STATE OF MICHIGAN

COURT OF APPEALS

LAWRENCE DePYPER, SR., JANE N. DePYPER, individually and as next friend of LAWRENCE R. DePYPER, JR.,

Plaintiffs-Appellants,

v

PAUL F. NAVARRO, D.O., PAUL F. NAVARRO, D.O., P.C., DOW CHEMICAL COMPANY, d/b/a MERRELL DOW PHARMACEUTICALS, INC., and MERRELL NATIONAL LABORATORIES, INC.,

Defendants-Appellees.

UNPUBLISHED
November 6, 1998

No. 191949
Wayne Circuit Court
LC No. 83-303467 NM

Before: Holbrook, Jr., P.J., and Young, Jr., and J.M. Batzer*, JJ.

PER CURIAM.

In this negligence and pharmaceutical products liability action, plaintiffs appeal as of right an order of the Wayne Circuit Court granting summary disposition in favor of defendants pursuant to MCR 2.116(C)(10). We affirm.

I. BACKGROUND

On February 2, 1983, plaintiffs filed a complaint against defendants in which they alleged that their minor son, Lawrence DePyper, Jr., was born with serious upper limb reduction birth defects that had been caused by Jane DePyper's ingestion during her pregnancy of Bendectin, a prescription antinausea drug manufactured by defendant Merrell Dow Pharmaceuticals, and commonly prescribed to expectant mothers experiencing morning sickness.[1] Plaintiffs' suit was eventually dismissed by the trial court on defendants' motion for summary disposition. However, in *DePyper v Navarro*, unpublished opinion per curiam of the Court of Appeals, issued 5/9/91 (Docket No. 116390) (hereinafter "*DePyper I*"), this Court reversed the trial court's grant of summary disposition, and remanded for a

* Circuit judge, sitting on the Court of Appeals by assignment.

Davis-Frye[2] hearing. As articulated by this Court, the relevant question to be resolved at the *Davis-Frye* hearing was: "Do impartial and disinterested experts in the field of teratology generally accept the methodology employed by plaintiffs' expert in accessing the impact of in vivo, in vitro, chemical structure and animal studies in determining teratogenity?" *DePyper I*, *supra* at 1. *In vivo* tests are tests which are performed "[i]n the living body, as opposed to the test-tube or other non-living experimental medium." 3 Schmidt, *Attorneys' Dictionary of Medicine and Word Finder* (New York: Matthew Binder, 1997), pp I-50 to I-51. Conversely, *in vitro* tests are performed "[i]n the test tube, or any other experimental medium not involving an animal or human being." *Id.* at I-50. "Chemical structure analysis is based on the theory that drugs with similar chemical structures may be expected to have similar properties and produce analogous effects." Bernstein, *The admissibility of scientific evidence after Daubert v Merrell Dow Pharmaceuticals, Inc*, 15 Cardozo L Rev 2139, 2178 (1994).

On remand, the lower court was presented written summaries submitted by six expert witnesses, three supporting plaintiffs' position and three supporting defendants' position. Plaintiffs' proofs also consisted of the transcribed testimony of the same three experts in *Havner v Bruce*, a 1991 Bendectin case tried in the 214 District Court, Nueces County, Texas (No. 88-3915-F). Additionally, the court heard from four independent expert witnesses appointed by the court pursuant to MRE 706(a).[3] The four independent experts were given the prepared statements of plaintiffs' and defendants' expert witnesses, as well as the testimony of plaintiffs' expert witnesses in *Havner*.[4] Thereafter, the trial court ruled that because the methodologies on which plaintiffs' experts relied in reaching the conclusion that Bendectin is a human teratogen were not generally accepted by experts in the field of teratology, their expert testimony was not admissible. The court then once again granted defendants' motion for summary disposition.

