OFFICE OF SPECIAL MASTERS

Nos. 00-759V; 01-221V; 99-609V;
99-591V; 99-628V

(Filed: August 5, 2003)

CAPIZZANO, ASHBY, ANALLA, RYMAN, and MANVILLE,	*	
Petitioners,	*	**TO BE PUBLISHED**
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

DECISION[1]

On June 11, 2003 and June 12, 2003 the undersigned conducted a hearing to address the general issue of whether the Hepatitis B vaccine can in fact cause rheumatoid arthritis. Rheumatoid arthritis is not an injury listed on the Vaccine Injury Table and thus does not benefit from the Act's presumed causation. 42 U.S.C. §300aa-14(a). Petitioners were represented by Mr. Ronald Homer and Ms. Sylvia Chin-Caplan. Respondent was represented by Ms. Catharine Reeves, Ms. Ann Donohue and Ms. Melonie McCall. The undersigned Chief Special Master also heard evidence in the five above captioned cases which argue that the Hepatitis B vaccine caused petitioners' rheumatoid arthritis.

On June 20, 2003 and on July 16, 2003 the undersigned issued Orders that directed the parties to file various documents introduced and discussed during the hearing and to file post-

[1]This Decision was originally filed on July 25, 2003. It was vacated and reissued on August 5, 2003 with several clerical corrections instituted by the court.

hearing briefs on the court's criteria[2] governing actual causation claims as discussed in Stevens v. Secretary of HHS, No. 99-594V, 2001 WL 387418 (Fed. Cl. Spec. Mstr. Mar. 30, 2001) as it relates to the issue of general causation. In the June 20, 2003 Order, the court also stated that it had made tentative findings with regard to the first prong of the Stevens test. The court found that

> [T]**entatively**, the undersigned finds the issue of medical plausibility (Prong 1) moot. That is because respondent's exhibit L, "Rheumatic Disorders Developed After Hepatitis B Vaccination" related four "rechallenge"[3] cases to the Hepatitis B vaccine. R. Ex. L (J.F. Maillefert, J. Sibilia et al., Rheumatic Disorders Developed After Hepatitis B Vaccination, Rheumatology, 1999:38:978-983 at 979). The Institute of Medicine (IOM) has stated that rechallenge is proof of causation. See Christopher P. Howson et al., Institute of Medicine, Adverse Effects of Pertussis and Rubella Vaccines, 48, 53 (1991). The IOM has also stated that where causation is proven, biologic plausibility is a given. Kathleen R. Stratton et al., Institute of Medicine, Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality, 21 (1994). Therefore, if the court affirms this tentative determination, petitioners will have met Prong 1 of Stevens and any rechallenge rheumatoid arthritis case, if proven successfully to be a rechallenge case, will be compensated.

This decision affirms the court's tentative findings on Prong 1 and provides the court's analysis and rationale for so doing.

Causation in Fact - Basic Principles

Causation in Vaccine Act cases can be established in one of two ways: either through the statutorily prescribed presumption of causation or by proving causation-in-fact. Petitioners must prove one or the other in order to recover under the Act. According to §13(a)(1)(A), claimants must prove their case by a preponderance of the evidence. This requires that the trier of fact "believe that the existence of a fact is more probable than its nonexistence before [the special master] may find in favor of the party who has the burden to persuade the [special master] of the fact's existence." Hodges v. Secretary of HHS, 9 F.3d 958, 963 (Fed. Cir. 1993) (Newman, J.,

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[2]Petitioner must provide (1) proof of medical plausibility, (2) proof of confirmation of medical plausibility from the medical community and literature, (3) proof of an injury recognized by the medical plausibility evidence and literature, (4) proof of a medically acceptable temporal relationship between the vaccination and the onset of the alleged injury, and (5) proof of the elimination of other causes. Stevens 2001 WL 387418, at *23-*26 as clarified in Watson v. Secretary of HHS, No. 96-639V, 2001 WL 1682537, at *8 (Fed. Cl. Spec. Mstr. Dec. 18, 2001), White v. Secretary of HHS, No. 98-426V, 2002 WL 1488764, at *5 (Fed. Cl. Spec. Mstr. May 10, 2002) and Althen v. Secretary of HHS, No. 00-170V, 2003 WL 21439669, at *9-*12 (Fed. Cl. Spec. Mstr. June 3, 2003) (Mot. For Review Pending).

