Golden Gate University Law Review

Volume 36
Issue 3 *Symposium Issue: California's Renewable Energy Sector*
Article 7

January 2006

Keeping Bad Science out of the Courtroom: Why Post-Daubert Courts Are Correct in Excluding Opinions Based on Animal Studies From Birth-Defects Cases

Dije Ndreu

COMMENT

KEEPING BAD SCIENCE OUT OF THE COURTROOM:

WHY POST-*DAUBERT* COURTS ARE CORRECT IN EXCLUDING OPINIONS BASED ON ANIMAL STUDIES FROM BIRTH-DEFECTS CASES

INTRODUCTION

Pregnant cats force-fed methylmercury.[1] Pesticides injected into the stomachs of pregnant rats.[2] These and other cruel animal experiments are done in the name of birth-defects research, resulting in animal suffering and, ultimately, death.[3] Although the medical establishment still considers animal testing necessary to ensure the safety of drugs and other substances,[4] courts of law are properly holding expert opinion

[1] K.S. Khera, *Teratogenic Effects of Methylmercury in the Cat: Note on the Use of This Species as a Model for Teratogenicity Studies*, 8 TERATOLOGY 293, 294 (1973).

[2] *See* Bourne v. E.I. du Pont de Nemours & Co., 189 F. Supp. 2d 482, 498 (S.D. W.Va. 2002) (explaining administration of pesticide in birth defects animal tests), *aff'd*, 85 F. App'x 964 (4th Cir. 2004).

[3] The Animal Welfare Act purportedly offers modest protection to animals used in laboratory testing. *See generally* Vasanth R. Shenai, Comment, *If Animal Rights Activists Could Write Federal Research Policy*, 4 ANIMAL L. 211, 214-215 (1998). However, the Animal Welfare Act does not cover mice, rats, or birds (these animals are excluded from the definition of "animal"). Katharine M. Swanson, Note, *Carte Blanche for Cruelty: The Non-Enforcement of the Animal Welfare Act*, 35 MICH. J. L. REFORM 937, 950 (2002). This exempts over 95% of research animals from protection. Shenai, *supra*, at 216. In addition, current regulations do not establish any minimum requirements of care in many situations. Swanson, *supra*, at 953-54.

[4] *See* UNITED STATES FOOD AND DRUG ADMINISTRATION, THE BEGINNINGS: LABORATORY

based on animal tests inadmissible to prove causation in birth-defects cases.[5]

Without question, birth defects are tragic.[6] A parent of a child born with defects will desperately search for answers.[7] It is natural for devastated parents to begin examining what they ate, drugs they took, and substances they were exposed to, in order to come up with a reason why they have suffered such a loss.[8]

To prove a particular substance caused a child's birth defects, the parent must prove that the substance in question can cause birth defects in humans generally.[9] Often, plaintiffs' experts will proffer animal studies that show a substance causes birth defects in animals, in an attempt to prove causation in humans.[10] This Comment examines the post-*Daubert* admissibility of such expert testimony in birth-defects cases at both the federal and state level, and it explores the resulting environmental policy issues.[11]

This Comment argues that courts should keep animal studies out of the courtroom in birth-defects toxic-torts cases. This will not only result in proper exclusion of unreliable evidence, but will also lead to valuable resources being directed to more worthy alternative tests, ultimately reducing human and animal suffering as birth defects are eradicated. Part I sets forth the evidentiary standards used to determine the admissibility of evidence and then presents background information on birth defects and how they are studied.[12] It also discusses the problems inherent with animal tests and the contrasting value of human data.[13] Part II explores the admissibility of animal studies in post-*Daubert* birth-

---

AND ANIMAL STUDIES, http://www.fda.gov/fdac/special/testtubetopatient/studies.html (last visited Feb. 3, 2006) (describing drug discovery process).

[5] *E.g.*, *Bourne*, 189 F. Supp. 2d at 501; Wade-Greaux v. Whitehall Labs., Inc., 874 F. Supp. 1441, 1482 (D.V.I. 1994), *aff'd*, 46 F.3d 1120 (3d Cir. 1994) (table).

[6] *See* Robert L. Brent, *Environmental Causes of Human Congenital Malformations: the Pediatrician's Role in Dealing With These Complex Clinical Problems Caused by a Multiplicity of Environmental and Genetic Factors*, 113 PEDIATRICS 957, 958 (2004).

