodies against the bacteria. These antibodies occasionally go on to attack the nervous system. Because the pathogenesis of GBS involves the body's own immune system, GBS is considered an autoimmune disease.

In addition to *C. jejuni*, other infectious agents are associated with GBS. Examples include *Haemophilius influenzae*. Importantly, this list of infectious agents does not include pneumococcus. See Jasti at 1176.

Of the potential infectious agents, Mr. Romine was not detected to suffer from any. The parties stipulated that the Secretary was not proposing an alternative cause for Mr. Romine's GBS. The doctors retained in this litigation also did not identify a cause of the GBS, other than potentially the Prevnar vaccine.

The doctors who treated Mr. Romine generally did not say the Prevnar vaccine caused his GBS. Some doctors memorialized a temporal sequence in which they recognized the Prevnar

vaccination preceded the onset of the GBS. See, e.g., Exhibit 4 at 38 (Dr. Kim: Mr. Romine "had a pneumonia shot a week prior to symptom onset"); see also Pet'r's Pre-Hearing Br., filed Sep. 30, 2024, at 25. These remarks carry relatively little significance on the question of vaccines as a cause. Cedillo v. Sec'y of Health & Hum. Servs., 617 F.3d 1328, 1347–48 (2010).

While most notations in the treatment records about Mr. Romine's receipt of Prevnar are not direct statements of causation, there is one unusual exception. On April 14, 2018, Nurse Maria Orito, a "CDI specialist," requested information from a doctor who had treated Mr. Romine during the hospitalization, Okkyung Kim. Exhibit 4 at 90. Before this case, Dr. Steinman was not familiar with the term "CDI." Tr. 60-61. It apparently means "clinical documentation improvement." To fill out this form, Nurse Ochoa gave Dr. Kim four choices:

- Possible, Probable or Suspected PNA Vaccine related to GBS.

- PNA Vaccine not related to GBS

- Other (specify)

- Unable to determine

Exhibit 4 at 90. Dr. Kim responded: "pneumonia vaccine probably related to GBS." Id.

Shortly after the discharge, a doctor informed government officials at the Centers for Disease Control and Federal Drug Administration that Mr. Romine developed GBS after receiving the Prevnar vaccine. Exhibit 79 (VAERS report, dated July 6, 2018).

After discharge, Mr. Romine went through recovery and he credited his family, especially his wife, for caring for him. Due to these efforts, Mr. Romine greatly improved. By the hearing in December 2024, Mr. Romine had returned to running his family business. He also enjoyed recreational activities such as golf, although at reduced levels.

II. Procedural History

A. Preliminary Materials

Mr. Romine initiated this case by filing a petition on March 29, 2019. The petition alleges that the Prevnar vaccine caused him to suffer GBS. This petition was originally assigned to a different special master. Mr. Romine periodically submitted medical records. The Secretary evaluated this material and recommended against an award of compensation. Resp't's Rep., filed April 20, 2020.

B. First Pair of Expert Reports

Mr. Romine supported his claim by filing a report from Dr. Sykes on July 7, 2020. Exhibit 11. Dr. Sykes cited nine medical articles. Exhibits 13-21. As discussed in the analysis, his opinion has largely been superseded by opinions from Dr. Steinman.

Before Mr. Romine filed a report from Dr. Steinman, the Secretary presented a report from a neurologist, David Alexander. Exhibit A (filed March 8, 2021). Dr. Alexander presented

some of the epidemiological studies discussed in the analysis. Otherwise, Dr. Alexander's report is largely overtaken by the reports from Dr. Whitton.

C. Second Pair of Experts

The level of complexity increased dramatically with the presentation of reports from Dr. Steinman for Mr. Romine and Dr. Whitton for the Secretary. Dr. Steinman frequently testifies on behalf of people seeking competition through the Vaccine Program. Special masters are generally familiar with his background as a neuroimmunologist.

In his first report, Dr. Steinman proposed that Mr. Romine's GBS was caused by the Prevnar vaccine. Broadly speaking, Dr. Steinman put forward two theories about how the Prevnar vaccine can cause GBS. The first theory was based upon phosphoglycerol. The second theory was based upon an asserted similarity between a component of the vaccine, CRM-197, and proteins found in the nervous system. Exhibit 22. Additional details about Dr. Steinman's opinions and the basis for those opinions are set out in the sections below.

The Secretary responded with a report from Dr. Whitton. Exhibit C.[2] Dr. Whitton, as discussed at length below, disagreed with many aspects of Dr. Steinman's opinion as to whether and how the Prevnar vaccine can cause GBS. Based upon this record, the presiding special master scheduled and entitlement hearing for December 3 through December 5, 2024. Order, issued June 29, 2022. On August 29, 2024, the case was reassigned to the undersigned.

Upon reassignment, the parties filed a great deal of material in a relatively short amount of time. Mr. Romine submitted a second report from Dr. Steinman. Exhibit 58.[3] A key revision concerned Dr. Steinman's protein-based theory. Dr. Steinman now opined that the CRM-197 portion of the vaccine cross-reacted with a protein known as PMP-22. Mr. Romine argued that he was entitled to compensation through a pre-hearing brief, submitted on September 30, 2024. With the pre-hearing brief, Mr. Romine filed five additional articles that Dr. Steinman had not discussed in any report. See Exhibits 73-77.[4] Of this group of articles, the most relevant is the article by Barbar.

The Secretary responded with both a second report from Dr. Whitton (Exhibit D) and a brief on October 30, 2024. Mr. Romine replied on November 12, 2024.

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[2] Technically, the first report was labeled as Exhibit B. However, a corrected version was filed on June 16, 2022 as Exhibit C.

[3] Mr. Raymond subsequently submitted a corrected version of this report as Exhibit 58.1 on November 26, 2024. This decision cites to the corrected report.

[4] Normally, the undersigned does not permit parties to file articles without a disclosure from an expert about the relevance of the article. Mr. Romine is exceptional because the undersigned was not the presiding special master when the hearing was scheduled.

In response to a suggestion from the undersigned, Dr. Steinman prepared a second supplemental report in which he attempted to show that some BLAST[5] searches do not return any positive results. Exhibit 80, filed November 25, 2024. This aspect turned out to be unintentionally complicated, despite everyone's good faith.

The hearing was held December 3 through December 5, 2024 in Los Angeles, California. Mr. Romine, Dr. Sykes, Dr. Alexander, and Dr. Steinman testified in person. Dr. Whitton testified by videoconference. The hearing was marred by an outburst by Dr. Steinman during Dr. Whitton's testimony, but that inappropriate remark and the episode that followed does not otherwise affect the outcome of Mr. Romine's case.[6]

After the hearing, the parties argued their cases through briefs. Mr. Romine presented his primary brief on February 28, 2025, and his reply on May 29, 2025. In between, the Secretary advanced his arguments via a brief filed on April 29, 2025. With the submission of Mr. Romine's reply, the case is ready for adjudication.

III. Standards for Adjudication

A petitioner is required to establish his case by a preponderance of the evidence. 42 U.S.C. § 300aa–13(1)(a). The preponderance of the evidence standard requires a "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." Moberly v. Sec'y of Health & Hum. Servs., 592 F.3d 1315, 1322 n.2 (Fed. Cir. 2010) (citations omitted). Proof of medical certainty is not required. Bunting v. Sec'y of Health & Hum. Servs., 931 F.2d 867, 873 (Fed. Cir. 1991).

Distinguishing between "preponderant evidence" and "medical certainty" is important because a special master should not impose an evidentiary burden that is too high. Andreu v. Sec'y of Health & Hum. Servs., 569 F.3d 1367, 1379-80 (Fed. Cir. 2009) (reversing special master's decision that petitioners were not entitled to compensation); see also Lampe v. Sec'y of Health & Hum. Servs., 219 F.3d 1357 (Fed. Cir. 2000); Hodges v. Sec'y of Health & Hum. Servs., 9 F.3d 958, 961 (Fed. Cir. 1993) (disagreeing with dissenting judge's contention that the special master confused preponderance of the evidence with medical certainty).

Because Mr. Romine is proceeding with an off-Table claim, he must establish that the Prevnar vaccine was the cause-in-fact of his GBS. Petitioners establish causation-in-fact by fulfilling the Althen prongs. Petitioners bear a burden "to show by preponderant evidence that the vaccination brought about [the vaccinee's] injury by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen v. Sec'y of Health & Hum. Servs., 418 F.3d

[5] The Basic Local Alignment Search Tool ("BLAST") is a program that compares biological sequences to identify similarities. For more details on BLAST and Dr. Steinman's use of it, see Section V.B.1 below.

[6] Dr. Steinman and counsel retaining Dr. Steinman are warned that any future violations of courtroom decorum may come with a more severe consequence.

1274, 1278 (Fed. Cir. 2005). Mr. Romine's case turns on Althen prong one, which requires Mr. Romine to present a theory explaining how Prevnar can cause GBS.

IV. Epidemiology

The analysis of whether Prevnar can cause GBS starts with epidemiology because epidemiology could be relevant to whatever theory is being proposed. See Tr. 239-40 (Dr. Steinman explaining that one paper provided epidemiology and another paper provided a mechanism). For a lengthy discussion of the value of epidemiologic studies in the Vaccine Program, see Tullio v. Sec'y of Health & Hum. Servs., No. 15-51V, 2019 WL 7580149, at *5-8 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), mot. for rev. denied, 149 Fed. Cl. 448, 475 (2020).

This section evaluates two types of studies. In the first type, which is discussed in section A, researchers looked to see whether people who received *vaccines* against pneumococcus developed GBS. In the second type, the question is whether people who are *infected* with the pneumococcus bacteria develop GBS.

A. Pneumococcal vaccines and GBS

Here, four articles explored whether people who received a vaccine against pneumococcus developed GBS at an increased incidence. These are Baxter, Haber, Tseng, and Yoon.

1. Baxter

This group of researchers investigated "the possible relationship between GBS and vaccinations." Baxter at 198. To do so, they consulted electronic medical records from Kaiser Permanente Northern California. Their study spanned 13 years and more than 30 million person-years. The researchers conducted two different types of analysis, a case-centered study and a cohort analysis. Id. at 198-99. In short, the researchers looked to see if people receiving various vaccines developed GBS more frequently. One of the vaccines was pneumovax 23 (labeled as PPV-23 in Baxter). The Baxter researchers did not study Prevnar because Prevnar was not available. Tr. 98, 110, 327. The researchers "found no evidence of an increased risk of GBS following any vaccination, as well as vaccinations combined." Baxter at 201. The researchers acknowledged that they "had limited power to fully assess the risk of GBS following vaccination due to the rarity of the outcome." However, they concluded that "the low numbers of GBS cases that were temporally associated with vaccination, coupled with our results, provide reassurance that the risk of GBS following any vaccine, including influenza vaccines, is extremely low." Id. at 203.

2. Haber

A group of researchers from the CDC consulted the VAERS database for adverse events following Prevnar 13. Special masters are familiar with the VAERS system. As explained in Haber, "VAERS is a national vaccine safety surveillance program run by CDC and the Food and Drug Administration (FDA). This early warning system is designed to detect possible safety issues with U. S.-licensed vaccines." Haber at 6631. A basic purpose of the vaccine adverse event reporting system is to surveil for potential problems that warrant further investigation. Dr. Whitton used a common phrase, asking whether there is a "red flag warning?" Tr. 328.

Often, an analysis of VAERS data can be unreliable because researchers do not know how many doses of a vaccine were given. Puckett v. Sec'y of Health & Hum. Servs., No. 21-1125V, 2024 WL 3160589, at *4 (Fed. Cl. Spec. Mstr. June 3, 2024) (citing cases); Ferguson v. Sec'y of Health & Hum. Servs., No. 17-1737V, 2021 WL 6276204, at *18 n.48 (Fed. Cl. Spec. Mstr. Dec. 10, 2021). The Federal Circuit has recognized difficulty in drawing conclusions from data when the denominator is not known. GHS Health Maintenance Organization, Inc. v. United States, 536 F.3d 1293, 1302 n.6 (Fed. Cir. 2008). In Haber, however, there is datum to fill the denominator. Haber researchers stated that in the study, approximately 16,000,000 doses were distributed. Haber at 6333; see also Tr. 98.[7]

In the relevant time, the VAERS database contained 10 reports of people age greater than 65 years old developing GBS. The question then becomes: do 10 reports of GBS raise concern? Dr. Alexander testified that the incidence of GBS in Haber was about 0.7 cases of GBS per million vaccine doses. Tr. 98. The usual background incidence of GBS is roughly 1.0 cases per million people. Yuki at 2294.

For adverse events generally, the Haber researchers stated: "We . . . did not identify any new safety concerns or unexpected [adverse events]." Haber at 6333. For the question of GBS specifically, the Haber researchers reported: "Our data mining analysis noted no disproportionate reporting for GBS." Haber at 6334. The Secretary's experts emphasize this aspect of the Haber article. Tr. 98 (Dr. Alexander), 329 (Dr. Whitton). Mr. Romine's experts, too, acknowledge this finding. Tr. 67 (Dr. Sykes), 199 (Dr. Steinman).

Mr. Romine's experts seem to focus on only the numerator, meaning the number of cases reported. Tr. 52 (Dr. Sykes: 10 patients with GBS), Tr. 200 (Dr. Steinman: "they saw 10 cases"). But, when considered in the context of the denominator (the population exposed to the vaccination), these reports in Haber resemble a case series. Case series are not a persuasive basis for finding causation. Virissimo v. Sec'y of Health & Hum. Servs., No. 24-1168V, 2025 WL 2439181, at *3 (Fed. Cl. Spec. Mstr. July 30, 2025); Cerrone v. Sec'y of Health & Hum. Servs., No. 17-1158V, 2023 WL 3816718, at *19 (Fed. Cl. June 1, 2023) (summarizing opinion of the Secretary's expert), mot. for rev. denied, 168 Fed. Cl. 745 (2023), aff'd, 146 F.4th 1113 (Fed. Cir. 2025); see also K.O. v. Sec'y of Health & Hum. Servs., No. 13-472V, 2016 WL 7634491, at *11-12 (Fed. Cl. Spec. Mstr. July 7, 2016) (discussing appellate precedent on case reports). Dr. Whitton was persuasive when, in the context of discussing Haber, he stated that the identification of some cases of GBS occurring after Prevnar is "absolutely not evidence of causation." Tr. 330.

