Grimes v. Hoffman-Laroche CV-92-54-B 09/28/95 P

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW HAMPSHIRE

Rhonda Grimes

v. Civil No. 92-cv-54-B

Hoffmann-LaRoche, Inc. and
Dr. Pierre G. Labrecque

MEMORANDUM AND ORDER

Rhonda Grimes sued Hoffmann-LaRoche ("Hoffmann") and her doctor, Pierre G. Labrecque, after developing cataracts which she claims were caused by taking Accutane, a prescription drug manufactured by Hoffmann. She contends that Dr. Labrecque negligently failed to warn her that Accutane could cause cataracts and negligently failed to use less obtrusive treatments before prescribing Accutane. She claims that Hoffmann is strictly liable for defectively designing Accutane and failing to warn her adequately of Accutane's side effects. She also claims that Hoffmann is liable based on a negligent failure-to-warn theory. Both defendants deny that Accutane caused Grimes' cataracts.

Grimes attempts to prove causation through the testimony of Dr. Sidney Lerman, an ophthalmologist with a recognized expertise

in evaluating photochemical effects on the eye. Defendants have moved pursuant to Federal Rule of Evidence 702 to exclude Dr. Lerman's testimony on the ground that it is unreliable when judged by the standard established by the Supreme Court in Daubert v. Merrell Dow Pharmaceuticals, Inc., 113 S. Ct. 2786, 2796 (1993). Anticipating success with this motion, defendants also move for summary judgment, claiming that Grimes cannot prove causation without Dr. Lerman's testimony. For the reasons that follow, I grant both motions.

DISCUSSION

I. MOTIONS TO EXCLUDE

A. The Legal Standard

After Daubert, expert testimony must satisfy three requirements in order to survive a Rule 702 objection: first, the expert must be qualified; second, the expert's testimony must be reliable; and third, it must "fit" the facts of the case. United States v. Shay, 57 F.3d 126, (1st Cir. 1995). Qualifications alone are insufficient to satisfy the rule's requirements if the expert's testimony is based on unreliable methodology or if it cannot reliably be applied to the facts in issue. Daubert v. Merrell Dow Pharmaceuticals, Inc., 43 F.3d

1311, 1319 (9th Cir. 1995) (expert's qualifications, conclusions, and assurances of reliability are not enough to satisfy requirements), petition for cert. filed (Aug. 1, 1995); Porter v. Whitehall Lab., Inc., 791 F. Supp. 1335, 1343 (S.D. Ind. 1992), aff'd, 9 F.3d 607 (7th Cir. 1993) ("expert is a conduit of facts and not merely a subjective speculator relying on stature alone").

Rule 702's reliability requirement demands that "the expert's opinion be based on the `methods and procedures of science' rather than on `subjective belief or unsupported speculation'; the expert must have `good grounds' for his or her belief." In re Paoli R.R. Yard PCB Litig., 35 F.3d 717, 742 (3d Cir. 1994) (quoting Daubert, 113 S. Ct. at 2795). Among the factors that a court should consider in determining the reliability of scientific testimony are: (1) whether the opinion can be or has been tested; (2) whether the theory or technique on which the opinion is based has been subjected to peer review and publication; (3) the technique's known or potential error rate; (4) the existence and maintenance of standards controlling the

technique's operations; and (5) "general acceptance."[1] Daubert, 113 S. Ct. at 2796-97; In re Paoli, 35 F.3d at 742. In evaluating these factors, the focus "must be solely on principles and methodology, not on the conclusions that they generate." Daubert, 113 S. Ct. at 2797.

The rule's "fit" requirement refers to the necessity of a connection between the expert's testimony and the facts of the case. Daubert, 113 S. Ct. at 2795-96. For example, if a plaintiff offers scientific testimony that a particular chemical causes cancer in rats in order to prove that the chemical also causes cancer in humans, the testimony will not fit the facts of the case and must be excluded unless the plaintiff also establishes that the expert can reliably extrapolate from rats to humans. In re Paoli, 35 F.3d at 743. Thus, the results of a scientifically reliable experiment or study will fail Daubert's fit requirement and be excluded unless the results can be linked

---

[1] The concept of general acceptance was first applied to expert testimony in Frye v. United States, 293 F. 1013, 1014 (D.C. Cir. 1923). There, the court stated that "while courts will go a long way in admitting expert testimony deduced from a well-recognized scientific principle or discovery, the thing from which the deduction is made must be sufficiently established to have gained general acceptance in the particular field in which it belongs." Id. at 1014.

through scientifically reliable means to the expert opinion it purports to support. See In re Paoli, 35 F.3d at 743, 744-45 n.12, 745 (Daubert's reliability requirement applies to each step in the expert's analysis).