II. *DAVIS-FRYE* ANALYSIS

Plaintiffs first argue that the trial court's grant of summary disposition was based on the erroneous conclusion that plaintiffs' expert witness testimony was inadmissible. We disagree. We review motions for summary disposition de novo in order to determine "whether the moving party was entitled to judgment as a matter of law." *Stehlik v Johnson (On Rehearing)*, 206 Mich App 83, 85; 520 NW2d 633 (1994). A trial court's admission of scientific evidence is reviewed for an abuse of discretion. *People v Haywood*, 209 Mich App 217, 224; 530 NW2d 497 (1995).

MRE 702 provides, in pertinent part, that "[i]f the court determines that recognized scientific . . . knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert . . . may testify thereto in the form of an opinion or otherwise." Under the terms of the *Davis-Frye* test, "the proponent of the evidence [in question] must show that the scientific principle or technique [underlying the testimony] has gained such general acceptance within the scientific community as to render the technique or principle, reliable." *People v Beckley*, 434 Mich 691, 718-719; 456 NW2d 391 (1990) (Brickley, J.). In other words, the proponent of the evidence must establish that the conclusion reached has been "deduced" from a technique or principle "sufficiently established to have gained general acceptance in the particular field in which it belongs." *Frye, supra* at 1014.[5]

After reviewing the record, we conclude that resolution of this issue comes down to an examination of one central question: "Does the methodology underlying the opinions advanced by plaintiffs' experts on the issue of the teratogenic effects of Bendectin place due emphasis on the role epidemiological studies should play in such an analysis?" [6]

A. Qualifications and Impartiality of Plaintiffs' Experts

As a preliminary matter, we briefly address plaintiffs' challenge to the qualifications and impartiality of the court appointed expert witnesses. Except for plaintiffs' challenge to the qualifications of Marilyn Preus, Ph.D.,[7] plaintiffs failed to raise these challenges below. Accordingly, we find that except for the issue of Dr. Preus's qualifications, plaintiffs' challenges are unpreserved. *Harvey v Security Services, Inc*, 148 Mich App 260, 265; 384 NW2d 414 (1986). On appeal, plaintiffs argue that Dr. Preus was unqualified because she has limited scientific expertise in the areas addressed at the *Davis-Frye* hearing. However, because plaintiffs' challenge to Dr. Preus's testimony at the *Davis-Frye* hearing was limited to her qualification to offer epidemiological testimony, we limit our review of her qualifications to this single matter. *Id.* ("Objections based on one ground are insufficient to preserve an appellate attack based on different grounds.").

A trial court's ruling regarding the qualification of an expert witness is reviewed for an abuse of discretion. *Carlton v St John General Hospital*, 182 Mich App 166, 171; 451 NW2d 543 (1989). After reviewing the record, we conclude that the hearing judge did not abuse her discretion when ruling that Dr. Preus was qualified to offer epidemiological testimony. Dr. Preus's educational and professional background establish that she is sufficiently qualified to offer her opinions in this area. Additionally, given our conclusions regarding plaintiffs' challenge to the qualification and impartiality of the defense experts, we necessarily conclude that plaintiffs' argument that they should not be required to pay their share of the court-appointed expert fees is without merit.

B. Examination of Expert Opinions

1. Plaintiffs' experts

Plaintiffs' expert witnesses agreed that epidemiological studies play a limited role in establishing the existence of a causal link between the ingestion of Bendectin and upper limb birth defects. Stuart Newman, M.D.,[8] acknowledged that in arriving at the conclusion that Bendectin is a human teratogen, he had not paid any significant attention to any epidemiological studies involving Bendectin. Dr. Newman indicated that in his opinion "[t]he generally accepted method of determining the ability of a substance to cause a teratogenic effect is to utilize all of the data available from any source as long as the studies are well done." Dr. Newman's conclusion about the teratogenic effects of Bendectin was based almost exclusively on his review of *in vitro* and *in vivo* animal studies. For example, Dr. Newman testified in the *Havner* case that because there is evidence from an *in vitro* study involving cells removed from chicken and mouse embryos that Bendectin can interfere with the process of chrondogenesis,[9] "that makes it a teratogen for cartilage development, skeletal development." In Dr. Newman's opinion, although "it is difficult to make direct extrapolations," nevertheless extrapolating conclusions about humans from animal studies is legitimate.[10]