3. Tseng

This group explored how the safety of the two pneumococcal vaccinations compared. Tr. 111, 330. The older vaccine was pneumovax (labeled as PPSV 23, see Tr. 111). The newer vaccine was Prevnar 13 (labeled as PCV 13). To determine whether one vaccine had more adverse events, the researchers consulted the Vaccine Safety Database (VSD). Tseng at 2. The VSD contains medical information about millions of people. Sparrow v. Sec'y of Health & Hum.

[7] Technically, the doses distributed could exceed the doses administered. But, the number of doses distributed can serve as a rough proxy for the number of doses administered. Likewise, the numerator (adverse events) may be affected by underreporting.

Servs., No. 18-295V, 2024 WL 1599165, at *19 (Fed. Cl. Spec. Mstr. Mar. 19, 2024) (the "VSD has data on >9 million subjects annually"), mot. for rev. denied, 173 Fed. Cl. 177 (2024), appeal docketed, No. 2025-1161 (Fed. Cir. Nov. 8, 2024). For more information about the VSD, see Dwyer v. Sec'y of Health & Hum. Servs., No. 03-1202V, 2010 WL 892250, at *67 n.284 (Fed. Cl. Spec. Mstr. Mar. 12, 2010); Werderitsh v. Sec'y of Health & Hum. Servs., No. 99-319V, 2005 WL 3320041, at *15 (Fed. Cl. Spec. Mstr. Nov. 10, 2005). The researchers searched specifically for GBS. Tseng at 3; Tr. 100. The incidence of GBS was not meaningfully different. Id. at 6 (Table 3); Tr. 332.

4. Yoon

These researchers wanted to evaluate the safety of pneumovax (labeled PPSV 23) among adults in Korea. They "assembled a large linked database by linking the Korea Immunization Registry Information System (KIRIS) to the National Health Information Database (NHID) from July 2018 to June 2021." Yoon at 2. Using this method, the researchers identified more than 1.8 million people who received the PPSV23 vaccine. Yoon at 9. The researchers were interested in GBS. They used a self- controlled risk interval. Id. at 3. The incidence rate ratio was less than one, meaning an association was not favored. Id. at 7 (figure 3). The authors concluded "our results corroborate previous findings that PPSV23 was not associated with a higher risk of serious systemic adverse events related to the cardiovascular, neurological, and immunological systems." Id. at 9; accord Tr. 333.

5. Summary

Collectively, these studies tend to reinforce each other in suggesting that an association between a pneumococcal vaccine and GBS has not been found, despite attempts to find such an association. A summary of these studies is:

Epidemiological Studies on Pneumococcal Vaccines and GBS			
Study & Year	Vaccine	Population	Finding
Baxter, 2013	Pneumovax	13 years and 30 million-person years	No increased risk
Haber, 2016	Prevnar	16 million doses distributed	No disproportionate reporting
Tseng, 2018	Prevnar and Pneumovax	Millions in Vaccine Safety Datalink	No difference in safety
Yoon, 2024	Pneumovax	1.8 million Koreans	No increased risk

Except for some discussion about Haber, neither Dr. Sykes nor Dr. Steinman testified about these epidemiological studies at length. In lieu of evidence, Mr. Romine attempts to minimize the value of epidemiological studies mostly through attorney's argument. See Pet'r's Reply at 12-20. One argument --- that the epidemiological studies had limitations including that

they were "not specifically focusing on GBS but rather adverse events in general" --- is mistaken. As noted, each of the studies did look for GBS specifically.

While it is true that these epidemiological studies have other limitations, all studies have some limitations. Martinez v. Sec'y of Health & Hum. Servs., No. 16-738V, 2022 WL 4884923, at *30 (Fed. Cl. Spec. Mstr. Sep. 9, 2022), mot. for rev. denied, 165 Fed. Cl. 76 (2023). It would be unusual for one study to be decisive. The Secretary is not burdened with an obligation to prove beyond a reasonable doubt that Prevnar cannot cause GBS. Instead, Mr. Romine bears a burden to present reliable evidence showing, more likely than not, that Prevnar can cause GBS. Although the burden rests with the petitioner, the Secretary can introduce evidence undermining a petitioner's case. Bazan v. Sec'y of Health and Hum. Servs., 539 F.3d 1347, 1353 (Fed. Cir. 2008). Here, the epidemiological studies on pneumococcal vaccines make the claim less likely, but not impossible.

B. Pneumococcus bacteria and GBS

The previous section addresses studies on pneumococcal vaccines and GBS. A different way of looking at the question is whether the *Streptococcus pneumoniae* bacteria is associated with GBS.

Reliable evidence supports a finding that streptococcal infections have not led to GBS. This finding is based upon two points. First, in Dr. Whitton's first report, he cited an article written by several people, including a doctor who has often assisted petitioners claiming compensation in the Vaccine Program, M. Eric Gershwin. Exhibit C at 9-11. Dr. Gershwin and colleagues did not list *Streptococcus pneumoniae* as being associated with GBS. See Exhibit C-19 (Jasti) at 1176. Second, Dr. Steinman had an opportunity to respond but did not provide a counterexample. See Exhibit 58. This pattern repeated at the hearing as again Dr. Whitton testified that the wild infectious bacteria has not been associated with GBS. Tr. 318-19. Again, Dr. Steinman could have answered this assertion but did not supply any information on this topic in his rebuttal.

Dr. Whitton explained why *Streptococcus pneumoniae*, unlike some other bacteria such as *C. jejuni*, is not likely to cause GBS. *Streptococcus pneumoniae*, as mentioned previously, is Gram positive. Dorland's at 1753. The types of bacteria that are associated with GBS are the opposite; they are Gram negative. Exhibit C at 10-11; Tr. 321. Dr. Steinman did not effectively rebut that distinction between Gram negative and Gram positive. See Tr. 138

If an analogy were to be drawn, then all things being equal, it would seem more reliable to start with the infectious agents to which the vaccine is directed rather than a different infectious agent such as *C. jejuni*. Mr. Romine's main argument is that all things are not equal. Dr. Steinman emphasizes that the sugars present in the naturally occurring bacteria differ from the sugars in Prevnar because the polysaccharides in the vaccine are conjugated to CRM-197. Exhibit 22 at 30, Tr. 137 (the vaccine is a patented invention). Dr. Whitton acknowledged that this point is "not unreasonable." Tr. 323.

Dr. Whitton's answer to this point is two-fold, although one point is more relevant in this context. Dr. Whitton's other point will be discussed in the context of Bryson antibodies below. Dr. Whitton points out that the immune responses to wild (or naked) pneumococcal

polysaccharides must be similar to a large degree to the immune responses to Prevnar because Prevnar is effective. Tr. 324. Dr. Whitton's reasoning seems sound. In any event, Dr. Steinman did not rebut it. See Gamboa-Avila v. Sec'y of Health & Hum. Servs., 166 F.4th 1318, 1322 (Fed. Cir. 2026) (ruling that special master was not arbitrary in rejecting Dr. Steinman's theory because, in part, the special master noted that the wild bacteria is not associated with GBS).

C. Synopsis on pneumococcal bacteria, pneumococcal vaccines and GBS

In sum, the Secretary has presented two similar, but not identical, points. First, four large-scale epidemiological studies have looked for an increased risk of GBS after vaccines against *Streptococcus pneumoniae*. They did not find an increased risk. Second, there appears to be no reports of a wild *Streptococcus pneumoniae* infection preceding GBS.

Together, these lines of evidence weigh against finding that Prevnar can cause GBS. But, these lines of evidence are not dispositive. Thus, the theory that Dr. Steinman proposes --- molecular mimicry --- is introduced next.

V. Molecular Mimicry

Molecular mimicry originated as a theory to explain how infectious organisms can evade the immune system of human beings. Tr. 514. The idea was that infectious organisms would benefit from resembling host tissue because the immune system is trained not to attack host tissues.

The theory of molecular mercury turned when Fujinami and Oldstone proposed that molecular mimicry could explain autoimmunity. Tr. 515; see also Tr. 228, 254. In the Vaccine Program, the theory of molecular mimicry is that when the human system responds to a foreign antigen (such as an infectious agent or vaccine), the immune system mistakenly targets human tissue leading to a disease. Tr. 56-57, 140, 335.

After Fujinami and Oldstone proposed molecular mimicry to explain autoimmune disease, other scientists also proposed this hypothesis. For example, in 1993, Dr. Steinman wrote an article for scientific America about molecular mimicry. Tr. 139. More than 100 Vaccine Program cases have been based upon molecular mimicry. Hoffman v. Sec'y of Health & Hum. Servs., No. 19-111V, 2024 WL 4444773, at *8 (Fed. Cl. Spec. Mstr. Sep. 13, 2024) (appendix).

Despite being proposed for decades in many contexts, demonstrated instances of molecular mimicry causing disease are rare. See Tr. 512. Here, Dr. Sykes cited an article by Lori J. Albert as one of five articles supporting an assertion: "The immune-mediate[d] mechanisms underlying Guillain-Barre Syndrome following vaccination are best explained by the molecular mimicry theory." Exhibit 11 at 4. On cross examination, the Secretary challenged Dr. Sykes by pointing out that Albert says: "No data convincingly demonstrate that mimicry is an important mechanism to the development of autoimmune disease in humans." Tr. 68; accord Exhibit 21 (Albert) at 3. In Dr. Alexander's direct testimony, he referred to the same sentence from Albert. Tr. 92.

Dr. Steinman was critical of Albert because it was published in 1999. Tr. 136, 226. Another article of the same generation also concluded that there are no good examples of

molecular mimicry. Rose; Tr. 468. As Dr. Steinman stated, since the 1990s, science has continued to evolve. Tr. 136.

One advancement was the sequencing of the entire human genome. This achievement was a foundation for the discovery that the composition of human proteins greatly overlaps with the composition of proteins in infectious organisms. See Bishara v. Sec'y of Health & Hum. Servs., No. 19-115V, 2023 WL 2799054, at *7 (Fed. Cl. Jan. 27, 2023) ("homology is common") (citing cases).

On the other hand, the intervening years have brought out some support from molecular mimicry as a theory to explain autoimmunity. Yuki linked *C. jejuni* to GBS through molecular mimicry. Yuki at 2292; Tr. 261. A second example is that a group of researchers including Dr. Steinman showed that molecular mimicry could explain how the Epstein-Barr virus can cause multiple sclerosis. Lanz; Tr. 173-76, 364-65.

Potentially based upon this work, Dr. Whitton acknowledges that viruses (but not necessarily vaccines that target viruses) can trigger autoimmunity through molecular mimicry. Tr. 451-52, See also Tr. 512. However, he also opines that molecular mimicry is not an easily falsifiable hypothesis. Tr. 513-14.

A. Appellate precedents on molecular mimicry

Because special masters are often called upon to evaluate the persuasiveness of the theory of molecular mimicry, the Court of Federal Claims and the Court of Appeals for the Federal Circuit have considered molecular mimicry in their appellate role. In December 2019, the undersigned identified the leading precedents as W.C. v. Sec'y of Health & Hum. Servs., 704 F.3d 1352 (Fed. Cir. 2013), and Caves v. Sec'y of Dep't. of Health & Hum. Servs., 100 Fed. Cl. 119 (2011), aff'd sub nom., 463 F. App'x 932 (Fed. Cir. 2012). Tullio v. Sec'y of Health & Hum. Servs., No. 15-51V, 2019 WL 7580149, at *12-14 (Fed. Cl. Spec. Mstr. Dec. 19, 2019), mot. for rev. denied, 149 Fed. Cl. 448 (2020). While Tullio describes those cases in more detail, their essence appears to be that although molecular mimicry is accepted in some contexts, special masters may properly require some empirical evidence to show that a particular vaccine can cause a particular disease.

In the next approximately four years, appellate authorities reviewing decisions involving molecular mimicry have generally endorsed the approach of looking for some evidence that persuasively shows that a portion of a vaccine resembles a portion of human tissue, which contributes to causing the disease, and that the immune system will respond to the relevant amino acid sequence. Chronologically, the list of more recent appellate cases begins with the opinion in Tullio, which denied the motion for review. 149 Fed. Cl. 448, 467-68 (2020).

Another example in which the Court of Federal Claims held that the special master did not elevate the petitioner's burden of proof in the context of evaluating the theory of molecular mimicry is Morgan v. Sec'y of Health & Hum. Servs., 148 Fed. Cl. 454, 476-77 (2020), aff'd in non-precedential opinion, 850 F. App'x 775 (Fed. Cir. 2021). In Morgan, the Chief Special Master found that petitioner had not presented persuasive evidence about a relevant antibody. Id. at 477. The Chief Special Master also noted that the articles about the relevant disease do not list the wild flu virus as potentially causing the disease. Id. When examining this analysis, the Court

of Federal Claims concluded: "the Chief Special Master did not raise the burden of causation in this case; petitioner simply failed to meet it." Id.

The Federal Circuit also evaluated the Chief Special Master's approach in Morgan. The Federal Circuit concluded: "We discern no error in the special master's causation analysis." 850 F. App'x 775, 784 (Fed. Cir. 2021).