[7] *Cf. id.* at 958.

[8] *Cf. id.* at 958, 964 (parents of children born with congenital malformations may suspect environmental exposure).

[9] *Cf.* Robert C. James, *Role of Toxicology in Toxic Tort Litigation: Establishing Causation*, 61 DEF. COUNS. J. 28, 30 (1994) (describing establishment of causation in toxic torts generally).

[10] *E.g.*, Daubert v. Merrell Dow Pharms., Inc., 43 F.3d 1311, 1314 (9th Cir. 1995); Castillo v. E.I. du Pont de Nemours & Co., 854 So. 2d 1264, 1267 (Fla. 2003).

[11] Much of the analysis below is also applicable to the admissibility of animal studies in other toxic-tort (e.g., cancer) cases, but those cases are outside the scope of this Comment.

[12] *See infra* notes 17-84 and accompanying text.

[13] *See infra* notes 85-142 and accompanying text.

defects cases and argues that exclusion is warranted.[14] Part II then urges redirection of resources to human studies and promising alternatives to animal tests, and it discusses the impact of excluding expert opinions based on animal tests from court cases.[15] Part III concludes by summarizing the case against admission of animal studies and the positives that would result from exclusion.[16]

I. BACKGROUND

A. ADMISSIBILITY OF SCIENTIFIC EVIDENCE

Scientific evidence, including expert testimony, is admitted into court hearings under two main evidentiary standards, known as the *Frye* and *Daubert* standards.[17] Federal courts follow the *Daubert* standard.[18] Just over half of all states have adopted the *Daubert* test in some form,[19] and the majority of remaining states follow the *Frye* standard of admissibility.[20]

1. The Frye "Generally Acceptable" Test

The short 1923 opinion in *Frye v. United States* concerned the admissibility of evidence derived from a crude precursor to the polygraph.[21] Frye was on trial for second-degree murder.[22] In his defense, he offered expert testimony claiming that results of a systolic blood pressure test showed he was being truthful when he denied committing the crime.[23] The trial court declined to admit the expert testimony and Frye was convicted.[24]

Upon appeal, the Court of Appeals for the District of Columbia

---

[14] *See infra* notes 143-231 and accompanying text.

[15] *See infra* notes 232-247 and accompanying text.

[16] *See infra* notes 248-252 and accompanying text.

[17] *See* Edward K. Cheng & Albert H. Yoon, *Does Frye or Daubert Matter? A Study of Scientific Admissibility Standards*, 91 VA. L. REV. 471, 471 (2005).

[18] *See id.* at 472 (noting that *Daubert* decision is legally binding on federal courts).

[19] David E. Bernstein & Jeffrey D. Jackson, *The Daubert Trilogy in the States*, 44 JURIMETRICS J. 351, 356 (2004).

[20] *Id.* at 355.

[21] Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 585 (1993). The polygraph is commonly referred to as a "lie detector." Michael D. Morgan, *Lying in the Heartland: Problems and Solutions Regarding Polygraph Evidence in Ohio Criminal Procedure*, 26 OHIO N.U. L. REV. 89, 91 (2000).

[22] Frye v. United States, 293 F. 1013, 1013 (D.C. Cir. 1923).

[23] *Id.*

[24] *Id.* at 1014.

Circuit affirmed the judgment, declaring, "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."[25] The court ultimately held that the systolic blood pressure deception test had "not yet gained such standing and scientific recognition among physiological and psychological authorities" and deemed the evidence inadmissible.[26]

This cryptic decision turned out to be one of the most debated in American jurisprudence.[27] Despite this debate, courts have generally interpreted the *Frye* test to consist of establishing whether a theory or technique has gained approval, or "general acceptance," of scientists in the relevant field.[28] Use of this standard allows courts to defer to the scientific community and avoid evaluating extremely technical or highly confusing information.[29] The *Frye* "general acceptance" test became "the dominant standard for determining the admissibility of novel scientific evidence at trial" and remained so for 70 years.[30]

2. *The Daubert Two-Prong Test*

Frye's dominance ended in 1993, when the United States Supreme Court announced a new standard for the admissibility of scientific evidence.[31] The *Daubert* decision created a more active role for federal courts, by requiring them to act as "gatekeepers" in determining whether scientific and other expert opinion evidence is admissible in court.[32]

In *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, infant plaintiffs alleged that Bendectin,[33] an anti-nausea drug, caused their birth defects.[34]

---

[25] *Id.*

[26] *Id.*

[27] Thomas Lyons, *Frye, Daubert, and Where Do We Go From Here?* 45 R.I.B.J. 5 (Jan. 1997) (noting that courts and commentators have debated over what constitutes "general acceptance" and how to define "particular field" and "relevant scientific community").