John Palmer, M.D.,[11] indicated that he had reviewed epidemiological studies examining the teratogenic effects of Bendectin. Dr. Palmer's reliance on such studies was, however, distinctly qualified. In Dr. Palmer's opinion, "[e]pidemological studies, while being helpful in determining whether or not a drug is a teratogen, would not be used solely to determine teratogenicity, partly because the studies are not experimental and difficult to control." Like Dr. Newman, Dr. Palmer opined that when trying to determine if a substance is a teratogen, a scientist should avail himself of as much data as possible. Accordingly, in addition to the epidemiological studies he reviewed, Dr. Palmer relied upon animal studies, pharmacological data, *in vitro* studies, drug experience reports and chemical structure analyses when concluding that Bendectin is a teratogen. Significantly, Dr. Palmer reached this conclusion even though he acknowledged that none of the epidemiological studies he examined had similarly found Bendectin to be a teratogen.

Shanna Swan, Ph.D.,[12] took Dr. Palmer's concession one step further when she acknowledged that she is not aware of any published study employing the traditional 95 percent confidence level that has shown that there exists a statistically significant relationship with limb reduction birth defects. Nevertheless, Dr. Swan testified in *Havner* that it was her "opinion that more probably than not, [Bendectin] . . . is associated with limb defects, specifically limb reduction defects." Much of Dr. Swan's testimony in *Havner* consisted of a critical critique of the epidemiological studies relied on by the *Havner* plaintiffs. In Dr. Swan's opinion, those studies were poorly constructed and poorly executed. Dr. Swan was particularly critical of the literature's reliance on the 95 percent confidence level. "[I]t's now considered very naï ve in statistical and epidemiological theory to view a confidence interval as a test of significance," Dr. Swan opined. According to Dr. Swan, traditionally confidence intervals have been used to classify the results obtained. If the results satisfied the set confidence interval, then they were classified as statistically significant. Conversely, if the confidence interval were not satisfied, the results were then dassified as nonsignificant. She concluded that such a statistical design is not helpful in analyzing epidemiological data.

2. Defendants' experts

Defendants' expert witnesses agreed that before a given substance can be classified as being a human teratogen, epidemiological data establishing the existence of an association between the substance and birth defects is essential. For example, Richard Miller, Ph.D.,[13] observed:

> Experts in the field of human teratology deem human data essential before it can conclude that an agent is a human teratogen. One standard requirement for human data is that it be comprised of two or more epidemiological studies of high quality with consistent findings. . . . *Epidemiological studies provide the only means of obtaining quantitative estimates regarding the strength and statistical significance of associations between agent exposures in pregnant women and abnormalities in their offspring*. . . . I have reviewed the epidemiologic literature for Bendectin and there is none which would support a conclusion that Bendectin causes human malformations in general or limb reduction defects in particular. (Emphasis added.)

Although he did not directly address the issue of epidemiological studies, Kenneth Chepenik, Ph.D.,[14] stated in his narrative that extrapolating results obtained in animal *in vitro* and *in vivo* studies "is neither generally accepted nor reliable." With respect to *in vitro* studies, Dr. Chepnik observed that "[t]o date, none of the proposed *in vitro* tests have been shown to be sufficiently accurate predictors of what will happen in either the laboratory animal or in human beings." As for *in vivo* studies, he stated:

> It is generally not accepted in the filed of teratology to draw definitive conclusions about what will happen in the human from *in vivo* laboratory animal testing. It is known and generally accepted that there are differences among species regarding metabolism of drugs and sensitivity of the embryo to insult by drugs. . . . This lack of agreement between effects in different species is also true for comparisons of laboratory animals to humans. *Thus, the only truly definitive data are those derived from human studies.*" (Emphasis added.)