Most other recent appellate cases follow this path. See, e.g., Dennington v. Sec'y of Health & Hum. Servs., 167 Fed. Cl. 640, 653-56 (2023) (finding the special master did not err in rejecting theory of molecular mimicry where petitioner did not specifically link vaccine and injury), mot. for review den'd, 167 Fed. Cl. 640 (2023), appeal dismissed, No. 2024-1214, 2024 WL 1255318 (Fed. Cir. Mar. 25, 2024); Duncan v. Sec'y of Health & Hum. Servs., 153 Fed. Cl. 642, 661 (2021) (finding the special master did not err in rejecting a bare assertion of molecular mimicry); Caredio v. Sec'y of Health & Hum. Servs., No. 17-79V, 2021 WL 6058835, at *11 (Fed. Cl. Dec. 3, 2021) (indicating that a special master did not err in requiring more than homology and citing Tullio); Yalacki v. Sec'y of Health & Hum. Servs., 146 Fed. Cl. 80, 91-92 (2019) (ruling that special master did not err in looking for reliable evidence to support molecular mimicry as a theory); but see Patton v. Sec'y of Health & Hum. Servs., 157 Fed. Cl. 159, 169 (2021) (finding that a special master erred in requiring petitioner submit a study to establish medical theory causally connecting flu vaccine to brachial neuritis).

This background information about molecular mimicry and how appellate authorities have treated molecular mimicry is helpful to understanding the way Dr. Steinman attempts to connect Prevnar and GBS. Dr. Steinman offered two ways that molecular mimicry could link Prevnar with GBS. One approach involves proteins and, as discussed below, this theme has four variations. The other approach is based upon polysaccharides. The protein-based theme is analyzed first because it is easier to understand due in part to the fact that Dr. Steinman has been relying upon BLAST searches in the Vaccine Program for more than a decade.

B. Protein Theory

Dr. Steinman's protein theory is comprised of a series of steps. Preliminary steps are Dr. Steinman's choice to use the BLAST program and the settings he selects in the computer program. Next, Dr. Steinman inputs information about vaccines into the program. He also inputs host (or human) proteins into the program. As a final step, Dr. Steinman presents the computer-generated results of the comparison. These steps are investigated below.

1. Proteins and BLAST program

The foundation for Dr. Steinman's protein-based theory is a computer program known as BLAST. Exhibit 22 at 24, Tr. 167-68. An understanding of the strengths and weaknesses of BLAST requires some understanding of how proteins are structured.

Proteins are the "principal constituents of the protoplasm of all cells." Dorland's at 1508. Proteins are composed of 20 amino acids. Id. A protein of average length will contain approximately 400 amino acids. Tr. 384.

Dr. Whitton compared the straightforward listing of the amino acids constituting a protein to the pearls on a necklace. This is known as the protein's linear structure. However, in nature,

proteins do not exist on a straight line. Instead, the proteins fold upon themselves creating something like a ball of string. The folding creates a three-dimensional shape. Thus, proteins are also known to have a tertiary structure as well as a linear structure. One component of the immune system, antibodies, recognizes a protein's nonlinear epitope. Tr. 521.

In the 1990s, a group of scientists wrote the BLAST program. Tr. 168, 375. The purpose was to allow researchers to determine if one protein was *evolutionarily* related to another protein. Tr. 375. Whether the BLAST program should be used to determine whether two proteins are related *immunologically* is disputed.

The BLAST program determines the degree of sameness in two proteins by aligning and comparing the linear sequence of amino acids. A scientific term for sameness in this context is "homology." Dorland's at 857-58. Over the years, Dr. Whitton has persuasively explained that some degree of homology between two proteins of average length is inevitable. Tr. 384; see J.C. v. Sec'y of Health & Hum. Servs., No. 17-69V, 2024 WL 3412625, at *18-19 (Fed. Cl. Spec. Mstr. May 16, 2024) (discussing opinion of the Secretary's expert who was not Dr. Whitton). The basic reason is that the given set of 20 amino acids can occur in a finite number of ways. There appears to be no dispute that some repetition of amino acids within short sequences (meaning sequences of approximately 10-12 amino acids in length) tends to appear in two average length proteins. See Silvanovich (2005) at 255 (figure 2), 258 ("the vast majority of matches identified using a sliding window size of six amino acids is simply a product of random chance and does not facilitate the identification of biologically meaningful allergenic characteristics of a protein"). An ensuing question is how to separate sequence homologies that occur by chance alone from sequence homologies that carry some biologic significance--either evolutionary or immunologically.

The authors of the Kerfeld & Scott article answer this question: E-values. Accord Tr. 380-81. As stated in the article, "understanding the steps in the calculation of an E-value provides an opportunity to show the relationship between how the algorithm works and fundamental principles of biochemistry and evolution." Kerfeld & Scott at 1. The article is written in the context of attempting to explain concepts such as "molecular evolution." Id. Kerfeld and Scott proposed that "many experienced researchers [are] simply using the default parameters because they do not know how to manipulate them or [are] accepting results with little understanding of their full meaning (or lack thereof)." Id. Although Kerfeld and Scott provide a reliable explanation for E-value, these authors do not propose any particular value as being significant. At best, Kerfeld and Scott seem to suggest that most researchers "draw an arbitrary line" at E<0.00001. Id. at 4. According to Dr. Whitton, the default E-value is 0.05. Tr. 392. Dr. Steinman did not contest Dr. Whitton's statement that the default in the BLAST program is 0.05.

A different article, one which Dr. Steinman cited originally, provides information about using BLAST to search for allergens.[8] To be clear, allergens are not exactly the same as a

[8] In his oral testimony, Dr. Steinman stated that Silvanovich was being "misused." Tr. 537. This statement reduces Dr. Steinman's credibility as he was the person who first cited Silvanovich. Exhibit 22 at 24. In his first report, Dr. Steinman accurately quotes from the Silvanovich article as stating "Thus, for large proteins and an expanding allergen database, a FASTA or BLAST bioinformatics search appears to be the optimum method for identifying

potentially auto-reactive protein. See H.C. v. Sec'y of Health & Hum. Servs., No. 16-4V, 2022 WL 2825395, at *8 n.28 (Fed. Cl. May 9, 2022) (discussing IgE). However, both processes involve immunoglobulins. In this context, Silvanovich states that "Bioinformatic analyses based on FASTA or BLAST algorithms provide a measure of reliability by providing cut-offs (35% identity over at least 80 amino acids), above which significant IgE cross reactivity may be expected to occur." Silvanovich (2005) at 258.

Silvanovich expanded this work in an article published in 2009. Again, in the context of allergens, they found "an *E*-score threshold 3.9E-07 or lower … conservatively identif[ied] known allergens and other proteins with potential for allergenic cross-reactivity." Silvanovich (2009) at S26. Other E-values would fail to screen out many false positives. Id. at S28-29. Dr. Whitton proposes this E-value as the standard. Exhibit C at 29-30, Tr. 382.

Dr. Steinman uses a different cutoff. He changes the BLAST default E-value from 0.05 to 10. Tr. 169-70, 547. This change is 200 times more lenient. Tr. 392.

Dr. Steinman justifies a cutoff of 10 based upon Wheeler. Tr. 248. Wheeler does, in fact state that an E-value of "'10' is designed to ensure that no biologically significant alignment is missed." Wheeler at 4. But, Wheeler continues: "'Expect Values' in the range of 0.001 to 0.0000001 are commonly used to restrict the alignments shown to those of high quality." Id. The difference between these terms ("biologically significant" and "high quality") is not readily apparent. See Tr. 248-50 (Dr. Steinman), 415-16 (Dr. Whitton).

Given the two competing pieces of evidence, Wheeler and the Silvanovich articles, the undersigned weighs Silvanovich as more persuasive. Silvanovich contains extensive data, reporting the number of false positives found with various E-values. Silvanovich also reports that its standard is endorsed by the World Health Organization. Wheeler does not contain anything to justify reliance upon its description. Furthermore, Wheeler itself recognizes that E-values with magnitudes much lower than 10 produce alignments of "high quality."

Dr. Steinman's use of a BLAST search with an E-value of 10 to identify immunologically relevant homologs is methodologically unsound. The process seems likely to fail to weed out many false positives that a more stringent E-value setting would reject. See Silvanovich (2009).

In his oral testimony, Dr. Whitton stated that he has been looking for confirmation of Dr. Steinman's methodology for years. Tr. 416. The undersigned can confirm that Dr. Whitton has sought this external support. Dr. Steinman's first report in this case, dated December 14, 2021, cited a paper by Root-Bernstein. Exhibit 22 at 24 (reference 26). However, Dr. Whitton demonstrated that the Root-Bernstein article is backwards as Root-Bernstein asserts that higher E-values are more meaningful. Exhibit C at 32-33; See also Root-Bernstein. In Dr. Steinman's second report, he withdrew his reliance on Root-Bernstein because of the Gautam articles and

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potential similarities between newly expressed proteins and known allergen." However, Dr. Steinman has taken this statement out of the context in which Silvanovich defined the way the BLAST program could be used to minimize false positives. To the extent that Dr. Steinman wants use to conclusion of Silvanovich to bolster his case, expecting Dr. Steinman to follow the methodology of Silvanovich is reasonable.

the Lanz paper discussed below. Exhibit 58 at 18. Subsequently, in a different case, Dr. Steinman testified that Root-Bernstein was "wrong," essentially agreeing with Dr. Whitton. Jossart v. Sec'y of Health & Hum. Servs., No. 15-1377V, 2024 WL 4100548, at *40 (Fed. Cl. Spec. Mstr. May 22, 2024); See also Morrison v. Sec'y of Health & Hum. Servs., No. 18-386V, 2024 WL 3738934, at *23 n.16 (Fed. Cl. Spec. Mstr. July 18, 2024) (quoting Dr. Steinman as testifying that there were "'problems with the methodology used in the Root-Bernstein paper.'").[9]

While Dr. Steinman deserves some credit for walking away from Root-Bernstein in his second report, there remains a question about why Dr. Steinman cited the paper in the first report. It would seem that experts using BLAST could have (and arguably should have) recognized on their own that "Root-Bernstein's description of the E-value is the polar opposite of its truth." Exhibit C at 33.

It seems telling that one of the articles Dr. Steinman cited to support his use of BLAST searches to identify potentially immunologically relevant homologues was wrong. The other papers Dr. Steinman cited also are not helpful in showing that Dr. Steinman's BLAST search method is reliable. For example, Lanz did not use BLAST searches. See Exhibit 62, Tr. 382 (Dr. Whitton), 560 (Dr. Steinman).

Another way of looking at BLAST searches is to see whether pharmaceutical companies are using BLAST searches to help discover medicines that could prevent or treat autoimmune diseases. If BLAST searches were useful, then pharmaceutical companies could use them. Dr. Steinman testified that pharmaceutical companies would not use BLAST searches. Tr. 253. Dr. Steinman is not aware of any companies that he helped found use BLAST searches.

In the context of trying to defend his use of BLAST, Dr. Steinman described BLAST as "a pretty clunky tool." Tr. 560. Although Dr. Steinman goes on to say that he used BLAST because it is a tool on hand, the record shows that other programs also allowed proteins to be compared for homology. Tr. 560.

Overall, Dr. Steinman has failed to demonstrate that using BLAST with an E-value set at 10 is a reliable method for identifying potentially immunologically relevant homologs. See J.C., 2024 WL 3412625, at *18 ("Effectively, BLAST results are probably better viewed as potentially enhancing an otherwise supported theory rather than being viable as a foundation for such a theory"). Because Dr. Steinman's first step---a decision to use BLAST with an E-value of 10---is methodologically unreliable, the ensuing steps that follow from the BLAST searches are also problematic. See LaLonde v. Sec'y of Health & Human Servs., 110 Fed. Cl. 184, 201 (2013) (ruling that special master was not arbitrary in rejecting petitioner's prong one evidence when the

[9] One of the earlier opinions finding that Prevnar can cause GBS noted the dispute between Dr. Steinman and Dr. Whitton over the reliability of the Root-Bernstein article. Gross v. Sec'y of Health & Hum. Servs., No. 17-1075V, 2022 WL 9669651 at *17 (summarizing Dr. Steinman's opinion) and *29 (summarizing Dr. Whitton's opinion) (Fed. Cl. Spec. Mstr. Sep. 22, 2022). However, the special master's analysis did not resolve this specific dispute. Given Dr. Steinman's oral testimony in Jossart and Morrison, this dispute can be resolved in favor of only Dr. Whitton.

petitioner's expert did not establish each step in his hypothesis), aff'd 746 F.3d 1334, 1340 (Fed. Cir. 2014); Mitchell v. Gencorp Inc., 165 F.3d 778, 782 (10th Cir. 1999) ("any step that renders the analysis unreliable renders the expert's testimony inadmissible. This is true whether the step completely changes a reliable methodology or merely misapplies that methodology"); see also Buen v. Sec'y of Health & Hum. Servs., No. 21-1314V, 2025 WL 2938046, at *25 (Fed. Cl. Spec. Mstr. Sept. 17, 2025) (special master finding that expert "did not provide evidence to support step one . . . of his seven-step mechanism," and "since the other six other steps of the seven-step theory rely on the first step, the entire mechanism fails"). Nevertheless, the remaining steps in Dr. Steinman's protein-based theory are also discussed.

2. Input of Vaccine Information into BLAST

The BLAST program requires its users to input two proteins for comparison. One of these proteins in this case is known as CRM-197. CRM-197 is used because it is the only protein in Prevnar. Tr. 168, 373. CRM-197 contains 597 amino acids. Tr. 184.

Because CRM-197 is (at least generally) safe, CRM-197 has been used as a conjugation protein in multiple vaccines. Broker at 200, Tr. 412. Potentially billions of doses of vaccines containing CRM-197 have been administered. Tr. 412 (Dr.Whitton: "if that sequence actually did trigger immune responses that cross-react with Contactin-1 to cause Guillain-Barre syndrome, I think with billions of doses have been given, we would know about it by now, but we don't.")

Although CRM-197 is contained in Prevnar (and other vaccines), no specific information about the immunogenicity of CRM-197 was provided. Instead, Dr. Steinman substituted a proxy for CRM-197, which is the diphtheria toxin. See Exhibit 22 at 28; See also Exhibit D at 19 (Dr. Whitton: "In both of his reports, Dr. Steinman equates [CRM-197] with diphtheria toxin"). After this substitution of diphtheria toxin for CRM-197, Dr. Steinman presented information about how the immune system responds to diphtheria toxoid by citing Raju. To add another level of complication, Raju immunized people with diphtheria *toxoid*, not diphtheria *toxin*. The article explained that "the key component of antidiphtheria vaccines is diphtheria toxoid (DTD), a partially denatured, non-toxic form of [diphtheria toxin]." Raju at 3207; See also Exhibit D at 19.