[28] *See* AMERICAN COLLEGE OF TRIAL LAWYERS, STANDARDS AND PROCEDURES FOR DETERMINING THE ADMISSIBILITY OF EXPERT EVIDENCE AFTER DAUBERT, *in* 157 F.R.D. 571, 571 (1994).

[29] *Id.* at 572.

[30] Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 585 (1993).

[31] *Id.* at 597.

[32] *Id.* at 589. As noted supra at note 19 and accompanying text, many states have adopted the *Daubert* test in some form; courts in those states must act as gatekeepers as well. Kamala London, Maggie Bruck, Stephen J. Ceci, & Daniel W. Shuman, *Disclosure of Child Sexual Abuse: What Does the Research Tell Us About the Ways That Children Tell?*, 11 PSYCHOL. PUB. POL'Y & L. 194, 219 (2005).

[33] Bendectin was prescribed to over 17 million women between 1957 and 1982. Daubert v. Merrell Dow Pharms., Inc., 43 F.3d 1311, 1313 (9th Cir. 1995).

[34] *Daubert*, 509 U.S. at 582.

To support this allegation, plaintiffs offered expert opinions based on animal tests, reanalysis of previously published epidemiological studies,[35] and other analyses.[36] The District Court for the Southern District of California granted defendant's motion for summary judgment, excluding plaintiffs' evidence because it did not meet the *Frye* "general acceptance" standard.[37]

The Court of Appeals for the Ninth Circuit declined to admit plaintiffs' expert testimony and affirmed the district court's judgment.[38] The court took issue with the experts' reanalysis of previously published studies.[39] The court found that this practice was generally accepted by the relevant scientific community only when subject to peer review; yet, plaintiff experts' reanalysis was not peer-reviewed.[40] Plaintiffs appealed, contending that the Federal Rules of Evidence[41] ("Rules," or "FRE" when referring to individual rules) superseded the *Frye* test.[42] The Supreme Court granted certiorari "in light of the sharp divisions among the courts regarding the proper standard for the admission of expert testimony."[43]

Since FRE 702 specifically governed expert testimony,[44] the adoption of the Rules played a large part in the "sharp divisions" among courts regarding what standard to use.[45] Federal judges began churning out a variety of decisions; some holding the new Rules incorporated the *Frye* standard, others holding the Rules established a new standard for the admissibility of scientific evidence, and yet others holding the Rules created a hybrid.[46]

The *Daubert* Court decided the issue by observing that nowhere in

---

[35] None of the more than 30 published epidemiological studies had found Bendectin to be teratogenic. *Id.*

[36] *Id.* at 583.

[37] *Id.*

[38] *Id.* at 584 (citing Daubert v. Merrell Dow Pharms., Inc., 951 F.2d 1128, 1131 (9th Cir. 1991)).

[39] *Id.*

[40] Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 584 (1993) (citing Daubert v. Merrell Dow Pharms., Inc., 951 F.2d 1128, 1131 (9th Cir. 1991)).

[41] Congress adopted the Federal Rules of Evidence in 1975. Pub. L. No. 93-595, § 1, 88 Stat. 1926 (1975).

[42] *Daubert*, 509 U.S. at 587.

[43] *Id.* at 585.

[44] The text of FRE 702 at the time *Daubert* was decided was as follows: "If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise." *Id.* at 588.

[45] *See* Lyons, *supra* note 27, at 6.