[3]A rechallenge case is one where adverse symptoms are noted after a dose of the vaccine, an additional dose of the vaccine is given, and the symptoms worsen.

dissenting) (citing Concrete Pipe and Products of California, Inc. v. Construction Laborers Pension Trust for Southern California, 508 U.S. 602 (1993), quoting In re Winship, 397 U.S. 358, 371-72 (1970) (Harlan, J., concurring)).

For presumptive causation claims, the Vaccine Injury Table lists certain injuries and conditions which, if found to occur within a prescribed time period, create a rebuttable presumption that the vaccine caused the injury or condition. 42 U.S.C. §300aa-14(a). Rheumatoid arthritis is not an injury listed on the Vaccine Injury Table and thus does not benefit from the Act's presumed causation. Id.

To demonstrate entitlement to compensation in an off-Table case, a petitioner must affirmatively demonstrate by a preponderance of the evidence that the vaccination in question more likely than not caused the injury alleged. See, e.g., Bunting v. Secretary of HHS, 931 F.2d 867, 872 (Fed. Cir. 1991); Hines v. Secretary of HHS, 940 F.2d 1518, 1525 (Fed. Cir. 1991); Grant v. Secretary of HHS, 956 F.2d 1144, 1146, 1148 (Fed. Cir. 1992). See also §§11(c)(1)(C)(ii)(I) and (II). To meet this preponderance of the evidence standard, "[a petitioner must] show a medical theory causally connecting the vaccination and the injury." Grant, 956 F.2d at 1148 (citations omitted); Shyface v. Secretary of HHS, 165 F.3d 1344, 1353 (Fed. Cir. 1999). A persuasive medical theory is shown by "proof of a logical sequence of cause and effect showing that the vaccination was the reason for the injury." Hines, 940 F.2d at 1525; Grant, 956 F.2d at 1148; Jay v. Secretary of HHS, 998 F.2d 979, 984 (Fed. Cir. 1993); Hodges, 9 F.3d at 961; Knudsen v. Secretary of HHS, 35 F.3d 543, 548 (Fed. Cir. 1994). Furthermore, the logical sequence of cause and effect must be supported by "[a] reputable medical or scientific explanation" which is "evidence in the form of scientific studies or expert medical testimony." Grant, 956 F.2d at 1148; Jay, 998 F.2d at 984; Hodges, 9 F.3d at 960.[4] See also H.R. Rep. No.

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[4]The general acceptance of a theory within the scientific community can have a bearing on the question of assessing reliability while a theory that has attracted only minimal support may be viewed with skepticism. Daubert v. Merrell Dow Pharmaceuticals, Inc., 509 U.S. 579, 594 (1993). Although the Federal Rules of Evidence do not apply in Program proceedings, the United States Court of Federal Claims has held that "Daubert is useful in providing a framework for evaluating the reliability of scientific evidence." Terran v. Secretary of HHS, 41 Fed. Cl. 330, 336 (1998), aff'd, 195 F.3d 1302, 1316 (Fed. Cir. 1999). In Daubert, the Supreme Court noted that scientific knowledge "connotes more than subjective belief or unsupported speculation." Daubert, 509 U.S. at 590. Rather, some application of the scientific method must have been employed to validate the expert's opinion. Id. Factors relevant to that determination may include, but are not limited to:

> whether the theory or technique employed by the expert is generally accepted in the scientific community; whether it's been subjected to peer review and publication; whether it can be and has been tested; and whether the known potential rate of error is acceptable.

Daubert v. Merrell Dow Pharmaceuticals, Inc., 43 F.3d 1311, 1316 (9th Cir. 1995) (Kozinski, J.), on remand from 509 U.S. 579 (1993); see also Daubert, 509 U.S. at 592-94.