In some ways, CRM-197 is similar to the toxin in diphtheria, but in other ways CRM-197 is different from diphtheria toxin. Of the 597 amino acids, CRM-197 and diphtheria toxin share 596. Just one amino acid differentiates CRM-197 from diphtheria toxin. Tr. 178, 373; See also Pet'r's Post-Hearing Br. at 26-27.

However, as Dr. Whitton explained without contradiction, the change in one amino acid has "profound immunologic consequences." Tr. 408; accord Exhibit D at 19-20. To start, people like Mr. Romine who received CRM-197 as part of a vaccine do not suffer the dangerous consequences of being exposed to diphtheria toxin. Tr. 409.

Whether the immune response to the diphtheria toxin can serve as a basis for inferring the immune response to CRM-197 is an issue on which Dr. Steinman and Dr. Whitton differ. In responding to Dr. Steinman's first report, Dr. Whitton asserted that: "The [Raju] paper tells us nothing about antibody responses to [diphtheria toxin] / [CRM-197]. . . In my opinion, these

facts render the Raju et al. paper almost irrelevant to petitioner's . . . theory of causation." Exhibit C at 37. Given this challenge from Dr. Whitton, Dr. Steinman might have addressed this critique. However, in Dr. Steinman's second report, he continued to rely upon Raju without addressing why Raju and diphtheria toxin assist with understanding how the body responds to what is actually in Prevnar, CRM-197. See Exhibit 58.1 at 21. Nevertheless, Dr. Whitton returned to this point, concluding in his second report that "while [CRM-197], diphtheria toxin, and diphtheria toxoid have very similar amino-acid sequences, the above biophysical, immunological, structural, and chemical differences mean that analyses of immune responses to diphtheria toxin / toxoid may not necessarily apply" to CRM-197. Exhibit D at 20.

The evidence in this case, including Dr. Steinman's lack of response, weighs against finding that the immune response to CRM-197 is likely to be sufficiently similar to the diphtheria toxin, which Dr. Steinman used in his BLAST search. At a basic and easy-to-understand level, diphtheria toxin causes people to have disease—CRM-197 does not. The difference between something that is dangerous and something that is safe is a big difference.

3. Input Of Host Proteins

To complete the pair of proteins to be compared in the BLAST program, Dr. Steinman compares CRM-197 to proteins allegedly implicated in GBS. Tr. 167. These four proteins are known as PMP22, P0, P2, and Contactin-1. Exhibit 22 at 24 (only Contactin-1), Exhibit 58 at 4. Thus, Dr. Steinman reported results in four BLAST searches. Id.

As for the searches regarding P0, P2, and Contactin-1, Dr. Steinman suggested that the evidence supporting involvement of these proteins was not as strong as evidence regarding PMP22. Tr. 264, 266.

Dr. Steinman's preferred protein is PMP22, which is peripheral myelin protein 22. Tr. 180, 197; Súkeníková at 160. PMP contains 160 amino acids.

The primary paper about PMP22 is Súkeníková. In 2024, these authors proposed that T cells can attack PMP22 to cause GBS. Súkeníková at 160; See also Tr. 181. As Dr. Whitton stated, Súkeníková and colleagues did not declare that pathology was established, but the authors were leaning that way. Tr. 413-14.

Súkeníková's hypothesis that PMP22 is attacked in GBS appears to be a new discovery. A different article from 2017 stated that PMP was not found in GBS. Hughes; See also Tr. 564. Whether Súkeníková's hypothesis becomes accepted depends upon additional work in the field. See Section VI.B. below (discussing peer review in the context of reliability).

Here, Súkeníková constitutes some basis for finding the portion of Dr. Steinman's opinion that asserts an attack on PMP22 can lead to GBS reliable. Whether the record, which contains some contradictory evidence, supports a finding that this aspect is persuasive is a more difficult question. Given the gaps and inadequacies in other parts of Dr. Steinman's opinion, addressing whether on a more likely than basis PMP22 can contribute to the pathogenesis of GBS is not required. This question can be reserved for another day.

4. Results of Comparison

Using the BLAST program, Dr. Steinman compared CRM-197 and PMP22. Exhibit 58.1 at 5. BLAST calculated an E-value of 0.015. Id.; See also Tr. 417.

Dr. Steinman reproduced the results of the BLAST search:

PMP22, partial [Homo sapiens]
Sequence ID: **CAG46751.1** Length: 160 Number of Matches: 2
Range 1: 30 to 82