He also criticized reliance on chemical structure analysis, stating that any opinion regarding causation "must be based upon the results of studies conducted on the actual compounds in question."

In his narrative, Richard Monson, M.D., Sc.D.,[15] was quite critical of the methodology employed by Dr. Swan. Not only did Dr. Monson state that the methodology relied upon by Dr. Swan is generally not accepted within the epidemiological community, but he also stated that "Dr. Swan uses this methodology in a way that may frequently lead to erroneous conclusions." In plain and unequivocal language, Dr. Monson concluded that "[o]ne cannot possibly conclude Bendectin causes human malformations in general or limb reduction defects in particular based upon any known, generally epidemiologic methodology."

3. Court appointed experts

The four court appointed experts agreed with defendants' experts about the importance of epidemiological studies. For example, in critiquing the narrative of Dr. Palmer, James Mills, M.D.,[16] opined that Dr. Palmer's "statement underestimates the importance of human data. . . . Indeed, human epidemiological studies must take priority over pharmacologic, in vitro, and animal studies. These other types of studies may provide supporting evidence." Dr. Preus testified at the *Davis-Frye* hearing that "if you are looking for . . . whether there is a real effect in humans, then you start with an epidemiological study, a positive epidemiological study." In the opinion of Mason Barr, Jr., M.D.,[17] under the generally accepted standard criteria for evaluating the teratogenic effect of a given substance, "human data are deemed essential to the confirmation of agents as human teratogens. These may be in the form of epidemiological data or case delineations." Further, Dr. Barr noted that "[w]hen neither the defect nor the exposure is rare, [as is the case with limb reduction defects and Bendectin ingestion] the standard practice in teratology is to rely heavily on epidemiological data to confirm or refute a suspicion of teratology." Finally, Philip Mirkes, Ph.D.,[18] confirmed in his narrative that his review of the body of epidemiological literature has failed to uncover a single study indicating that there exist an association between Bendectin and limb reduction birth defects.

C. Conclusions

After carefully reviewing in its totality the evidence in the record, we conclude that plaintiffs have failed to establish that the scientific methodology underlying their opinions "has gained such general acceptance within the scientific community as to render the [methodology] . . . reliable." *Beckley, supra*, 434 Mich at 719. In making their argument, plaintiffs' experts both implicitly and explicitly acknowledge that they did not follow the accepted methodology for examining the teratogenic effect of a given substance. Indeed, the gist of the argument put forth by plaintiffs' experts is that the prevailing methodology is inadequate, particularly the reliance on epidemiological studies. In essence, plaintiffs' experts are arguing that the prevailing methodology, the traditional scientific paradigm should be replaced. We do not feel an appellate court is well suited either by temperament or expertise to sort through competing articulations concerning what constitutes proper scientific methodology, or to pass judgment on the question of when it is time to replace an existing scientific paradigm with another.