I begin my review of defendants' challenge to the admissibility of Dr. Lerman's testimony by describing his opinion on causation and the methodology he used in reaching that opinion. I then review his methodology in light of Rule 702's requirements. In doing so, I am mindful that the burden lies with Grimes to demonstrate by a preponderance of the evidence that the rule's requirements have been met. Daubert, 113 S. Ct. at 2796 n.10.

B. Dr. Lerman's Testimony

Dr. Lerman proposes to testify that Accutane "played a role" in the development of Grimes' cataracts. In reaching this ultimate conclusion, Dr. Lerman necessarily must also conclude that therapeutic doses of Accutane will cause cataracts in certain humans under certain conditions. Stated differently, Dr. Lerman's conclusion that Accutane was the specific cause of Grimes' cataracts is necessarily based, in part, upon his opinion that Accutane is a general cause of cataracts when it is taken in therapeutic doses. See, e.g., Wade-Greaux v. Whitehall Lab., 874

F. Supp. 1441, 1448 (D.V.I. 1994) (discussing concepts of specific and general causation), aff'd without op., 46 F.3d 1120 (3d Cir. 1994).

Rather than relying on epidemiological data, Dr. Lerman bases his general causation opinion primarily on scientific theory, an in vitro experiment, and what he considers certain "generally accepted" scientific facts.[2] Simply stated, his theory is that: (1) Accutane is a "photosensitive" drug; (2) that gets into the lens when taken in therapeutic doses; (3) becomes "photobound" to normally transparent lens protein after being exposed to normal levels of ultraviolet radiation; and (4) alters the lens protein in such a way as to produce opacities in the lens, otherwise known as cataracts. Dr. Lerman defines a photosensitive drug as "a compound whose chemical structure endows it with the ability to absorb optical radiation (UV and visible) and undergo a primary photochemical reaction resulting in the generation of highly reactive and relatively long-lived

[2] Dr. Lerman also bases his opinion in part on the fact that there have been anecdotal reports of cataracts in patients who have taken Accutane. However, no epidemiological studies have been done which establish any relationship between Accutane and cataracts and Dr. Lerman does not contend that causation can be proved by anecdotal evidence alone.

intermediates (triplets, radicals and ions) that can cause chemical modifications in other (nearby) molecules of the biologic system." Sidney Lerman, "Photosensitizing Drugs and their Possible Role in Enhancing Ocular Toxicity," Ophthalmology, Vol. 93, No. 3, (March 1986). According to Dr. Lerman, photobinding occurs when a photosensitive drug is exposed to ultraviolet light and becomes "cross linked" or bound to surrounding tissue. This process is potentially significant in the development of cataracts, according to Dr. Lerman, because when a photosensitive chemical becomes photobound with lens protein, it remains in the lens rather than diffusing out and its phototoxic effect is exacerbated.[3]

The research Dr. Lerman conducted to test his theory involved the use of ultraviolet spectroscopy and high performance liquid chromatography ("HPLC") to compare various samples of lens protein.[4] The samples used during the tests were taken from

---

[3] The lens is surrounded by a thin membrane called the aqueous humor. The membrane allows compounds of a certain size, weight, and chemical structure to diffuse in and out of the lens. Molecules that are too large or that become bound to lens protein molecules cannot diffuse out of the lens.

[4] Ultraviolet spectroscopy is a method of identifying an unknown compound by comparing the frequency of ultraviolet light absorbed by that compound with the frequency absorbed by a known

(1) Grimes and another patient who had developed cataracts after taking Accutane; (2) age-matched[5] normal lenses; (3) age-matched cataractous lenses from patients who had not taken Accutane; (4) age-matched normal lenses that were incubated in Accutane, exposed to ultraviolet radiation, and dialyzed;[6] and (5) age-

---

compound. See 13 Encyclopedia Britannica 527-28 (Phillip Goeth ed.) (1991). Ultraviolet spectroscopy can also be used to measure the amount of a compound known to absorb a specific frequency of ultraviolet light present in a sample by measuring the amount of ultraviolet light absorbed at the known frequency. High performance liquid chromatography is another method of identifying unknown compounds by comparing them with known compounds. See Van Nostrand Reinhold Encyclopedia of Chemistry 252-54 (Douglas M. Considine, ed.) (1984). During this process, different compounds will move through a thin tube filled with solid supports and liquid at different rates. By comparing the rate at which an unknown compound moves through the tube with the movement rate of known compounds, the unknown compound may be identified. See id.

[5] Age-matched lenses are used for comparison purposes because the lens changes as a person ages.