Score	Expect	Method	Identities	Positives	Gaps	Frame
21.6 bits(44)	0.015()	Composition-based stats.	18/53(34%)	25/53(47%)	0/53(0%)	

```
Query  479  VGNGVHANLHVAFHRSSSEKIHSNEISSDSIGVLGYQKTVDHTKVNSKLSLFF  531
            VGNG   +L       SSS  +H    SS +  +    Q T+  + + S LSLF
Sbjct  30   VGNGHATDLWQNCSTSSSGNVHHCFSSSPNEWLQSVQATMILSIIFSILSLFL  82
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Dr. Steinman opined that this combination could be immunologically relevant because, in part, of the Gautam standard. See Exhibit 22 at 24 (technically discussing Gautam in context of Contactin-1); Exhibit 58.1 at 5 (citing three papers by Gautam, published in 1992, 1993, and 1998). However, there are limits to the value of the Gautam papers.

A fundamental point is that homology is not necessarily the same as likely immunological mimics. Dr. Whitton provided an example that is easy to understand. The flu virus has different strains that share a high degree of molecular overlap. This homology does not mean that a person's responses to the strains are the same, because the vaccine contains multiple strains. If homology by itself were sufficient, then multiple strains in the flu vaccine would be unnecessary. Tr. 471-72. Similarly, Prevnar itself contains multiple strains of the *Streptococcus pneumoniae* bacteria. If molecular mimicry were sufficient, then the vaccine would not contain multiple strains. Tr. 323-26; See also Morrison, 2024 WL 3738934, at *22 (noting that although CRM-197 shares all but one amino acid with diphtheria toxin, people are immunized with diphtheria toxoid, not CRM-197, to protect against diphtheria).

Further, the articles contain examples of instances in which searches of computer databases did not produce an immunologically relevant substance. A prominent example is Wucherpfennig. Exhibit 1003; Tr. 277-87.[10] Another example is Varrin-Doyer. See also Tr. 285-88.

With an understanding that homology does not always equal shared immunogenicity, the Gautam papers can be reviewed. In a previous case in which Dr. Steinman relied upon the Gautam papers, the undersigned set out the steps that the Gautam researchers, including Dr. Steinman, followed. Sparrow v. Sec'y of Health & Hum. Servs., No. 18-295V, 2024 WL 1599165, at *24 (Fed. Cl. Spec. Mstr. Mar. 19, 2024), mot. for rev. denied sub nom. Sparrow on behalf of L.S. v. Sec'y of Health & Hum. Servs., 173 Fed. Cl. 177 (2024), appeal docketed, No. 25-1161 (Fed. Cir. Nov. 8, 2024). Before conducting their experiments, Gautam and colleagues knew that the first 11 amino acids that formed myelin basic protein were involved in creating a

[10] Wucherfennig is more thoroughly discussed in the context of the testability of Dr. Steinman's theory as part of the Daubert analysis in section VI.C., below.

disease known as experimental autoimmune encephalitis ("EAE") in genetically modified mice. Gautam (1992) at 605. Because of this background knowledge, the Gautam researchers did not search a computerized database like BLAST to find potential homologs. See Exhibit D at 24 (Dr. Whitton noting that Gautam did not use BLAST). The researchers were interested in learning whether all 11 amino acids were necessary to cause disease in mice. Thus, the researchers varied the sequences of amino acids that were injected into mice. As reflected in table 1 from Gautam (1992), different combinations of amino acids produced different results. Gautam (1992) at 607. For example, changing one amino acid reduced the incidence of disease from 80 percent to 15.7 percent. In Sparrow, "Dr. Steinman acknowledged that a change in one amino acid could make a big difference." 2024 WL 1599165, at *25. Therefore, Sparrow found that "5 amino acids out of 12 work sometimes but not always." Id.

Accordingly, there is abundant evidence that changing one amino acid can produce dramatically different substances. One example is CRM-197 and diphtheria toxin. Another example is the peptides given to the mice in the Gautam experiments. A third example, which is discussed in more detail in section VI.C., below, is the Wucherpfennig article. If there were any doubt about this principle, the Federal Circuit recently cited the United States Supreme Court for a statement that "even a minor change of chemical structure can alter an antibody's functionality." Seagen, Inc. v. Daiichi Sankyo Co., Ltd., 160 F.4th 1322, 1333 (Fed. Cir. 2025), citing Amgen v. Sanofi, 598 U.S. 594, 614-15 (2023).

In this case, during the pre-hearing status conference, the parties were advised to review Sparrow and for their experts to be prepared to discuss it. During his testimony, Dr. Steinman was asked about this finding in Sparrow, and he agreed that the Gautam papers show that four amino acids might work but they do not have to work. Tr. 253.

The bottom line is that the record supports finding that relatively short sequence homology can be a basis for immunogenicity. Dr. Whitton admits as much. Tr. 383, 398, 468. But to find that CRM-197 and PMP22 are so sufficiently similar that they do, in fact, cause GBS is an additional step. As Dr. Steinman has not presented a reliable foundation for this leap, Mr. Romine's case falls short of preponderant evidence.

In this respect, Dr. Steinman did not follow the methodology that Gautam, others, and he used in their experiments. See Kumho Tire Co. v. Carmichael, 526 U.S. 137, 152, 119 S.Ct. 1167, 143 L.Ed.2d 238 (1999) ("[The objective of Daubert's gatekeeping requirement] is to make certain that an expert, whether basing testimony upon professional studies or personal experience, employs in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field").

In the Gautam experiments, after the researchers identified homology at different levels, the researchers tested to see whether the homologous peptides induced an immunologic reaction. In contrast, Dr. Steinman essentially ended his work without taking the potentially more informative and more meaningfully step of testing for immunogenicity. This lack of investigation creates a gap within Dr. Steinman's opinion. See Cedillo v. Sec'y of Health & Hum. Servs., 617 F.3d 1328, 1339 (Fed. Cir. 2010) (recognizing that a court may find that there is a gap between the data and the opinion).

Dr. Whitton introduced additional evidence to undermine Dr. Steinman's assertion that the homologs that the BLAST search identified were immunologically relevant. As reflected in the chart taken from Dr. Steinman's report, the BLAST search aligned approximately 50 amino acids. In the query, the amino acid sequence begins at 479 and ends at 531. In the subject, the amnio acid sequence begins at 30 and ends at 82.

From this sequence of about 50 amino acids, Dr. Steinman selected the first nine amino acids of each sequence (VGNGVHANL and VGNGHATDL). Exhibit 58.1. Dr. Steinman states that five of these nine are identical. Id.,[11] Tr. 184; See also Pet'r's Post-Hearing Br. at 34. Pursuant to Dr. Steinman's theory, this portion of CRM-197 (VGNGVHANL) is the basis for the autoimmune reaction with Prevnar.

Dr. Whitton entered the key sequence of nine amino acids found in CRM-197 (VGNGVHANL) into BLAST. (This is different from Dr. Steinman, who entered the sequence for the entire CRM-197). Exhibit D at 16. Dr. Whitton reported that a match was found between at least a portion of this sequence and PMP22, but with an E-value of 3,817. Id. Again, higher E-values are less meaningful. Thus, according to Dr. Whitton, the "BLAST algorithm is informing us that this homology is a matter of random chance." Id. Dr. Whitton described his process in his oral testimony. Tr. 417-21. But, there was not any persuasive rebuttal testimony.

5. Summary on Protein Theory

For the reasons explained above, the evidence does not weigh in favor of finding that Dr. Steinman's theory that the CRM-197 portion of Prevnar can cross react with PMP22 is either sound, reliable, or persuasive. Reasons for rejecting this theory start with the lack of association between either pneumococcal vaccine and GBS and the lack of association between *Streptococcus pneumoniae* infections and GBS. See section IV. Additional flaws specific to the protein theory include:

> Problems in using the BLAST program with an E-value set to 10 to identify immunologically relevant homolog;
>
> An unsupported assumption that the immune response to CRM-197 is similar to the immune response to diphtheria toxoid, which was studied in Raju;
>
> Assuming that identifying a homology at a level of 5 out of 12 is the same as demonstrating immunogenicity when Gautam and other papers show that shared immunogenicity is only possible.

Accordingly, Mr. Romine does not prevail upon his first attempt to satisfy the first prong of Althen.

[11] Technically, Dr. Steinman states five out of ten but that was because Dr. Steinman inadvertently introduced an extra amino acid. See Exhibit D (Dr. Whitton's report) at 16; Tr. 419.

C. Phosphoglycerol Theory

1. Definition Of Terms and Introduction

Dr. Steinman's other theory is a variation on molecular mimicry, which is often based upon proteins as just discussed. This other theory is sufficiently complicated that Dr. Steinman stated that he never expected to be discussing X-ray crystallography in the Vaccine Program. Tr. 154. Unlike the protein-based theory, this theory is based upon polysaccharides. Polysaccharides are a type of carbohydrate. Dorland's at 1471. They are sometimes referred to as "sugars."

Some polysaccharides contain phosphoglycerol. Tr. 340. A "glycerol" is an alcohol found in many lipids. Dorland's at 784. Lipids, in turn, are types of fats. Dorland's at 1048. A phospholipid is a lipid containing phosphorus, such as phosphoglycerides. Dorland's at 1416. Phospholipids are "the major form of lipids in all cell membranes." Id.; accord Tr. 342. Phospholipids are present in myelin. Tr. 341.

Two of the polysaccharides in Prevnar 13 have phosphoglycerol attached to them. These are the polysaccharides for strains 18C and 23F. Tr. 143. The phosphoglycerol in 18C is needed to develop immunogenicity. Chang; Tr. 146-47, 154, 357.

From a starting point that the immune response to the 18C component of Prevnar responds at least, in part, to the phosphoglycerol, Dr. Steinman proposes that the immune response can be misdirected and can cause GBS. Dr. Whitton raises multiple points against this opinion. These are discussed below starting with the points that are easiest to understand.

2. Anti-phospholipid syndrome

In Dr. Whitton's second report, he reasoned that if Dr. Steinman's opinion that antibodies against phospholipids can cause GBS were correct, then people who suffer from diseases involving antibodies against phospholipids would have increased incidences of GBS. Exhibit D at 12. This reasoning seems appropriate, especially because Dr. Steinman did not contest it. Essentially, Dr. Whitton is asking: how does Dr. Steinman's theory play out in the real world among people who have the allegedly harm-inducing antibodies? When Dr. Whitton consulted recent reviews about anti-phospholipid syndrome, they did not associate anti-phospholipid syndrome and GBS. Exhibit D at 12, citing Knight and Bröker.

Dr. Whitton testified that anti-phospholipid syndrome is not associated with GBS. Tr. 371. Dr. Steinman did not address this point in rebuttal. Likewise, the Secretary argued this point (Resp't's Post-Hearing Br. at 24), but Mr. Romine did not address this in his reply.

This point carries great value. Cf. Whitecotton v. Sec'y of Health & Hum. Servs., 81 F.3d 1099, 1108 (Fed. Cir. 1996) ("Congress desired the special masters to have very wide discretion with respect to the evidence they would consider and the weight to be assigned that evidence").[12] As Dr. Whitton acknowledges, this is not "a hard and fast rule." Tr. 371. Yet, there

[12] The undersigned has not located any opinions from special masters addressing how the lack of association between anti-phospholipid syndrome and GBS affects claims that anti-phospholipid antibodies cause GBS. Cf. Mullins v. Sec'y of Health & Hum. Servs., No. 19-

is an underlying logic to seeing the reported consequences to producing anti-phospholipid antibodies. By citing review articles about anti-phospholipid syndrome, Dr. Whitton has made a reasonable effort to attempt to prove a negative. Dr. Whitton's effort is reinforced by the lack of response from Mr. Romine and Dr. Steinman. Mr. Romine and Dr. Steinman had opportunities to contradict Dr. Whitton's assertion by presenting articles or even case reports showing someone linked anti-phospholipid syndrome and GBS. No such evidence was presented, leaving Dr. Whitton's assertion unrebutted.

3. Phospholipids in GBS generally

Using similar logic, Dr. Whitton makes another point against Dr. Steinman's theory. Dr. Whitton opines that in GBS, the immune system most often targets gangliosides, not phospholipids. Tr. 342. Dr. Whitton's opinion appears correct. Except for Nakos, which is discussed below, other articles do not hypothesize that phospholipids are the subject of the immune system's attack in GBS. Admittedly, the pathogenesis of GBS is not understood completely. This lack of awareness means that the possibility that some GBS cases could involve phospholipids cannot be closed off with a door nailed shut. On the other hand, special masters are required to resolve cases based upon the existing evidence, not hypothetical developments in hypothetical future cases. 42 U.S.C. § 300aa–13(a); Sharpe v. Sec'y of Health & Hum. Servs., 964 F.3d 1072, 1084 (Fed. Cir. 2020). Here, a preponderance of evidence supports a finding that phospholipids are not likely to be involved in causing GBS. This evidence includes how working neurologists treat their GBS patients. Neither Dr. Sykes nor Dr. Alexander routinely test for anti-phospholipid antibodies in people with GBS. Tr. 76, 96.

a) *Nakos*

For the proposition that antibodies against phospholipids cause GBS, Mr. Romine relies upon Nakos. See Pet'r's Pre-Hearing Br. at 17; Pet'r's Post-Hearing Br. at 18-19, 61. Nakos was published in 2005. The authors explained that due to similarities between the lipopolysaccharides of *C. jejuni* and the epitopes of gangliosides, "a cross-reaction of the antibodies against micro-organisms could recognize gangliosides of the nerves." Nakos at 1402. "It is not established, however, whether apart from gangliosides other lipid antigens are also recognized as targets for antibodies in GBS." Id. The researchers therefore investigated "whether anti-phospholipid antibodies are present in serum samples of GBS patients without known autoimmunity disorders." Id.. The investigation involved nine patients with GBS and nine controls. Id. Before the people with GBS were treated with γ-globulin, a serum sample was obtained. Serum samples were also taken on the first, second, fifth, and eighth days of the treatment. Id. at 1402. The researchers "detected a wide range of anti-phospholipid antibodies

320V, 2024 WL 4045424, at *33-34, 43-45 (Fed. Cl. Spec. Mstr. Aug. 8, 2024) (special master noting phosphoglycerol as one of three specific molecular mimicry homologies proposed by petitioner, but finding that even absent the three proposed homologies, molecular mimicry was a sound and reliable theory).

in patients with idiopathic GBS. . . . [W]hereas none of the controls demonstrated any anti-phospholipid activity under our experimental conditions." Id. at 1405.

The authors propose two explanations for this observation. One is that the anti-phospholipids contributed to the pathogenesis of GBS; the other is that the anti-phospholipid antibodies were a consequence of GBS. Nakos at 1406. Both Dr. Steinman and Dr. Whitton discussed this portion of the article. Tr. 206, 363. A third possibility is that the anti-phospholipid antibodies are "epiphenomena."

The Nakos researchers also noted "in our cases there was no relationship between the presence of anti-phospholipid antibodies and outcome, nor to the severity of the disease, probably due to the limited number of patients and variety of GBS." Nakos at 1407. To Dr. Whitton, this statement was important because in most (but not all) autoimmune diseases, the presence of an autoantibody tends to correlate with the severity of the disease. Tr. 363; See also Tr. 555 (Dr. Steinman's testimony not really answering a question on this topic).

Nakos does not persuasively establish that anti-phospholipid antibodies contribute to the pathogenesis of GBS. First, the authors literally do not reach this conclusion. Second, the article was written in 2005. So, it is approximately two decades old. Dr. Steinman cited only this article to discuss anti-phospholipid antibodies and GBS. Presumably, if there were any follow up or additional support for this proposition, Dr. Steinman would have cited it. Third, the leaders in GBS who wrote the review articles have not cited Nakos. Fourth, the current practice among neurologists as reflected in care delivered by Dr. Sykes and Dr. Alexander does not align with a view that anti-phospholipids antibodies cause GBS. See Tr. 362.