[46] *Id.*

the text of FRE 702 was "general acceptance" established as an absolute prerequisite to admissibility.[47] As the Supreme Court pointed out, the drafting history was also silent on the *Frye* test.[48] This silence on the part of the drafters, coupled with the permissive backdrop of the Rules, led the Court to find that "the *Frye* test was displaced by the Rules of Evidence."[49] However, this did not mean that the Rules placed no limits on the admissibility of scientific evidence.[50]

Based on its interpretation of FRE 702, the *Daubert* Court established gatekeeping requirements for federal courts.[51] Prior to admitting an expert scientific opinion, a federal court must make two determinations.[52] Under the first prong of the *Daubert* test, the court must determine whether the reasoning or methodology underlying the opinion is sufficiently reliable.[53] The *Daubert* Court equated reliability with trustworthiness.[54]

Under the second prong of the *Daubert* test, the court must determine whether the opinion is helpful to the trier of fact (whether it "fits" the facts of the case).[55] The *Daubert* Court gave an example of how the "fit" test works, noting that although knowledge of the phases of the moon may assist the trier of fact in ascertaining whether a certain night was dark, evidence that the moon was full on a certain night would not assist the trier of fact in determining whether an individual behaved irrationally on that night.[56]

To evaluate both the reliability and helpfulness of scientific evidence, the *Daubert* Court offered several non-exclusive factors for courts to consider.[57] One factor was whether a theory or technique can be or has been tested.[58] Another factor was whether such theory or technique has been subjected to peer review and publication.[59] The remaining factors were the known or potential rate of error of the theory

---

[47] *Daubert*, 509 U.S. at 588.

[48] *Id.*

[49] *Id.* at 589. The court ultimately remanded the case back to the Ninth Circuit. *Id.* at 598. The Ninth Circuit excluded plaintiff's experts under the second, "fitness" prong of the *Daubert* test. Daubert v. Merrell Dow Pharms., Inc., 43 F.3d 1311, 1322 (9th Cir. 1995).

[50] *Daubert*, 509 U.S. at 589.

[51] *Id.*

[52] *Id.* at 589-91.

[53] *Id.* at 589-90.

[54] *Id.* at 590 n.9.

[55] *Id.* at 591.

[56] Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 591 (1993).

[57] *Id.* at 593-94.

[58] *Id.* at 593.

[59] *Id.*

or technique, and whether the theory or technique is generally accepted[60] in the relevant scientific community.[61]

As seen with *Frye*, the *Daubert* opinion sparked much debate.[62] Nevertheless, *Daubert* is considered one of the most important evidence cases ever decided.[63]

B. SUITABILITY OF ANIMAL DATA TO PROVE A SUBSTANCE CAUSES BIRTH DEFECTS IN HUMANS

1. Occurrence and Causes of Birth Defects

Out of every 1,000,000 pregnancies, 30,000 result in severe congenital malformations.[64] In the United States alone, 120,000 newborns are born with severe birth defects each year.[65] Medical experts attribute 15-25% of human congenital malformations observed during the first year of life to genetic causes and estimate that 65-75% have an unknown cause.[66] Experts suspect that environmental conditions cause the remaining 10%, with less than 1% of the overall total attributed to prescription drugs, other chemicals, high-dose ionizing radiation, and hyperthermia.[67]

Although external agents are thought to cause only 10% of congenital anomalies, the resulting birth defects compromise the quality of life of millions of people and rack up health-care costs totaling billions of dollars every year.[68] Unsurprisingly, study in this area "continues to be a burgeoning area of medical research in the quest for the eradication of preventable birth defects."[69]

---

[60] The *Daubert* court acknowledged that general acceptability, although not required, was still a relevant factor for courts to consider. *Id.* at 594.

[61] *Id.*

[62] *See generally* Bernstein & Jackson, *supra* note 19, at 352 (discussing debate over whether *Daubert* was more or less permissive than *Frye*).

[63] Paul L. Giannelli, *Daubert Revisited*, 41 No. 3 CRIM. L. BULL. 5 (2005).

[64] Brent, *supra* note 6, at 958. A congenital malformation is a physical defect present at birth, due to a problem with development of a structure during the embryonic state. Examples of severe congenital malformations include cleft palate, spina bifida, and limb reduction. MedicineNet.com, Definition of "congenital malformation," http://www.medterms.com/script/main/art.asp?articlekey=2820 (last visited Feb. 5, 2006).

[65] Brent, *supra* note 6, at 958.