99-908, Pt. 1, at 15 (1986), reprinted in 1986 U.S.C.C.A.N 6344. While petitioner need not show that the vaccine was the sole or even predominant cause of the injury, petitioner bears the burden of establishing "that the vaccine was not only a but-for cause of the injury but also a substantial factor in bringing about the injury." Shyface, 165 F.3d at 1352-53. Petitioners do not meet their affirmative obligation to show actual causation by simply demonstrating an injury which bears similarity to a Table injury or to the Table time periods. Grant, 956 F.2d at 1148. See also H.R. Rep. No. 99-908, Pt. 1, at 15 (1986), reprinted in 1986 U.S.C.C.A.N 6344. Nor do petitioners satisfy this burden by merely showing a proximate temporal association between the vaccination and the injury. Grant, 956 F.2d at 1148 (quoting Hasler v. United States, 718 F.2d 202, 205 (6th Cir. 1983), cert. denied, 469 U.S. 817 (1984) (stating "inoculation is not the cause of every event that occurs within the ten day period [following it]. . . . Without more, this proximate temporal relationship will not support a finding of causation.")); Hodges, 9 F.3d at 960. Finally, a petitioner does not demonstrate actual causation by solely eliminating other potential causes of the injury. Grant, 956 F.2d at 1149-50; Hodges, 9 F.3d at 960.

Discussion

The court addresses petitioners' Table and off-Table claims in light of these governing principles. This court has adopted an appropriate analytical framework for resolving off-Table cases, see Stevens, 2001 WL 387418.

Stevens determined that epidemiology, while not a prerequisite to compensation under the Program, is the most desirable and probative direct evidence of causation-in-fact.[5] See Stevens, 2001 WL 387418, at *13. By presenting a reliable and relevant epidemiologic study indicating a relative risk greater than two and establishing that the vaccinee falls within the parameters of the group associated with the statistically significant relative risk, petitioners can successfully prove causation in a particular case more probable than not (assuming, of course, respondent fails to prove a factor unrelated). Id.

In the absence of such controlling epidemiological evidence, petitioners may prove causation-in-fact with circumstantial evidence by satisfying the undersigned's five prong causation standard. Stevens, 2001 WL 387418. This five-prong standard requires that petitioner provide (1) proof of medical plausibility that the vaccine received can cause the injury alleged, (2) proof of confirmation of medical plausibility from the medical community and literature, (3) proof of an injury recognized by the medical plausibility evidence and literature, (4) proof of a medically acceptable temporal relationship between the vaccination and the onset of the alleged injury, and (5) proof of the elimination of other causes for the alleged injury. Id. at *23-*26. See also Althen, 2003 WL 21439669, at *9-*12; White, 2002 WL 1488764, at *11-*17; Watson, 2001 WL 1682537, at *19-*28.

[5]Other desirable evidence includes "dispositive clinical or pathological markers" or "vaccine footprints" evidencing a direct causal relationship between the alleged injury and the vaccine received. Stevens, 2001 WL 387418, at *14.

Prong One is satisfied by "proffering a medically or scientifically supported mechanism by which a vaccine component could cause the injury alleged." Stevens, 2001 WL 387418, at *23, *24. **Prong Two** requires that petitioner submit confirmation from peer-reviewed literature or the relevant medical community that it is "thinking about" or "seeing and reporting a suspected or potential association" between the alleged injury and the vaccine received. Id. at *24; Althen, 2003 WL 214396669, at *12-*14. Relating the evidence to the vaccine received ensures that petitioner's theoretically plausible mechanistic theory advances to what Daubert requires – *objective* confirmation within the relevant medical community for the injury and vaccine at issue. Stevens, 2001 WL 387418, at *24; see also Althen, 2003 WL 21439669, at *12 (n. 29). **Prong Three** is straightforward and requires that petitioner "demonstrate that the vaccinee *in fact* suffered the injury which is associated with the vaccine under the preceding prongs" – petitioner will typically look to the medical records for this evidence. Stevens, 2001 WL 387418, at *25 (italics in original). Under **Prong Four**, petitioners must satisfactorily prove that the onset of the injury alleged in Prong Three occurred within a medically appropriate time frame according to the scientific or medical evidence presented in Prongs One and Two. Id. Finally, **Prong Five** commands that petitioners affirmatively demonstrate that the treating physicians employed reasonable efforts to consider and rule out known, apparent alternate causes – a critical tool in this proof is the physician's differential diagnosis. Id. at *26; White, 2002 WL 1488764, at *12, *17; Watson, 2001 WL 1682537, at *23-*26. Petitioners are not required to eliminate "potential *unknown, unidentified, speculative, unapparent, or spontaneous causes* with or without a subclinical nature." Stevens, 2001 WL 387418, at *26 (italics in original). See also White, 2002 WL 1488764, at *13 (opining that petitioner can successfully demonstrate that the vaccine caused her injury by "show[ing] either that the infection was not apparent or her treaters eliminated the infection as the cause of her illness."); Watson, 2001 WL 1682537, at *23-*26 (clarifying Prong Five and stating that "[n]either the Act nor caselaw requires petitioner to rule out unapparent infections – to do so would demand proof of causation beyond a reasonable doubt – a standard well beyond what is required, by the Act or in traditional tort litigation.")