[6] Dialysis is a technique which can be used to determine whether a compound has become bound to proteins in a sample. After a compound has been added to the sample, the sample and a small amount of solution are placed in a semi-porous bag through which proteins are too large to diffuse. The bag is then placed in a beaker of the solution. If the compound does not bond with the proteins, it will diffuse out of the bag into the surrounding solution. Conversely, if it does bond with the protein, it will not diffuse into the surrounding solution because the compound protein material is too large to fit through the pores of the bag.

matched normal lenses that were incubated in Accutane and dialyzed without first being exposed to ultraviolet radiation.[7]

The spectroscopy results revealed that lens material taken from lenses that had been exposed to Accutane and ultraviolet radiation showed greater absorbency to ultraviolet radiation between 330-390 nanometers[8] than lens material taken from both the lenses that had not been exposed to Accutane and the lenses that had been incubated in Accutane but not exposed to ultraviolet radiation prior to dialysis. The HPLC results also revealed an "anomalous peak" which was present only in the analysis of the lens material taken from the lenses of the Accutane patients and the lenses incubated in Accutane and exposed to ultraviolet radiation before dialysis.

Dr. Lerman contends that his experiment proves both that when Accutane is taken in therapeutic doses it can enter the

---

[7] I cannot determine from Dr. Lerman's deposition testimony whether he conducted spectroscopy and HPLC tests on the samples he obtained from both Grimes and the other Accutane patient. I am also unable to determine from the evidence how many age-matched normal lenses and cataractous lenses Dr. Lerman used in his research. Nevertheless, I assume for purposes of analysis that Dr. Lerman performed spectroscopy tests and HPLC tests on the lens material taken from both Accutane patients. I also assume that he used multiple control samples.

[8] A nanometer is a measuring unit for wavelengths of light.

lens, and that if Accutane enters the lens and is exposed to ultraviolet radiation, it becomes photobound to lens protein. According to Dr. Lerman, the experiment proves the first point because samples of the lens protein taken from the Accutane patients showed the same increased absorbency to certain wave lengths of ultraviolet radiation during spectroscopy and the same anomalous peak during HPLC testing as was shown by his analysis of the lens protein that had been incubated in Accutane and exposed to ultraviolet radiation prior to dialysis. Dr. Lerman reasons that the only plausible explanation for the anomalous peak and the increased ultraviolet absorbency seen in the lens material taken from the Accutane patients is that the Accutane they were taking, or one of its metabolites, entered their lenses. He also contends that the experiment proves the second point because he detected the anomalous peak and increased ultraviolet absorbency only in the lens material that had been exposed to both Accutane and ultraviolet radiation before dialysis. According to Dr. Lerman, the sample that was exposed to Accutane but not ultraviolet radiation did not exhibit the anomalous peak and increased ultraviolet absorbency because the Accutane in the sample did not become bound to the lens protein and was removed during dialysis. Finally, he concludes that

Accutane produces cataracts because, he argues, it is "generally accepted" that cataracts will result whenever a photosensitive chemical becomes photobound to lens protein.

C. Analysis

Assuming without deciding that Dr. Lerman's experiment is a scientifically reliable way of determining that therapeutic doses of Accutane will enter the lens and become photobound to lens protein if exposed to ultraviolet radiation, he must still have a reliable basis for concluding that Accutane will produce cataracts if it enters the lens and becomes photobound.[9] Otherwise, his opinion cannot satisfy Daubert's fit requirement because the results of his experiment cannot be linked reliably to the opinion they purport to support.

In completing the final step in his analysis, Dr. Lerman relies on what he considers to be the generally accepted scientific fact that photosensitive chemicals that enter the lens

[9] Defendants argue that Dr. Lerman's experiment is flawed because: (1) the sample he took from Grimes' lens was tainted; (2) he failed to use adequate controls; and (3) he has failed to account for other innocent explanations that are also consistent with his result. I need not consider these contentions because I conclude that Dr. Lerman's testimony should be excluded even if his experiment was methodologically sound.

and become photobound to lens protein will produce cataracts.[10] In a letter filed with the court after the hearing concluded, Dr. Lerman explained his view.

> It is universally accepted that many forms of radiation can cause cataracts. Two forms of radiation, namely, x-rays and ultraviolet radiation, are well known cataractogenic agents.
>
> The role of [U.V. absorbing] photosensitizers in the generation of cataracts is primarily due to the fact that they enhance UV action on the lens in which they are photobound to lens protein.
>
> It therefore follows that the demonstration of such photobinding clearly shows that it can and will initiate and enhance the formation of a cataract.