[66] *Id.* at 959.

[67] *Id.*

[68] Jarrod Bailey, Andrew Knight, & Jonathan Balcombe, *The Future of Teratology Research is In Vitro*, 19 BIOGENIC AMINES 97, 97-98 (2005).

[69] *Id.* at 97.

2. *Teratology*

Teratology is the study of birth defects caused by external chemical or physical agents.[70] A teratogen is "[a] substance (chemical, virus, or radiation) that can cause malformations in an embryo or fetus."[71] The science of teratology began in the 1920s and 30s, when pigs fed high-fat or vitamin A-deficient experimental diets gave birth to malformed piglets.[72]

To evaluate substances for teratogenicity (the ability to cause birth defects), teratologists[73] study human epidemiological data and conduct toxicological experiments to study suspected teratogens.[74] Teratologists conduct both *in vivo* (using live animals) and *in vitro* (using animal or human cells in a test tube or similar media) experiments.[75]

During a typical *in vivo* animal toxicology experiment, a range of doses of a particular substance is given to animals, and the outcomes are compared to those of control animals.[76] The administration of the substance can take several forms, including oral ingestion, injection under the skin, and injection into the stomach of the animal.[77] Mice, rats, and rabbits are the animals most commonly experimented on.[78] Cats, dogs, ferrets, pigs, and even non-human primates, such as monkeys, are also used.[79] In order to control costs and ensure sufficient adverse responses, toxicologists usually expose animals to high doses of the

---

[70] *Id.*

[71] American Chemical Society Glossary of Green Chemistry Terms, http://www.chemistry.org/portal/a/c/s/1/acsdisplay.html?DOC=greenchemistryinstitute%5cglossary_mz.html (last visited Feb. 5, 2006).

[72] Bailey, Knight, & Balcombe, *supra* note 68, at 98. The piglets predominantly suffered lack of eyes. *Id.*

[73] Scientists who study teratology. *See* Merriam-Webster Medline Plus online Medical Dictionary, http://www2.merriam-webster.com/cgi-bin/mwmednlm?book=Medical&va=teratologist (last visited Feb. 20, 2006).

[74] *Cf.* Robert L. Brent and David A. Beckman, *Teratogens*, in ENCYCLOPEDIA OF REPRODUCTION, Volume 4, 735 (Ernst Knobil ed., 1999); EXPERIMENTAL TOXICOLOGY: THE BASIC ISSUES 220-21 (Diana Anderson and D.M. Conning eds., Royal Society of Chemistry 2d ed. 1993).

[75] *See* Robert L. Brent, *Utilization of Animal Studies to Determine the Effects and Human Risks of Environmental Toxicants (Drugs, Chemicals, and Physical Agents)*, 113 PEDIATRICS 984, 987 (2004). For the remainder of this Comment, the terms "animal studies," "animal tests," and "animal experiments" shall refer to *in vivo* studies, unless otherwise noted.

[76] Bailey, Knight, & Balcombe, *supra* note 68, at 101.

[77] *See generally id.* at 120.

[78] *Id.* at 101.

[79] *See id.* at 102; Jack L. Landau & W. Hugh O'Riordan, *Of Mice and Men: The Admissibility of Animal Studies to Prove Causation in Toxic Tort Litigation*, 25 IDAHO L. REV. 521, 533 (1989).

substance under study.[80]

After the animal experimentation phase of an *in vivo* study is complete, the data obtained is entered into a mathematical model to predict how humans might respond to the substance.[81] Researchers first compute the animal dose-response relationship based on the typically high-dose data.[82] Next, they scale the animal data to estimate the human dose-response relationship at the higher doses.[83] Researchers then attempt to extrapolate downward using complex biostatistical calculations to estimate the dose-response relationship in humans at lower levels of exposure.[84]

3. *Validity of the Extrapolation from Animal Studies to Show Teratogenicity in Humans*

a. Problems with Extrapolating from Animals to Humans

It is unreliable to extrapolate from animal studies that show a substance causes birth defects in animals to prove the substance causes birth defects in humans.[85] Extrapolation from animal experiments to humans has distinct disadvantages.[86] For example, species differ in their susceptibility to the formation of birth defects.[87] Within a species of animal, susceptibility varies further among different strains, individuals, and phenotypes.[88]

Predicting human teratogenicity based on animal tests is further confounded by differences in dosage levels and routes of administration of a substance.[89] In addition, the stress of laboratory handling, which can

---

[80] Bert P. Krages II, Comment, *Rats in the Courtroom: The Admissibility of Animal Studies in Toxic Tort Cases*, 2 J. ENVTL. L. & LITIG. 229, 241-42 (1987).