Fortunately, under *Davis-Frye* a court is not required to address such matters. Rather, the court is asked to decide whether the proponent of the evidence has established that a sufficient evidentiary foundation exists to admit expert testimony addressing the teratogenic effects of a given substance. In order to satisfy this burden, the party offering such testimony must show that the conclusions drawn are supported by sound epidemiological evidence. See *Nelson v American Sterilizer (On Remand),* 223 Mich App 485, 495; 566 NW2d 671 (1997) (observing that "the reliability of plaintiff's expert testimony is undercut by the epidemiological studies relied upon by defendants"); *Daubert v Merrell Dow Pharmaceuticals, Inc* 727 F Supp 570, 575 (SD CA, 1989) (observing that under a *Davis-Frye* analysis, "expert opinion which is not based on epidemiological evidence is not admissible to establish causation")[19]; *Richardson v Richardson-Merrell, Inc*, 857 F2d 823, 830 (CA DC, 1988) (observing that under a *Davis-Frye* analysis, *in vitro, in vivo,* and chemical structure analysis "are not capable of proving causation in human beings in the face of overwhelming epidemiological evidence"). We conclude that plaintiffs have failed to meet this burden. [20] To the extent that plaintiffs' experts are arguing that the methodology they have employed has gained general acceptance within the relevant scientific community (e.g., Dr. Swan's assertions regarding the recognized usefulness of the 95 percent confidence level), we further conclude that their argument is unsupported by the record. Therefore, having found that the hearing court did not abuse its discretion in rejecting plaintiffs' expert testimony under *Davis-Frye*, we furthermore conclude that the grant of summary disposition with regard to defendant Dow Pharmaceuticals was proper.

III. SUMMARY DISPOSITION IN FAVOR OF DR. NAVARRO

Finally, we disagree with plaintiffs' assertion that the trial court erred in granting summary disposition in favor of Dr. Navarro. In their complaint, plaintiffs alleged that Dr. Navarro breached his duty of care by prescribing and providing Bendectin to Jane DePyper during her pregnancy, and by failing to warn her of possible harmful effects the drug might have on her pregnancy. However, plaintiffs failed to support these accusations with expert testimony either establishing the applicable standard of care or that Dr. Navarro had breached the applicable standard of care. See, e.g., *Birmingham v Vance,* 204 Mich App 418, 421; 516 NW2d 95 (1994) ("Expert testimony is required in medical malpractice cases to establish the applicable standard of care and to demonstrate that the defendant

somehow breached that standard."). Further, we reject plaintiffs' characterization of their claim against Dr. Navarro as being a products liability claim. We are aware of no Michigan authority indicating that a physician may be held liable under a products liability theory for the prescription of a drug. The primary function of a physician is to provide care, not to manufacture or distribute products. *Ayyash v Henry Ford Health Systems*, 210 Mich App 142, 146; 533 NW2d 353 (1995). Products liability theories should not be applied to physicians whose prescription of a drug is only incidental to the provision of medical services. *Id.* at 146-147.

Affirmed.

/s/ Donald E. Holbrook, Jr.
/s/ Robert P. Young, Jr.
/s/ James M. Batzer

[1] During the period between 1957 and 1982, Bendectin was prescribed for approximately 30 million woman around the world. *Turpin v Merrell Dow Pharmaceuticals, Inc*, 959 F2d 1349, 1351 (CA 6, 1992). More than 17.5 million women in the United States took the drug during the same time period. *Daubert v Merrell Dow Pharmaceuticals, Inc (On Remand)*, 43 F3d 1311, 1313 (CA 9, 1995) (hereinafter "*Daubert II*"); *Turpin, supra* at 1351.

[2] *People v Davis*, 343 Mich 348; 72 NW2d 269 (1955); *Frye v United States*, 293 F 1013 (CA DC, 1923).

[3] MRE 706(a) reads in pertinent part:

> *Appointment*. The court may on its own motion or on the motion of any party enter an order to show cause why expert witnesses should not be appointed, and may request the parties to submit nominations. The court may appoint any expert witness agreed upon by the parties, and may appoint expert witnesses of its own selection.

[4] Neither plaintiffs' nor defendants' experts, and only two of the four independent experts testified at the *Davis-Frye* hearing.

[5] In this way, the generally recognized technique or principle acts as the major premise in an evidentiary syllogism. Once accepted by the court, the technique or principle can then can applied by the expert witness to the case specific facts (which are governed by MRE 703) to yield the expert's opinion. See Imwinkelried, Evidentiary Distinctions, ch 7, pp 119-122.