b) Ho

The second article on which Dr. Steinman relied to support the proposition that anti-phospholipid antibodies can cause GBS is Ho. Dr. Steinman is a co-author of this paper, which was published in 2012.

Ho and colleagues studied multiple sclerosis. Tr. 158, 359. Thus, Dr. Steinman extends Ho to inform GBS by a three-step reasoning: (1) Ho shows phospholipid antibodies cause multiple sclerosis, (2) multiple sclerosis is like GBS, (3) therefore, by substitution, phospholipid antibodies cause GBS. Many of the previous adjudications split on the second step.

However, the undersigned finds more problem with accepting the first premise as preponderantly established. Like Nakos, Ho was published more than 10 years ago. And like Nakos, Ho seems to have received little attention.

Ho proposed that because, in the authors' views, anti-phospholipid antibodies cause multiple sclerosis and phospholipid antibodies ameliorated multiple sclerosis, phospholipids could be a therapeutic treatment for multiple sclerosis. Ho (abstract) at 9. Dr. Steinman and other researchers obtained patents for their discoveries. Exhibits 82-83.

Dr. Steinman and his employer, Stanford University, attempted to market the patent to pharmaceutical companies. Tr. 299. However, for whatever reason, the patentees "could not get pharma sufficiently bold enough to test in humans." Tr. 297.[13]

Perhaps due to the lack of follow up, neurologists such as Dr. Sykes do not routinely test their multiple sclerosis patients for anti-phospholipid antibodies. Tr. 74. Dr. Whitton also noted that the Lanz paper proposes a protein as the target of autoimmune attack in multiple sclerosis, and does not mention phospholipids as a possible target. Exhibit D at 11. Finally, although far from dispositive, the undersigned's experience in reviewing cases and literature on multiple sclerosis is also consistent with a finding that doctors generally do not associate anti-phospholipid antibodies with multiple sclerosis.

Even if Ho were a reliable basis for finding that some multiple sclerosis cases are caused by attacks on phospholipids, there would remain the question about whether multiple sclerosis can be the basis of inference for GBS. As noted previously, special masters have not viewed the transferability of Ho to GBS the same. See, e.g., Bielak v. Sec'y of Health & Hum. Servs., No. 18-761V, 2023 WL 35509, at *16 (Fed. Cl. Spec. Mstr. Jan. 3, 2023).

4. Summary

A recap of these points is worthwhile. From two perspectives, Dr. Steinman's opinion that anti-phospholipid antibodies cause GBS is not reliable. Doctors have some understanding of the consequences of anti-phospholipid antibodies and these consequences do not include GBS. The other viewpoint is from what is understood about GBS. People with GBS are generally not monitored or treated for having anti-phospholipid antibodies.

Therefore, Dr. Steinman's theory can be rejected even without considering the immunology. But, the immunology is discussed next.

5. Immunology

The immunology at the heart of Dr. Steinman's phospholipid opinion is complicated but ultimately relies upon a handful of articles. In a nutshell, the immunologic aspect of the phospholipid theory is a variation of the molecular mimicry theory. The phospholipid theory differs from the more typical molecular mimicry theory because the phospholipid theory is based upon an alleged similarity in carbohydrates, not proteins. See Tr. 197, 337. This difference is not disqualifying in any respect.

The foundation of the phospholipid theory is that a group of researchers found that the protective response to strain 18C in Prevnar requires a response to a phosphoglycerol moiety. Chang; exhibit 22 at 14-15, Tr. 146-47. Dr. Whitton agrees with this finding. Tr. 357.[14]

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[13] Dr. Steinman cautioned against reading too much into the lack of funding by recounting a story that an inventor of checkpoint inhibitors, Jim Allison, was not funded for many years. After receiving funding, he eventually won a Nobel Prize. Tr. 298.

[14] There remains an unfortunate lack of clarity as to whether Dr. Steinman is proposing a phosphocholine head group or phosphoglycerol. See exhibit C at 17, exhibit D at 2-3, Tr. 338.

On the foundation of Chang, Dr. Steinman adds two articles by Bryson (a 2016 article and the supplemental material to that article) and with the addition of Bryson, Dr. Whitton interposes an objection, or at least a qualification. Dr. Steinman asserts that "The Bryson paper demonstrates that the immune response to S. pneumoniae serotype 23F after Pneumovax 23 vaccine targets the phosphoglycerol in the polysaccharide capsule of serotype 23F." Exhibit 22 at 18. Over the next three pages, Dr. Steinman explains part of the work done by Bryson and colleagues and reproduces various images. This explanation is the basis for Dr. Steinman's statement that: "The data from the Bryson article demonstrates UNEQUIVOCALLY that the immune response to the serotype 23F component of Pneumovax 23 targets the phosphoglycerol in serotype 23F." Id. at 21. Dr. Whitton agrees that the antibodies (which are known in the Prevnar litigation as "Bryson antibodies") "recognize a larger structure, of which the glycerophosphate is just one part." Exhibit C at 21; see also Tr. 350 (Dr. Whitton stating that the Bryson antibodies recognize a phosphate group). The larger structure is known as "L rhamnose." Exhibit C at 21. "L rhamnose," in turn, is "a component . . . of lipopolysaccharides of some gram-negative bacteria." Dorland's at 1612; accord Tr. 210 (Dr. Steinman agreeing that L rhamnose is a bacterial sugar that is part of serotype 23F). This qualification is important to Dr. Whitton because antibodies do not recognize just the glycerophosphate. If antibodies recognized only glycerophosphate, then the antibodies would recognize glycerophosphates in the strains other than 23F, making vaccination against other strains unnecessary. Exhibit C at 21. In Dr. Steinman's second report, Dr. Steinman did not respond to Dr. Whitton's discussion of the Bryson antibodies. See Exhibit 58.1.

Nevertheless, Dr. Whitton expanded upon his earlier discussion of the Bryson antibodies in his second report. Here, Dr. Whitton stated that an antibody grasps an antigen through points of contact that resemble the fingertips of a glove. Exhibit D at 8. For the Bryson antibody on which Dr. Steinman is relying, the antibody has nine fingers / points of contact. Id.; see also Tr. 214-15 (Dr. Steinman agreeing there are nine points of contact). Of these nine, eight are with a saccharide residue. Exhibit D at 8; see also Tr. 216-17 (Dr. Steinman agreeing that eight points of contact are with a sugar). The remaining point of contact is between the antibody and "the oxygen atom . . . in the phosphate." Exhibit D at 8. This emphasis on the binding with the saccharide, to Dr. Whitton, reinforces his earlier point that an antibody sees phosphoglycerol only in the context of a specific polysaccharide. Dr. Whitton repeats his earlier argument that if antibodies saw only phosphoglycerol, then the Prevnar vaccine would not need to contain the polysaccharides for both strain 18C and 23F. Id. at 9.

On cross-examination, Dr. Steinman came around to Dr. Whitton's point of view, at least in part. Dr. Steinman agreed: "The sugars are really important. But the paper goes on to say that the phosphate group of phosphoglycerol is another major determinant. . . . They're both important." Tr. 211-12. When pressed further on cross-examination, Dr. Steinman stated: "You can't ignore the phosphoglycerol, and I don't want to ignore the rhamnose. So maybe we should say we agree." Tr. 212.

Dr. Whitton's oral testimony repeated much of the foundation for this complicated immunology. See Tr. 344-52, 517 ("It's crystal -- crystallography clear that these antibodies see

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More clarity would be better. But the lack of reliability of Dr. Steinman's phosphoglycerol theory does not turn on this point.

phosphate as part of larger epitope, the rest of the epitope being the bacterial sugars"). He emphasized that the Bryson antibodies do not recognize the phosphate alone, but that the Bryson antibodies recognize a phosphate in the context of a particular polysaccharide. Tr. 353. Dr. Whitton again repeated that the specific polysaccharide affects the immune response because vaccines contain both strain 18C and 23F, which have different sugars. Tr. 353.

All of this background helps to understand why Dr. Whitton contests Dr. Steinman's opinion that the immune system's response to Prevnar can lead to a cross-reaction to myelin, causing GBS. To refresh, myelin contains phospholipids. See Exhibit D at 9. A simple definition of a "lipid" is that a lipid is a fat. Dorland's at 1048. Dr. Whitton asserted, without any contradiction, that polysaccharides and phospholipids have "completely different molecular structure[s]." Exhibit D at 9; accord Tr. 356 (Dr. Whitton: "lipids are very different structurally from sugars, very different, completely different").

Dr. Whitton, then, raised the key point: given that Bryson antibodies recognize phosphate in the context of specific polysaccharides and given that polysaccharides differ from phospholipids found in myelin, why would an antigen that sees a phosphate in the context of a specific sugar (such as L rhamnose) also see that phosphate in the context of a phospholipid? See Exhibit D at 9. Dr. Whitton created a visual aid to help illustrate his reasoning:

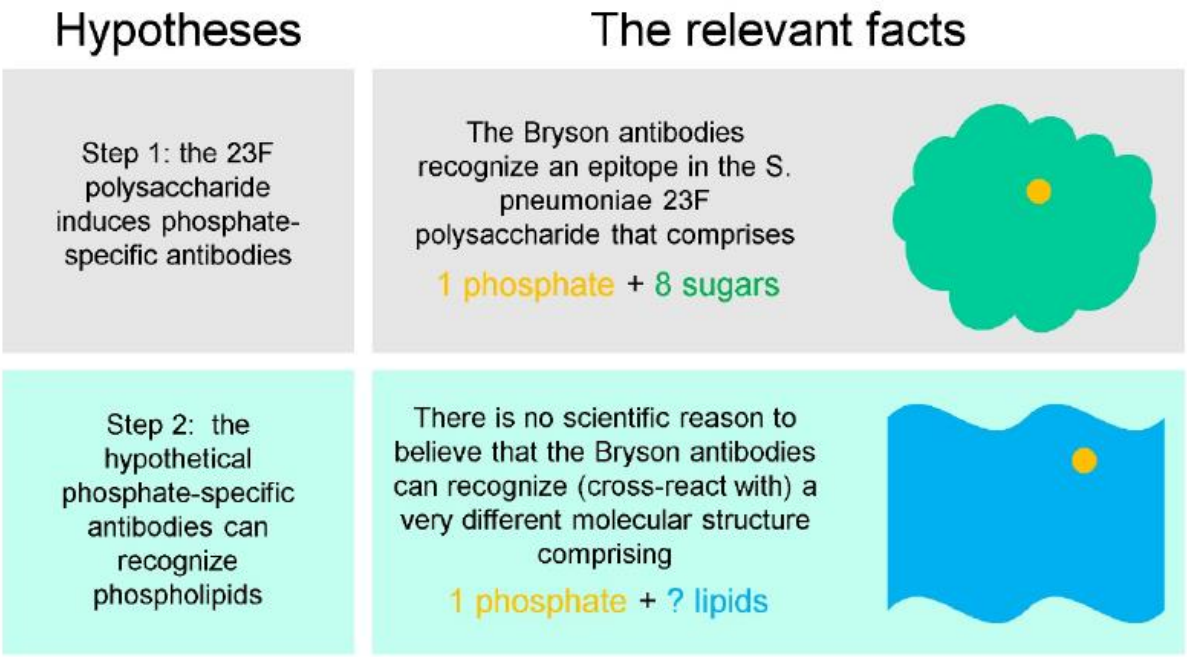

Exhibit D at 13.[15] Dr. Whitton explained that in the first row, the yellow dot represents a phosphate group. The green cloud in the first row represents a polysaccharide. In the second row, the phosphate group is still a yellow dot, but it is now depicted in the context of a lipid,

[15] For completeness, it should be noted that Dr. Whitton's chart contains a third row that is not reproduced above. Dr. Steinman agrees with how Dr. Whitton has summarized the steps in his theory (the left column). Tr. 551-53. Dr. Steinman does not agree with Dr. Whitton's criticisms (the right column).

represented by the blue waving flag. Tr. 356. Dr. Whitton asserted that "Dr. Steinman presents no data whatsoever to support his speculation that the extremely specific Bryson antibodies … can 'see' a structure comprising [phosphate + lipid]." Exhibit D at 9 (brackets in original). Referring to his visual aid, Dr. Whitton reiterated his assessment: "And so the notion that antibodies that recognize the yellow dot and the green cloud can somehow turn around and recognize a yellow dot on this completely different blue [lipid], there's no credible scientific reason to believe that that's the case." Tr. 356.

Dr. Steinman attempted to answer this criticism in his rebuttal testimony by discussing Barbar. Tr. 532-24. Barbar was an article that Mr. Romine had filed without an accompanying disclosure from Dr. Steinman. This late disclosure appears to have imposed minimal, if any, prejudice upon the Secretary as Dr. Whitton also commented upon Barbar. Exhibit D at 25.

Barbar has received relatively little attention from special masters. In general, in opinions that find Prevnar can cause GBS, the ruling mentions Dr. Steinman's reliance upon Barbar but without any substantive analysis of the article. E.g, Datte v. Sec'y of Health & Hum. Servs., No. 18-2V, 2025 WL 1565894, at *9 (Fed. Cl. Spec. Mstr. May 9, 2025); Anderson v. Sec'y of Health & Hum. Servs., No. 18-484V, 2024 WL 557052, at *13 n.33 (Fed. Cl. Spec. Mstr. Jan. 17, 2024) (identifying Barbar). The most detailed analysis of Barbar was in the context of an opinion that found that the petitioner had failed to establish that Prevnar can cause GBS. Jaye v. Sec'y of Health & Hum. Servs., No. 20-672V, 2024 WL 3691413, at *4-5 (Fed. Cl. Spec. Mstr. July 18, 2024).

In this case, Dr. Steinman relies upon Barbar to assert that antibodies attach to a phosphate group. Tr. 155-56, 534; see also Pet'r's Post-Hearing Br. at 20-21. Although Dr. Whitton might prefer the more specific term "phenylphosphocholine," see Exhibit D at 25, additional refinement seems unnecessary. Barbar does not contradict Dr. Whitton's basic reasoning---Bryson antibodies respond to specific pneumococcal polysaccharides. One type of Bryson antibody could attach to the phosphoglycerol component strain 18C. A different Bryson antibody attaches to the phosphoglycerol component of strain 23F as shown in Bryson itself. The main point is that different polysaccharides require the inclusion of different strains in Prevnar.

Barbar appears not to help Dr. Steinman with this conundrum. If an antibody to strain 18C does not induce an immune response to strain 23F (and both 18C and 23F are polysaccharides), then why would the immune response to one of them also cross-react with a much different substance, a phospholipid? Dr. Steinman appears to be equating sugars and fats without any persuasive basis. This is far too big of a gap to credit.[16] See Cedillo, 617 F.3d at 1339.

[16] In an effort to be transparent, the undersigned discloses this understanding of Barbar could be subject to modification. The science underlying Barbar is complicated. The testimony about Barbar, whether contained in Dr. Whitton's second report or Dr. Steinman's oral presentation, was not especially clear. The lack of clarity does not assist Mr. Romine because he bears the burden of proof and an unclear presentation is not consistent with a persuasive presentation.

6. Summary on Phosphoglycerol Theory

For the reasons explained above, the evidence does not weigh in favor of finding that Dr. Steinman's theory that the phosphoglycerol theory is either sound, reliable, or persuasive. Reasons for rejecting this theory start with the lack of association between either pneumococcal vaccines and GBS and the lack of association between *Streptococcus pneumoniae* infections and GBS. See section IV. Additional flaws specific to the phosphoglycerol theory include:

> The lack of association between people suffering from anti-phospholipid syndrome and GBS;
>
> The lack of persuasive support for the assertion that the pathogenesis of GBS involves phospholipids;
>
> The lack of a persuasive basis for finding that antibodies produced in response to a phosphate in the context of a polysaccharide can cross-react with a phosphate in the context of a phospholipid.

Accordingly, Mr. Romine does not prevail upon his second attempt to satisfy the first prong of Althen.

VI. **Daubert**

The foregoing analysis is an analysis that special masters typically employ. Due to the differences in outcome, which are discussed further in Section VIII, a separate approach is presented below.

The Federal Circuit has stated special masters may use Daubert "as a tool or framework for conducting the inquiry into the reliability of the evidence." Terran v. Sec'y of Health and Hum. Servs., 195 F.3d 1302, 1316 (Fed. Cir. 1999). In light of Terran's endorsement of the Daubert factors, Mr. Romine's argument that evaluating an expert's opinion according to Daubert erroneously elevates petitioner's burden (Pet'r's Post-Hearing Br. at 57) is rejected. Potentially relevant factors include:

> (1) whether a theory or technique can be (and has been) tested;
>
> (2) whether the theory or technique has been subjected to peer review and publication;
>
> (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and,
>
> (4) whether the theory or technique enjoys general acceptance within a relevant scientific community.

Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579, 592-95, 113 S.Ct. 2786, 125 L.Ed.2d 469 (1993). As with any Daubert evaluation, the factors need to be employed flexibly. Kumho Tire Co., Ltd. v. Carmichael, 526 U.S. 137, 141-42, 119 S.Ct. 1167, 143 L.Ed.2d 238 (1999).

A. Testability

The first Daubert factor is "whether a theory or technique can be (and has been) tested." "Testability" depends, at least in part, on what aspect of the opinion is being addressed. For example, with respect to the point regarding general causation---whether pneumococcal vaccines can cause GBS---epidemiological studies can be thought of as one way to look for data confirming or refuting the hypothesis. As discussed in section IV above, investigations have not found an increased incidence of GBS among people receiving pneumococcal vaccines. Thus, on this particular point, the testability factor weighs against finding Dr. Steinman's opinion reliable.