[81] *Id.* at 233.

[82] *Id.* at 242.

[83] *Id.* Scaling is typically premised on body weight or surface area. *Id.* at 240.

[84] *Id.* at 242.

[85] *See* David E. Bernstein, *The Admissibility of Scientific Evidence After Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 15 CARDOZO L. REV. 2139, 2176 (1994) (noting that just because a substance is found to be teratogenic in animals does not mean it causes similar effects in humans).

[86] *See* REFERENCE MANUAL ON SCI. EVIDENCE 346 (Fed. Jud. Center, 2d ed. 2000) (noting differences in absorption, metabolism and other factors and problems with extrapolating from high dosage studies).

[87] Janine E. Polifka & J.M. Friedman, *Clinical Teratology: Identifying Teratogenic Risks in Humans*, 56 CLINICAL GENETICS 409, 416 (1999); *see also* Krages, *supra* note 80, at 236 (discussing interspecies variability with animal studies generally).

[88] Bailey, Knight, & Balcombe, *supra* note 68, at 138. Phenotypes are the physical and physiological traits of an organism. NEIL A. CAMPBELL, BIOLOGY G-16 (4th ed. 1996); *see also* Landau & O'Riordan, *supra* note 79, at 541-42; Krages, *supra* note 80, at 236.

[89] Joe G. Hollingsworth & Eric G. Lasker, *The Case Against Differential Diagnosis:*

impair animal health, can also skew the outcomes of birth-defects testing.[90] Anatomical differences between laboratory animals and humans, along with differences in the absorption, excretion, and metabolism of a substance, can also affect results.[91] Moreover, animal tests can miss more subtle signs of birth defects like learning or behavioral difficulties.[92]

b. Arguments for Using Animal Studies

Because of the inherent problems with animal tests, few people claim that animal tests are reliable enough to establish legal causation.[93] Nevertheless, some commentators tout the ability of researchers to isolate the effects of exposure and control all aspects of the animals' lives,[94] and one even claims that animal studies are preferable to human

Daubert, Medical Causation Testimony, and the Scientific Method, 37 J. HEALTH L. 85, 93 (2004) (observing that a high-dose study resulting in adverse effects in animals cannot be extrapolated into a scientifically reliable conclusion that the substance can cause such effects in humans at normal exposure levels and that because of the routes of administration used in animal studies, they do not reflect real-world risks and cannot be extrapolated); REFERENCE MANUAL ON SCI. EVIDENCE, *supra* note 86, at 346; *see also* Bernstein, *supra* note 85, at 2173 (stating high dose animal studies have little relevance in toxic suits alleging causation in humans); Brent & Beckman, *supra* note 74, at 742; Polifka & Friedman, *supra* note 87, at 416.

[90] Bailey, Knight, & Balcombe, *supra* note 68, at 138.

[91] Brent, *supra* note 75, at 988; *see also* REFERENCE MANUAL ON SCI. EVIDENCE, *supra* note 86, at 346; Krages, *supra* note 80, at 235; James, *supra* note 9, at 30. Body weight, surface area, or other bases of extrapolating from animals to humans do not adequately account for the significant physiological, metabolic, excretive and absorptive differences between animals and humans. Landau & O'Riordan, *supra* note 79, at 547.

[92] Bailey, Knight, & Balcombe, *supra* note 68, at 100; *see also* REFERENCE MANUAL ON SCI. EVIDENCE, *supra* note 86, at 420 (noting difficulty of testing for nonspecific human symptoms such as nausea, headache, and weakness in animals).