Notwithstanding Dr. Lerman's undeniable expertise, this broad assertion is insufficient to establish the reliability of his conclusion on this point for three independent reasons. First, an expert cannot establish that a fact is generally accepted merely by saying so. In this case, Dr. Lerman has failed to identify any authoritative source which recognizes as generally accepted the proposition that all photosensitive chemicals

---

[10] Grimes does not contend that any of Daubert's alternative criteria can be used to establish the reliability of the final step in Dr. Lerman's opinion. Therefore, I will only consider whether the scientific propositions on which his opinion is based are generally accepted.

produce cataracts when they become photobound to lens protein. In the absence of such authority, I find his testimony on the point to be unpersuasive. Second, even if it were generally accepted that some photosensitive chemicals will produce cataracts if they become photobound to lens protein, that general proposition would not fit the facts of this case unless one could reliably draw an analogy between those photosensitive chemicals and Accutane. See, e.g., Federal Judicial Center, Reference Manual on Scientific Evidence 83-84 (1994) [hereinafter Reference Manual] (suggesting that an expert who bases an opinion on a proposed analogy that has not been investigated should not be permitted to testify because he is offering a "hunch" rather than an "explanatory theory . . ."). In the present case, Dr. Lerman has failed to identify any scientifically reliable basis for concluding that Accutane causes cataracts simply because other photosensitive drugs cause cataracts.[11] Finally, even if it

---

[11] In certain circumstances, toxicologists have relied on similarities in the chemical structures of two compounds to draw an analogy between an established toxic effect exhibited by one chemical and an anticipated toxic effect in another. This technique is referred to as the identification of Structure Activity Relationships ("SAR"). Reference Manual, supra, at 203; but see David E. Bernstein, The Admissibility of Scientific Evidence after Daubert v. Merrell Dow Pharmaceutical, Inc., 14 Cardozo L. Rev. 2139, 2178-79 (1994) ([c]hemical structure

could reliably be claimed that all photosensitive chemicals that become photobound to lens protein will produce cataracts if they are present in certain concentrations, that proposition would be irrelevant here unless there were some basis in the record to conclude that Grimes had taken a sufficient dose of Accutane to produce cataracts. Dr. Lerman has not attempted to determine the amount of Accutane that he claims reached Grimes' lenses. Nor has he stated how much of a photosensitive drug must be present in the lens to produce a cataract. Without such information, it would not be possible to reliably opine that therapeutic doses of Accutane cause cataracts simply because it is generally accepted that unspecified doses of other photosensitive drugs produce cataracts when they become photobound. See, e.g., Reference Manual, supra, at 201 ("[T]he expert should offer an opinion as to whether the dose to which the plaintiff was exposed was sufficient to cause the disease."). See also Turpin v. Merrell

---

analysis is an example of a scientific technique that has valid scientific uses but is not properly used to prove causal association, much less individual causation"). Although Dr. Lerman testified about his research into Psoralan, another photosensitive drug which he claims produces cataracts, he did not claim that Accutane has a similar chemical structure to Psoralan. Thus, even if the identification of an SAR between the compounds could in some circumstances provide a reliable basis for drawing an analogy between the compounds, that technique is inapplicable here.

Dow Pharmaceuticals, Inc., 959 F.2d 1349, 1360 (6th Cir. 1992) (failure to indicate dose used in studies left analytical gap between evidence presented and inference to be drawn about whether therapeutic doses of medication caused the disease), cert. denied, 113 S. Ct. 84 (1992).

In summary, even if I were to assume that Dr. Lerman's experiment is methodologically sound, I must still exclude his opinion on general causation because the final essential step in the formulation of that opinion is based on an untested assumption which fails Daubert's reliability and fit requirements. Since his opinion on specific causation is necessarily based on his opinion concerning general causation, that testimony must be excluded as well. Accordingly, I grant defendants' motions to exclude.

II. SUMMARY JUDGMENT

"Summary judgment is `mandate[d] . . . against a party who fails to make a showing sufficient to establish the existence of an element essential to that party's case and on which that party will bear the burden of proof at trial.'" Flanders & Mederios, Inc. v. Bogosian, slip op. at 21-22 (1st Cir. Sept. 13, 1995) quoting Celotex Corp. v. Catrett, 477 U.S. 317, 322 (1986).

Since it is undisputed that causation is an essential element of Grimes' claims, see, e.g., LeFavor v. Ford, 135 N.H. 311, 313 (1992), and I have excluded the only evidence Grimes points to in order to prove causation, defendants' summary judgment motion must be granted.

CONCLUSION

Defendants' Motions in Limine to exclude Dr. Lerman's expert opinion testimony (document nos. 38, and 41) and defendants' Motions for Summary Judgment (document nos. 37 and 42) are granted.[12] The clerk shall issue judgment for the defendants.

SO ORDERED.

_____
Paul Barbadoro
United States District Judge

September 28, 1995

cc: Edward Van Dorn, Esq.
Michael Lehman, Esq.
John D. Winter, Esq.
John E. Friberg, Esq.

[12] I did not rely on Dr. Dillon's testimony in reaching these decisions. Therefore, plaintiff's Motion to Exclude Portions of Expert Testimony of Dr. James Dillon (document no. 69) is deemed moot.