On the other hand, for the narrower point of specific causation---whether Prevnar caused Mr. Romine's GBS---the analysis is different. Purely from a theoretical perspective, this aspect could be tested by re-administering another dose of Prevnar to see what happens to Mr. Romine. If he again developed GBS, he would have experienced the paradigm known as challenge-rechallenge. Challenge-rechallenge, in turn, is usually accepted as evidence of causation. Capizzano v. Sec'y of Health & Hum. Servs., 440 F.3d 1317, 1322 (Fed. Cir. 2006).

However, for ethical reasons, we do not ask human beings to participate in experiments that could harm them. Thus, on the question of specific causation, Daubert's testability factor is neutral. Due to the lack of testing on Mr. Romine, Dr. Steinman's opinion should neither be credited as reliable nor rejected as unreliable.

Rather than experiment on people, researchers often use animal models. Lanz; Miura; Tr. 257. Dr. Steinman could inject mice with Prevnar to see whether the animals develop a neurologic disease like GBS. Tr. 309. Dr. Whitton could, too. Tr. 525-27.

The lack of testing, which is a Daubert factor, tends to undermine the reliability of Dr. Steinman's opinion.

B. Peer review

For one commenter's assessment of peer review, See Susan Haack, "Peer Review and Publication: Lessons for Lawyers," 36 Stetson L. Rev. 789 (2007). As this article illustrates, publication of a manuscript after peer review does not mean the article is reliable. For example, the authors could present fraudulent data that peer-reviewers are unlikely to detect. Id. at 802-03. Dr. Steinman and Dr. Whitton agreed that papers containing fraud can survive peer review. Tr. 504, 557. When Dr. Steinman reviews a manuscript as a peer reviewer, he is, in his words, "lenient," as he is "not awarding a Nobel Prize." Tr. 222. In Dr. Whitton's role as an editor of the journal Virology, he was uncertain how much time reviewers spent on each article. Tr. 498. One article reported the average amount of time was less than three hours. Effie J. Chan, "The 'Brave New World' Of Daubert: True Peer Review, Editorial Peer Review, And Scientific Validity," 70 N.Y.U. L. Rev. 100, 118 (1995).

All this background is to say that the appearance of an article in a peer-review journal does not correlate with reliability. Tr. 501. The Supreme Court itself recognized: "Publication (which is but one element of peer review) is not a sine qua non of admissibility; it does not necessarily correlate with reliability." Daubert, 509 U.S. at 593. Instead, as Dr. Steinman testified, peer review is "a good opening for reliability." Tr. 557.

Here, Dr. Steinman has not submitted his opinion that Prevnar can cause GBS for peer review. Tr. 301-02. This is surprising in the sense that (a) Dr. Steinman has written hundreds of articles appearing in peer-reviewed journals (See Exhibit 60 (updated curriculum vitae)) and (b) Dr. Steinman's opinion that attacks on phospholipids cause GBS would constitute a "major discovery about GBS that others in the field more well-versed in the specific study of peripheral neuropathies have fully missed." Gamboa-Avila v. Sec'y of Health & Hum. Servs., No. 18-925V, 2023 WL 6536207, at *27 (Fed. Cl. Spec. Mast. Sept. 11, 2023), mot. for rev. denied, 170 Fed. Cl. 441 (2024), aff'd, 166 F.4th 1318 (Fed. Cir. 2026).

Dr. Steinman explained that his reluctance to author a paper about Prevnar harming recipients was due to the current environment. Dr. Steinman worried that he would be targeted like Dr. Fauci, who maintained that people should be mandated to wear masks to prevent the spread of COVID during the pandemic. Tr. 305-07.

Another type of peer review is the process of seeking a grant. Lawrence S. Pinsky, "The Use of Scientific Peer Review and Colloquia to Assist Judges in the Admissibility Gatekeeping Mandated by Daubert," 34 Hous. L. Rev. 527, 559-60 (1997). As of his testimony in the hearing in December 2024, Dr. Steinman had not sought a grant to investigate whether Prevnar can cause GBS from any national organization dedicated to GBS or the National Institute of Health. However, Dr. Steinman stated he would apply for a grant from NIH, which his former colleague Jay Bhattacharya leads. Tr. 313.[17]

In short, there has not been any peer-review of Dr. Steinman's theory that Prevnar can cause GBS. Thus, the Daubert factor of peer review does not support the reliability of Dr. Steinman's opinion that Prevnar can cause GBS.

C. **Potential rate of error**

As to the potential rate of error, there is very little evidence. One small aspect of Dr. Steinman's overall theory that could be seen as having an error rate concerns the use of computerized databases to identify immunologically relevant mimics. See section V.B.1, above.

Some of the foundational work on molecular mimicry was done by Kai Wucherpfennig. Tr. 140-41. For one article, Wucherpfennig and his colleague Jack L. Strominger, another "giant in the field" (Tr. 278), used a computer database to search for amino acid sequences similar to the amino acid sequences for myelin basic protein. Wucherpfennig & Strominger at 607. They found 129 possible mimics in various infectious agents such as the human papillomavirus and herpes simplex virus. Id. at 696, 698. Wucherpfennig and Strominger tested to see whether these potential mimics actually reacted to myelin basic protein. Of the 129 potential mimics, 7 viral peptides and 1 bacterial peptide (or approximately 6%) stimulated T cells. Id. at 696.

Although Wucherpfennig & Strominger could be viewed as providing some math quantifying an error rate, it is important not to overstate its significance. Wucherpfennig & Strominger is only one study. The researchers also used a database different from BLAST. See

[17] Whether NIH would fund Dr. Steinman's research into Prevnar and GBS will be interesting to consider in any future Prevnar-GBS cases. Dr. Whitton suggested that this grant application would not be received well. Tr. 509-10.

Wucherpfennig & Strominger at 697 (identifying the databases as PIR and SwissProt). Therefore, the study does not provide conclusive evidence about the likelihood of error in a search for immunologically relevant homologs using BLAST. If Wucherpfennig & Strominger is worth anything, it would weigh against a finding that the protein theory based upon BLAST searches is reliable. If Wucherpfennig & Strominger is worth nothing, then the Daubert factor of error rate is neutral.

D. General Acceptance

The final Daubert factor is "general acceptance." Although Capizzano states special masters cannot require "general acceptance in the scientific and medical communities," 440 F.3d at 1325, Terran endorses a special master's consideration of this factor.

Whether Dr. Steinman's theory is generally accepted depends at least in part on the level of generality. At a high level of abstraction, molecular mimicry as a theory is recognized in the medical community. Dr. Whitton emphasized that he did not deny the possibility of molecular mimicry; Dr. Whitton stated that molecular mimicry might occur with viruses but not with vaccines. Tr. 451-52.

This high level of abstraction, in turn contributes, in part, to some special masters accepting that Prevnar can cause GBS. See, e.g., Mullins, 2024 WL 4045424 at *42-45; Simeneta v. Sec'y of Health & Hum. Servs., No. 18-859V, 2024 WL 4881411, at *30-33 (Fed. Cl. Spec. Mstr. Oct. 31, 2024). However, "a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case." Broekelschen v. Sec'y of Health and Hum. Servs., 618 F.3d 1339, 1345 (Fed. Cir. 2010).

In the context of reviewing a special master's assessment of molecular mimicry, the Federal Circuit held that "the special master found that '[m]olecular mimicry is a well-regarded theory in some contexts,' . . .but correctly required additional evidence showing that molecular mimicry can cause the influenza vaccine to significantly aggravate multiple sclerosis." W.C., 704 F.3d at 1360 (citing Broekelschen, 618 F.3d at 1345 (holding "a petitioner must provide a reputable medical or scientific explanation that pertains specifically to the petitioner's case").

In the context of the more specific issue of whether Prevnar can cause GBS, there is not persuasive evidence that the medical community accepts this theory. As noted above, Dr. Steinman has not submitted his views to a journal for publication. Thus, there is a general absence of literature.[18] The epidemiological studies have investigated the possibility and have not detected an increased incidence. Articles about GBS list multiple potential causes, including some vaccines, but do not list either *Streptococcus pneumoniae* or Prevnar. See, e.g., van Doom at 940-41; van den Berg at 470-71. Mr. Romine has not presented any persuasive evidence that the medical community accepts Prevnar as causing GBS. Thus, this factor weighs against finding the theory reliable.

[18] The record in this case contains one case report. However, Mr. Romine did not include it in any briefing. Even special masters who have credited the theory have questioned the usefulness of this article.

E. Falsification

Another factor that may contribute to assessing the reliability of an expert's theory is whether the theory is falsifiable. Daubert, 509 U.S. at 593. Dr. Steinman did not provide a clear answer as to whether, in his view, the theory of molecular mimicry is falsifiable. Tr. 227, 239. In Dr. Whitton's view, the theory of molecular mimicry would be very difficult to falsify. Tr. 513.

A challenge to falsifying molecular mimicry is that relatively few details are known about how autoimmune diseases develop. Even after more is learned about the pathogenesis of some autoimmune diseases or the pathogenesis of some specific cases of specific autoimmune diseases, there is likely to remain some residual area of indeterminacy. This remnant creates a space that molecular mimicry could occupy. In other words, until the pathogenesis of GBS is established for all cases, there remains a chance that molecular mimicry would explain a minority of cases.

The lack of falsifiability can contribute to a finding that an expert's opinion is not reliable. See In re: Paraquat Prod. Liability Lit., 730 F.Supp.3d 793, 841 (N.D. Ill. 2024) (granting motion to exclude expert's opinion that an exposure to a herbicide caused Parkinson's disease), appeal docketed sub nom. (among others), Coward v. Syngenta AG, No. 24-1967 (7th Cir. May 16, 2024).

F. Summary on Daubert

Proponents of an expert's opinion are not required to demonstrate that the opinion passes all the Daubert criteria. The Daubert criteria should be employed flexibly.

But, for Dr. Steinman's theory that Prevnar can cause GBS, it is difficult to see how the theory passes any of the Daubert factors. At best, some criteria are either neutral or not applicable. But for other criteria, the theory does not measure up.

The evidence does not support a finding that the theory is either reliable or persuasive. Its lack of reliability means Mr. Romine cannot prevail. See Vaccine Rule 8(b)(1) (directing special masters to consider all "reliable" evidence); see also MLC Intellectual Property, LLC v. Micron Technology, Inc., 10 F.4th 1358, 1373 (Fed. Cir. 2021) (affirming a Daubert order excluding an expert's opinion regarding reasonable royalty rate for failure to apportion); MicroStrategy Inc. v. Business Objects, S.A., 429 F.3d 1344, 1355-56 (Fed. Cir. 2006) (stating a "district court has the responsibility to exclude an expert opinion that overlooks factors that render the testimony unreliable and/or speculative" and ruling that the district court's exclusion of the expert reports was not an abuse of discretion).[19]

[19] Although MLC Intellectual Property and MicroStrategy are set in a posture in which a district court excluded an expert's opinion, Dr. Steinman's opinion has not been excluded. It has been considered fully.

VII. Additional Comments

Mr. Romine, like any petitioner, is required to demonstrate his claim with preponderant, not certain, evidence. Even under the preponderant standard, there are many gaps in his evidence.

General	How likely is Prevnar to increase the incidence of GBS when four epidemiologic studies, of which the smallest involved 1.8 million people, have not detected any increase in the incidence of GBS among people receiving pneumococcal vaccines?
General	How likely is Prevnar to cause GBS when the underlying infection is not associated with GBS?
Protein Theory	How likely is the method of using BLAST to search for immunologically relevant homologs to produce reliable results when Dr. Steinman appears to be the only person using this technique?
Protein Theory	How reliable is the assertion that linear sequence homology between CRM-197 and PMP22 can cause a cross-reaction when this hypothesis has not been tested?
Phosphoglycerol Theory	How reliable is the assertion that the immune system attacks phospholipids to cause GBS when review articles about GBS do not mention this idea?
Phosphoglycerol Theory	How reliable is the assertion that anti-phospholipid antibodies contribute to the pathogenesis of GBS when people who suffer from anti-phospholipid syndromes do not experience a higher incidence of GBS?

VIII. Comparisons of Results in Other Cases

The resolution of Mr. Romine's claim that Prevnar caused him to suffer GBS is based upon an analysis of the evidence and arguments presented in this case. While special masters have found the evidence does not preponderate in favor of finding that Prevnar can cause GBS in some persuasive decisions, in other cases, petitioners presenting the same claim have prevailed. The differences in outcomes are not easily explained by a difference in evidence as Dr. Steinman and Dr. Whitton frequently (but not exclusively) have been paired in these cases. But see Datte v. Sec'y of Health & Hum. Servs., No. 18-2V, 2025 WL 1565894, at * 18 n.12 (Fed. Cl. Spec. Mstr. May 9, 2025) ("it is still important to look closely at respondent's expert presentation in each case"). Instead, this disparity in outcome may be attributable to how special masters have evaluated the evidence. See Jaye, 2024 WL 3691413, at *17 n.20 (suggesting that the acceptance of a petitioner's evidence amounts to "an exercising in lowering the preponderant standard") (emphasis in original). This "split" in outcome is not necessarily bad. See Lampe v. Sec'y of Health & Hum. Servs., 219 F.3d 1357, 1368 (Fed. Cir. 2000) (recognizing that special masters may weigh evidence differently). Strictly from a legal perspective, different outcomes are permissible because special masters do not bind each other. Boatmon v. Sec'y of Health &

Hum. Servs., 941 F.3d 1351, 1358 (Fed. Cir. 2019); but see Gamboa-Avila, 166 F.4th at 1323-24 (Fed. Cir. 2026) (expressing concern about differences in outcome).

Nevertheless, it is worthwhile to set forth the points where the present decision parts company with other rulings finding in favor of compensation. The discussion below roughly follows the organization of the sections above.

A. Epidemiology

Section III.A., above, evaluated studies by Baxter, Haber, Tseng, and Yoon. It concluded that although the studies are not perfect, they collectively weigh against the proposition that a pneumococcal vaccine causes GBS.

Some cases finding that Prevnar can cause GBS, by contrast, appear to have given the epidemiology studies less weight mainly because petitioners are not required to present epidemiology to prevail. Datte, 2025 WL 1565894, at *18 (noting the special master had considered three of the four epidemiological studies and finding that they do not "cast significant doubt on the viability of Dr. Steinman's theory"); Koller v. Sec'y of Health & Hum. Servs., No. 16-439V, 2021 WL 5027947, at *22 (Fed. Cl. Spec. Mstr. Oct. 8, 2021).

This statement of law---that petitioners are not required to support their claims with epidemiology---is of course correct. Althen, 418 F.3d at 1279-81. But, when epidemiology is available, a special master may consider that form of evidence. Lampe, 219 F.3d at 1365 ("An epidemiological study may be probative medical evidence relevant to a causation determination"); McCollum v. Sec'y of Health and Hum. Servs., 760 Fed. App'x 1003, 1008 (Fed. Cir. 2019) (special master's consideration of an epidemiologic study did not raise petitioner's burden of proof). In this case, the epidemiology includes four studies of which the *smallest* involved 1.8 million people. It would seem that if a pneumococcal vaccine were increasing the incidence of GBS, one of these studies would have detected an uptick. Opinions such as Datte and Koller have not persuasively explained why the epidemiologic studies do not undermine the claim that pneumococcal vaccines can cause GBS.