[93] Bernstein, *supra* note 85, at 2173 (noting that "with exception of a few on the fringe," scientists agree that high-dose animal studies are not reliable for determining harm to humans from low-dose exposures). For examples of such individuals, *see, e.g.,* Carl Cranor, *Scientific Interferences in the Laboratory and the Law*, 95 AM. J. PUB. HEALTH (SUPPLEMENT) S121, S122 (2005); Erica Beecher-Monas, *A Ray of Light for Judges Blinded by Science: Triers of Science and Intellectual Due Process*, 33 GA. L. REV. 1047, 1066-67 (1999) (urging that high-dosage extrapolations from animals provide realistic indications of human causal relationships). For example, Beecher-Monas states that differences in routes of administration are irrelevant, because "if one accounts for solubility differences, the route of exposure makes little difference." Erica Beecher-Monas, *The Heuristics of Intellectual Due Process: A Primer for Triers of Science*, 75 N.Y.U. L. REV. 1563, 1620 (2000). This is contrary to other authorities, *e.g.,* Polifka & Friedman, *supra* note 87, at 410 (noting that route of exposure is important since it affects absorption of substance).

[94] *See, e.g.,* Michael D. Green, *Expert Witnesses and Sufficiency of Evidence in Toxic Substances Litigation: The Legacy of Agent Orange and Bendectin Litigation*, 86 NW. L. REV. 643, 654 (1992); REFERENCE MANUAL ON SCI. EVIDENCE, *supra* note 86, at 345, 414.

studies because of this.[95] However, because human exposures are typically variable and intermittent, aspects not replicated in animal tests, "the exposure experience in animals, although well controlled and measured, is a poor representation of human exposure scenarios."[96] Furthermore, although exposure dose, other environmental factors, and genetic conditions can be controlled in animal studies, there is still the problem of extrapolating across species, from animals to humans, which is a very uncertain process.[97]

Some scientists and policy-makers justify extrapolation from animal studies simply on the basis that it is often the only information available.[98] Several commentators, even while acknowledging the limitations of animal tests, have adopted this rationale in urging the admissibility of expert opinions based on such tests when human data is scarce or not available.[99] However, simply because animal studies are the only evidence or the best evidence available in a case does not make them admissible under *Daubert*; the evidence must still be reliable and fit the facts of the case.[100] Moreover, this argument would not work with other types of evidence. For example, it is unlikely that a court would find admissible a crude test that detected a particular controlled

---

[95] Beecher-Monas, *The Heuristics of Intellectual Due Process: A Primer for Triers of Science*, 75 N.Y.U. L. REV. 1563, 1608 (2000); Erica Beecher-Monas, *A Ray of Light for Judges Blinded by Science: Triers of Science and Intellectual Due Process*, 33 GA. L. REV. 1047, 1065 (1999).

[96] Irva Hertz-Picciotto, *Epidemiology and Quantitative Risk Assessment: A Bridge from Science to Policy*, 85 AM. J. PUB. HEALTH 484, 485 (1995).

[97] LEON GORDIS, EPIDEMIOLOGY 184 (2d ed. 2000).

[98] Bernstein, *supra* note 85, at 2174; *see, e.g.*, Robert M. Sussman, *Science for Judges II: The Practice of Epidemiology and Administrative Agency Created Science: Science and EPA Decision-Making*, 12 J.L. & POL'Y 573, 584 (2004) (noting rationale for making chemical safety decisions based on animal studies); Krages, *supra* note 80, at 245 (commenting on political pressure forcing regulators to rely on animal studies in absence of better alternatives). In fact, reliance on animal studies is so engrained, despite wide recognizance of their drawbacks and lack of reliability, that some researchers insist on using animals even when adverse human effects are well known. *E.g.*, Theodore A. Slotkin, *Fetal Nicotine or Cocaine Exposure: Which One Is Worse?*, 285 J. PHARMACOLOGY & EXPERIMENTAL THERAPEUTICS 931, 933 (1998) (claiming animal studies on the effects of nicotine are needed despite knowledge of the adverse effects of smoking on pregnancy).

[99] *See, e.g.*, Erica Beecher-Monas, *A Ray of Light for Judges Blinded by Science: Triers of Science and Intellectual Due Process*, 33 GA. L. REV. 1047, 1065-66 (1999) (recognizing complex issues involved with extrapolation, but advocating admissibility of animal studies since they are often the primary source of information regarding health effects of chemicals with so few good human studies available); REFERENCE MANUAL ON SCI. EVIDENCE, *supra* note 86, at 405 (stating that ability of animal experiments to accurately predict human responses to chemical exposures is subject to debate, yet noting they provide "best" information in absence of human data). *Cf.* Sabrina Strawn & Marvin S. Legator, *Epidemiology and Toxic Torts: Animal Studies Yield Valid Insights*, TRIAL, Apr. 1991, at 60, 63 (calling for acceptance of animal data in toxic torts cases because human proof might not be available).