[6] Human teratogens are "drugs and chemical substances known to cause permanent deformities and malfunctions in the [human] fetus." Schmidt, *supra* at T-53. "Epidemiological studies are statistical studies of human populations used by scientists in an attempt to determine correlations between certain factors and human disease." Bernstein, *supra* at 2167.

[7] The record indicates that Dr. Preus's Ph.D. is in "Biology (Human Genetics)."

[8] The record indicates that Dr. Newman's Ph.D. is in Chemistry.

[9] "The formation or growth of cartilage." Schmidt, *supra* at C-186.

[10] In explaining why such extrapolations can be done, Dr. Newman made the following observations in the *Havner* case:

> A study on a single species is a little more difficult to extrapolate because there are some differences as I mentioned between species, but if you find something that prevails across species, you use a number of different species and you find similar things hold. For example, in species as far from one another as chickens and mice. Chickens and mice are much further from one another than mice are from humans. If something prevails in those species and then you take a third species like rats and you find the same thing prevails, then you can be awfully sure that the same thing will prevail in humans.

[11] The record indicates that in addition to being a medical doctor, Dr. Palmer has a Ph.D. in Pharmacology.

[12] The record indicates that Dr. Swan holds a Ph.D. in statistics. Additionally, Dr. Swain testified in the *Havner* case that as of that time she had served as "chief of the reproductive epidemiology program in a group called the Special Epidemiological Studies Program" in California for approximately nine years.

[13] The record indicates Dr. Miller's Ph.D. is in Pharmacology/Toxicology and Physiology. Dr. Miller stated in his narrative that he has been "trained as a teratologist."

[14] The record indicates that Dr. Chepenik's Ph.D. is in Human Anatomy.

[15] The record indicates that Dr. Monson "received a Medical Doctor degree from Harvard Medical School in 1963 and a Doctorate in Epidemiology and Biostatistics from the Harvard School of Public Health in 1969."

[16] The record indicates that Dr. Mills received his Doctor of Medicine from New York Medical College. He also holds a Master in Science from the University of Pennsylvania. At the time of the *Davis-Frye* hearing, Dr. Mills was an Associate in the Department of Epidemiology at The John Hopkins University.

[17] The record indicates that Dr. Barr received his Doctor of Medicine from George Washington University. At the time of the *Davis-Frye* hearing, Dr. Barr was serving as Director of the Human Teratology Unit at C.S. Mott Children's Hospital.

[18] The record indicates that Dr. Mirkes's Ph.D. is in Zoology.

[19] *Daubert I* was affirmed by the Ninth Circuit Court of Appeals in *Daubert v Merrell Dow Pharmaceuticals, Inc*, 951 F2d 1128 (CA, 9) (1991). The federal appellate court decision was vacated and the case remanded to the district court in *Daubert v Merrell Dow Pharmaceuticals, Inc*, 509 US 579; 113 S Ct 2786; 125 L Ed 2d 469 (1993). Because the action taken by the United States Supreme Court was based on its rejection of the *Davis-Frye* rule, as well as the differently worded Federal Rule of Evidence (FRE 702), *id*. at 587-589, the legal principles advanced in *Daubert I* are still relevant in Michigan.

[20] Plaintiffs' argument appears to be better suited for a jurisdiction evaluating the admissibility of expert witness testimony under the standard established in *Daubert v Merrell Dow Pharmaceuticals, Inc*, 509 US 579; 113 S Ct 2786; 125 L Ed 2d 469 (1993). Under this standard (the aptly named *Daubert* standard), the proponent of scientific expert testimony need only show that the methodology underlying that testimony is sound. *Id.* at 592-593. As the United States Court of Appeals for the Ninth Circuit observed on remand in *Daubert II* in analyzing the methodology underlying proffered scientific expert testimony under *Daubert* standard, "the court and the parties are not limited to what is generally accepted; methods accepted by a minority in the scientific community may well be sufficient." We do not mean to imply that the testimony of plaintiffs' experts at issue here would necessarily be admissible under Daubert.