During the hearing, the court heard extensive testimony related to Prong 1 including a detailed discussion of a theory that immunization may trigger the onset of disease in patients who have a genetic susceptibility. Tr. at 13-24, 28, 76, 161-162. However, it is not necessary to discuss this theory in great detail because the court found that respondent's exhibit L, "Rheumatic Disorders Developed After Hepatitis B Vaccination"which related four "rechallenge" cases to the Hepatitis B vaccine to be persuasive on the issue of biologic plausibility. R. Ex. L (J.F. Maillefert, J. Sibilia et al., Rheumatic Disorders Developed After Hepatitis B Vaccination, Rheumatology, 1999:38:978-983 at 979).

In addition to the Maillefert study the court also relied on the findings of the Institute of Medicine (IOM) on the issue of rechallenge and biological plausibility to be persuasive. The IOM has determined that "increasing severity of the event with increasing dose number would tend to support a causal interpretation. See Christopher P. Howson et al., Institute of Medicine, Adverse Effects of Pertussis and Rubella Vaccines, 48 (1991). Stated differently, the IOM has determined that one of the considerations to be made in inferring causality is the "strength of

association with increased exposures" and that "causality is strengthened by evidence that the risk of occurrence of an outcome increases with higher doses or frequencies of exposure." Id. at 53; Kathleen R. Stratton et al., Institute of Medicine, Adverse Events Associated with Childhood Vaccines: Evidence Bearing on Causality, 21 (1994).

Petitioners' expert, Dr. Bell, testified that the Maillefert study provided evidence of three rechallenge cases where a further vaccine injection caused a worsening of the patient's complaints. Tr. at 38-39. Respondent's expert Dr. Moulton, testified that "positive rechallenge for a rare event can be of interest to the medical community." Tr. at 135, 136. Dr. Moulton also testified that the IOM's report sa[id] that "if there is convincing evidence of recurrence of an adverse event with rechallenge it raises the level of suspicion higher of a possible causal relationship." Tr. at 201. After the first day of testimony, the court concluded, "based upon Maillefert's article describing the rechallenge case ... I will tentatively for [the] purpose of tomorrow's [hearing] accept the biologic plausibility of Hepatitis B causing RA." Tr. at 249.

In Stevens, the court found that Prong 1 is satisfied by "proffering a medically or scientifically supported means by which a vaccine component could cause the injury alleged." Stevens, 2001 WL 387418, at *23, *24. Here the court finds the Maillefert Study, the IOM criteria and the expert testimony persuasive evidence that the petitioners have met Prong 1. In essence, rechallenge cases are such strong proof of causality that it is unnecessary to determine the mechanism of cause – it is understood to be occurring.

As to the current status of the above captioned Hepatitis B rheumatological cases, the court is awaiting additional filings due July 25, 2003 and post hearing briefs due on August 25, 2003 before reaching a final decision on those cases. These filings will address the strength of the parties' evidence in relation to Prong 2 of the Stevens test.

Lastly, the court wishes to reiterate that despite excellent presentation by counsel, credible testimony from well-credentialed experts and solid medical literature during the hearing, the ultimate outcome of the Hepatitis B rheumatological cases before the court remains problematic. The court in its June 20, 2003 Order, and in previous conversations with counsel, has attempted to focus the resolution of these cases through eliminating some issues and

narrowing others. The court again strongly urges the parties to begin reviewing the individual cases against this guidance to determine the weak cases – which should be dismissed, the cases with strong evidence – which should be compensated, and lastly those cases with evidentiary "holes" – which may either be settled or litigated. The court stands ready to assist the parties in any way the parties find appropriate.

IT IS SO ORDERED.

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Gary J. Golkiewicz
Chief Special Master