Section IV.B. above also discussed whether an infection with *Streptococcus pneumoniae* is associated with GBS. Section IV.B. credited the opinion from Dr. Whitton that the wild-type infection is not associated with GBS and relied in part on difference between Gram positive bacteria and Gram negative bacteria.

In this regard, the undersigned respectfully disagrees with the portion of Byrd v. Sec'y of Health & Hum. Servs., No. 20-1476V, 2024 WL 4003061, at *30 (Fed. Cl. Spec. Mstr. July 8, 2024), that states that "*potential* mimicry between components of the gram-positive [*Streptococcus pneumoniae*] bacteria . . . has not been ruled in or out" (emphasis added). This reasoning seems to place the burden of disproving the reliability of the asserted theory on the Secretary, when actually the burden of proving (ruling in) the reliability of the theory rests with the petitioner.

As one special master has noted, "it is generally accepted that a number of different infectious antigens can cause GBS, including unspecified upper respiratory infections," and "this background information has partly informed the special masters' analysis of a petitioner's theory of causation with respect to GBS" in other cases. Bartoszek v. Sec'y of Health & Hum. Servs.,

No. 17-1254V, 2024 WL 4263604 at *18 (Fed. Cl. Spec. Mstr. Aug. 7, 2024). The undersigned, though mindful of this context, affords less weight to the general acceptance of multiple antigens as pathogenic. Mr. Romine's case rests not upon these other multiple antigens, but rather, a specific vaccine against pneumonia caused by the *Streptococcus pneumoniae* bacteria. Petitioners are responsible for presenting a theory that is specific to their case. Broekelschen, 618 F.3d at 1345. Furthermore, Mr. Romine did not persuasively analogize *Streptococcus pneumoniae* to any of these other "different infectious antigens."

Thus, the undersigned finds more persuasive the reasoning in cases such as Gamboa-Avila, 166 F.4th at 1322, Trollinger v. Sec'y of Health & Hum. Servs., No. 16-473V, 2023 WL 2521912, at *28 (Fed. Cl. Feb. 17, 2023), mot. for rev. denied, 167 Fed. Cl. 127 (2023), that found the absence of an association between wild bacteria and GBS weakens the claim that the vaccine against the wild bacteria causes GBS.

B. Molecular Mimicry Generally

The present decision cites many cases from appellate authorities that have examined whether a special master's treatment of molecular mimicry was legally sound. Those cases have generally (but not universally) held that the special masters do not err when requiring some persuasive and reliable evidence to support molecular mimicry as a proposed mechanism for an autoimmune disease process.

This reliance on appellate authorities regarding molecular mimicry distinguishes the present case from some cases finding that petitioners prevail on a theory that Prevnar can cause GBS. Some cases in which petitioners prevailed have cited rulings from special masters about the sufficiency of molecular mimicry that have not always engaged with the appellate authorities cited in section V.A. of the present decision. See, e.g., Anderson, 2024 WL 557052, at *31.

C. Protein-Based Theory

The heart of the differences in outcomes for these cases concerns how special masters have evaluated Dr. Steinman's theory that a protein found in Prevnar is sufficiently similar to a human protein that a cross-reaction can lead to GBS. Within this broad topic, there are several places where the analysis differs.

A fundamental point is whether a BLAST search with an E-value of 10 is a reliable methodology. It appears that most opinions start with an assumption that Dr. Steinman is following a reliable methodology. For example, Simeneta, 2024 WL 4881411, at *15 and *25, noted the conflict between Dr. Steinman's opinion and the Secretary's expert's opinion about E-values but did not determine how the evidence on this point preponderated. The same is true for Anderson, in the sense that the special master summarized Dr. Whitton's opinion but did not specifically address whether the significance of E-values diminished the reliability of Dr. Steinman's use of BLAST searches in general. Instead, Anderson stated that many of Dr. Whitton's criticisms "relate to either collateral issues or identify issues that are not material." 2024 WL 557052, at *31.

In the undersigned's view, the way BLAST searches are used---or more precisely, not used in the world outside of litigation---is one factor to consider in determining the reliability of Dr. Steinman's methodology. Contrary to Mr. Romine's arguments (see Pet'r's Post-Hearing Br.

at 34-35), evaluating the reliability of an expert's methodology does not raise a petitioner's burden on proof. Here, the evidence preponderates in favor of finding that Mr. Romine has not established the reliability of this methodology.

Assuming that this methodology is reliable, the next part is to consider the inputs into the BLAST program. As to the portion from the vaccine (CRM-197), special masters have disagreed at times. The present decision finds that CRM-197, which is in Prevnar, is not sufficiently similar to the diphtheria toxin, which is what Dr. Steinman used. This result---finding that there is not persuasive evidence of immunologic similarity between diphtheria toxin and CRM-197---is consistent with one opinion from a special master that addressed this issue. Morrison v. Sec'y of Health & Hum. Servs., No. 18-386V, 2024 WL 3738934, at *21-22 (Fed. Cl. Spec. Mstr. July 18, 2024). By way of contrast, another opinion found that CRM-197 is "immunologically indistinguishable" from diphtheria toxin. Musick v. Sec'y of Health & Hum. Servs., No. 18-451V, 2025 WL 2452232, at *15 (Fed. Cl. Spec. Mstr. July 8, 2025). A third category of cases is one in which special masters have recognized the competing opinions but have not stated how the evidence on this issue preponderated. See, e.g., Simeneta, 2024 WL 4881411, at *25 (summarizing Dr. Whitton's report that Raju "did not reach any conclusions about antibody responses to the diphtheria toxin in [CRM-197]").

Finally, in discussing the Gautam papers, the present decision attempts to distinguish homology from immunogenicity. As explained in Sparrow, 2024 WL 1599165, at * 24, a finding that two proteins share homology at a level of 5 out of 12 amino acids is not the same as finding that the two proteins likely cross-react. But, the rulings finding in favor of a Prevnar-GBS connection have not engaged with this additional step.

These differences help explain why this decision finds that Dr. Steinman's protein-based theory is not persuasive. The other theory is one based on polysaccharides.

D. Polysaccharide-Based Theory

In Mr. Romine's case, Dr. Whitton appears to have raised a new criticism of Dr. Steinman's theory involving antibodies against phospholipids—that people who have anti-phospholipid antibodies appear not to have any increased incidence of GBS. See section V.C.2 above. As this was a new point, special masters have not had the occasion to weigh the value of Dr. Whitton's observation.

Whether any anti-phospholipid antibodies are associated with GBS is another place of departure. Opinions crediting Dr. Steinman's theory have looked upon Dr. Steinman's reliance on Nakos and Ho favorably. However, this decision declines to extend the observations from the Nakos and Ho articles to the present case in part because the articles were written more than 10 years ago and appear not to have achieved a general acceptance in the medical field.

Within the polysaccharide-based theory, a final place where special masters have weighed the evidence differently concerns the Bryson antibodies. See section V.C.5 above. The present decision finds that Dr. Whitton has persuasively questioned how Dr. Steinman can explain how antibodies that can recognize an epitope in the context of a sugar (L rhamose) can also recognize the same epitope in the context of a lipid.

E. Daubert

The preceding paragraphs have attempted to highlight places in the analysis where special masters have differed. An earlier section (section VI) of this decision added a new prism through which to evaluate the evidence---the test for the reliability of an expert's opinion as set out in Daubert. By Daubert's metrics of reliability, Mr. Romine has failed to establish the reliability of Dr. Steinman's opinion. This method of analysis fits within Federal Circuit precedent. See Cedillo, 617 F.3d at 1339 ("By inclusion of the terms 'relevant and reliable,' Vaccine Rule 8(b)(1) necessarily contemplates an inquiry into the soundness of scientific evidence to be considered by special masters"). By way of contrast, other special masters have not shown how Dr. Steinman's opinion passes through any of the Daubert gates.

F. Summary on Comparisons to Other Cases

Within the bounds of controlling law reflected in precedent from the Federal Circuit and the Vaccines Rules, special masters evaluate evidence. These assessments at times may differ and this variance is not necessarily problematic as "Congress desired the special masters to have very wide discretion with respect to the evidence they would consider and the weight to be assigned that evidence." Whitecotton v. Sec'y of Health & Hum. Servs., 81 F.3d 1099, 1108 (Fed. Cir. 1996). To the extent that similarity in outcomes is desirable, the undersigned has attempted to explain where the analysis differs. If additional appellate litigation were to occur, then a reviewing authority may provide greater guidance on the various points of departure. Notably, none of the previous rulings finding a causal connection between Prevnar and GBS have been the subject of a motion for review. This lack of appellate review contrasts with some of the decisions finding the other way. In cases in which petitioners have challenged a special master's decision finding that preponderant evidence did not support a finding of entitlement, petitioners have achieved no appellate success.

IX. Conclusion

Mr. Romine received a vaccine to protect him from becoming infected with *Streptococcus pneumoniae* and developed GBS within about two weeks. Mr. Romine alleges that the vaccine caused the GBS. Although Mr. Romine has presented some evidence to support his claim, the evidence does not preponderate in his favor. He has not presented a reliable theory to explain how Prevnar can cause GBS. Accordingly, he is not entitled to compensation.

The Clerk's Office is instructed to enter judgment in accord with this decision unless a motion for review is filed. Information about filing a motion for review, including the deadline, can be found in the Vaccine Rules, which are available on the website for the Court of Federal Claims.

IT IS SO ORDERED.

s/Christian J. Moran
Christian J. Moran
Special Master

Appendix: Articles Cited[1]

1. Elisar Barbar et al., Binding of Phenylphosphocholine-Carrier Conjugates to the Combining Site of Antibodies Maintains a Conformation of the Hapten, 35 BIOCHEMISTRY 2958 (1996); filed as Exhibit 73.

2. Roger Baxter et al., Lack of Association of Guillain-Barré Syndrome With Vaccinations, 57 CLIN. INFECT. DIS. 197 (2013); filed as Exhibits A-5 and C-6.

3. Michael Bröker et al., Biochemical and biological characteristics of cross-reacting material 197 (CRM197), a non-toxic mutant of diphtheria toxin: Use as a conjugation protein in vaccines and other potential clinical applications, 39 BIOLOGICALS 195 (2011); filed as Exhibit 43 and D-5.

4. Steve Bryson et al., Structures of Preferred Human IgV Genes-Based Protective Antibodies Identify How Conserved Residues Contact Diverse Antigens and Assign Source of Specificity to CDR3 Loop Variation, 96 J. IMMUNOL. 4723 (2016) filed as Exhibit 40; and Supplemental Material, filed as Exhibit 42.

5. Janoi Chang et al., Relevance of O-acetyl and phosphoglycerol groups for the antigenicity of Streptococcus pneumoniae serotype 18C capsular polysaccharide, 30 VACCINE 7090 (2012); filed as Exhibit 36.

6. Anand M. Gautam et al., A Polyalanine Peptide with only Five Native Myelin Basic Protein Residues Induces Autoimmune Encephalomyelitis,176 J EXP. MED. 605 (1992); filed as Exhibit 46.

7. Anand M. Gautam et al., Minimum structural requirements for peptide presentation by major histocompatibility complex class II molecules: Implications in induction of autoimmunity, 91 PROC. NATL. ACAD. SCI. U.S.A. 767 (1994); filed as Exhibit 47.

[1] Although this appendix provides bibliographic information for articles cited in the decision, all articles have been considered.

8. Anand M. Gautam et al., A viral peptide with limited homology to a self peptide can induce clinical signs of experimental autoimmune encephalomyelitis, 161 J. IMMUNOL. 60 (1998); filed as Exhibit 48.

9. Penina Haber et al., Post-licensure surveillance of 13-valent pneumococcal conjugate vaccine (PCV13) in adults aged ⩾19 years old in the United States, Vaccine Adverse Event Reporting System (VAERS), June 1, 2012-December 31, 2015, 34 VACCINE 6330 (2016); filed as Exhibits 52, A-7, and C-7.

10. Peggy P. Ho et al., Identification of Naturally Occurring Fatty Acids of the Myelin Sheath That Resolve Neuroinflammation, 4 SCI. TRANSL. MED. 137 (2012); filed as Exhibit 38.

11. Richard A. C. Hughes et al., Guillain-Barré syndrome in the 100 years since its description by Guillain, Barré, and Strohl, 139 BRAIN 3041 (2016); filed as Exhibit C-26.

12. Anil K. Jasti et al., Guillain-Barré syndrome: causes, immunopathogenic mechanisms and treatment, 12 EXPERT REV. CLIN. IMMUNOL. 1175 (2016); filed as Exhibit C-19.

13. Cheryl A. Kerfeld and Kathleen M. Scott, Using BLAST to teach "E-value-tionary" concepts, 9 PLOS BIOL. e1001014 (2011); filed as Exhibit C-29.

14. Jason S. Knight et al., Antiphospholipid syndrome: advances in diagnosis, pathogenesis, and management, 380 BMJ e069717 (2023); filed as Exhibit D-3.

15. Yumako Miura et al., Contactin 1 IgG4 associates to chronic inflammatory demyelinating polyneuropathy with sensory ataxia, 138 BRAIN 1484 (2015); filed as Exhibit 45.

16. G. Nakos et al., Anti-phospholipid antibodies in serum from patients with Guillain-Barré syndrome, 31 INTENSIVE CARE MED. 1401 (2005); filed as Exhibit 35.

17. Tobias V. Lanz et al., Clonally expanded B cells in multiple sclerosis bind EBV EBNA1 and GlialCAM, 603 NATURE 321 (2022); filed as Exhibit 62.

18. R. Raju et al., Epitopes for human CD4+ cells on diphtheria toxin: structural features of sequence segments forming epitopes recognized by most subjects, 25 EUR. J. IMMUNOL. 3207 (1995); filed as Exhibit 51.

19. Robert Root-Bernstein, Rethinking Molecular Mimicry in Rheumatic Heart Disease and Autoimmune Myocarditis: Laminin, Collagen IV, CAR, and B1AR as Initial Targets of Disease, 2 FRONT. PEDIATR. 1 (2014); filed as Exhibit 49.

20. N. R. Rose and I. R. Mackay, Molecular mimicry: a critical look at exemplary instances in human diseases, 57 CELL MOL. LIFE SCI. 542 (2000); filed as Exhibit C-22.

21. Andre Silvanovich et al., The value of short amino acid sequence matches for prediction of protein allergenicity, 90 TOXICOL. SCI. 252 (2006); filed as Exhibit 50.

22. Andre Silvanovich et al., The use of E-scores to determine the quality of protein alignments, 54 REGUL. TOXICOL. PHARMACOL. S26 (2009); filed as Exhibit C-31.

23. L. Súkeníková et al., Autoreactive T cells target peripheral nerves in Guillain-Barré syndrome, 626 NATURE 160 (2004); filed as Exhibit 59.

24. Hung Fu Tseng et al., Pneumococcal Conjugate Vaccine Safety in Elderly Adults, 5 OPEN FORUM INFECT. DIS. 1 (2018); filed as Exhibits A-10 and C-8.

25. Biana van den Berg et al., Guillain–Barré syndrome: pathogenesis, diagnosis, treatment and prognosis, 10 NAT. REV. NEUROL. 469 (2014); filed as Exhibit C-15.

26. Pieter A. van Doom et al., Clinical features, pathogenesis, and treatment of Guillain-Barré syndrome, 7 LANCET. NEUROL. 939 (2008); filed as Exhibit C-9.

27. Michel Varrin-Doyer et al., Aquaporin 4-specific T cells in neuromyelitis optica exhibit a Th17 bias and recognize Clostridium ABC transporter, 72 ANN. NEUROL. 53 (2012); filed as Exhibit 1002.

28. David Wheeler and Medha Bhagwat, BLAST QuickStart: example-driven web-based BLAST tutorial, 395 METHODS MOL. BIOL. 149 (2007); filed as Exhibit 68.

29. K. W. Wucherpfennig and J. L. Strominger, Molecular mimicry in T cell-mediated autoimmunity: viral peptides activate human T cell clones specific for myelin basic protein, 80 CELL 695 (1995); filed as Exhibit 1003.

30. Dongwon Yoon et al., Cardiovascular, Neurological, and Immunological Adverse Events and the 23-Valent Pneumococcal Polysaccharide Vaccine, 7 JAMA NETW. OPEN e2352597 (2024); filed as Exhibit D-1.

31. Nobuhiro Yuki and Hans-Peter Hartung, Guillain-Barré Syndrome, 366 N. ENGL. J. MED. 2294 (2012); filed as Exhibit 21.