[100] Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 589-91 (1993).

substance with only 50% accuracy merely because it was the only test available for detecting such drug.

c. Quantification of the Poor Predictability of Animal Tests

In 2005, a comprehensive, systematic study of existing animal birth-defects data, *The Future of Teratology Research is In Vitro*, examined and quantified the poor predictability of animal tests.[101]

The study's authors, Bailey, Knight, and Balcombe, scrutinized existing animal data and evaluated the agreement between animal results and known effects in humans for a variety of substances.[102] They determined both positive predictability, the percentage of known human teratogens that caused birth defects in animals, and negative predictability, the percentage of known human non-teratogens that did not cause birth defects in animals.[103] The study also looked at inter-species variability.[104]

The results exposed the wide discrepancies found between animal and human teratogenicity.[105] For example, an analysis of responses of 12 different animal species to 11 groups of known human teratogens showed great disarray in the data.[106] Positive predictability ranged from 40% to 75% for any individual animal species.[107] A similar analysis of 35 substances linked with human birth defects showed that only 56% of 139 individual combinations of animal species and substances were positive.[108]

The study also discussed a Food and Drug Administration ("FDA") report that analyzed responses of mice, rats, rabbits, hamsters, and monkeys to 38 known human teratogens and likewise showed low predictability, with a mean of only 60% for correct positives from any one of these species.[109] These analyses indicate that at least 40% of

---

[101] Bailey, Knight, & Balcombe, *supra* note 68.

[102] *Id.* at 105.

[103] *Id.*

[104] *Id.* at 105, 110.

[105] *Id.* Large discrepancies between different animal species were also revealed. *Id.*

[106] Bailey, Knight, & Balcombe, *supra* note 68, at 105.

[107] *Id.*

[108] *Id.*

[109] Bailey, Knight, & Balcombe, *supra* note 68, at 105 (analyzing United States Food and Drug Administration Caffeine: Deletion of GRAS Status, Proposed Declaration that no Prior Sanction Exists, and Use on an Interim Basis Pending Additional Study, 45 Fed. Reg. 69,817, 69,823 (proposed Oct. 20, 1980) [hereinafter FDA Report]). The FDA report was part of a Federal Register notice announcing that the FDA was proposing to remove caffeine from a list of substances considered safe. This proposal was based on FDA's findings that caffeine caused teratogenic effects in animals. The proposal was later withdrawn. Withdrawal of Certain Proposed Rules and Other

known human teratogens would not be identified via animal tests.

In addition, the FDA report evaluated the responses of different animal species to 165 compounds known not to cause birth defects in humans.[110] As determined by Bailey *et al.*, the FDA report showed a mean negative predictive value of 54% for any of these species.[111] Combined with the positive predictive value of 60% for known human teratogens, this results in a mean value of 57%, "little better than the 50% that would have been obtained by pure chance."[112]

The unreliability of animal tests in predicting human birth defects is further demonstrated by taking into account all substances for which some birth-defects data, both positive and negative, has been determined in animals. Bailey *et al.*'s analysis of 1,396 individual substances tested in more than one animal species revealed that 30% demonstrated discordance (a mixture of positive, equivocal and negative results).[113] This kind of variability is not useful for predicting human birth defects.[114] Further demonstrating the poor predictability of animal experiments, Bailey *et al.* found that fewer than 2.3% of 1,223 animal teratogens characterized as definite, probable, and possible were linked to human birth defects.[115]

d. Why Extrapolation from Animals to Humans is the Relevant Direction to Analyze

The FDA report's trumpeting that 37 of 38 animal studies conducted on known human teratogens showed a positive result in at least one animal species is of dubious merit.[116] It seems logical that if a substance, already known to cause birth defects in humans, is tested on enough animal species, eventually one species is bound to exhibit birth defects.[117] Indeed, the validity of established animal-based methods is questionable, considering that such benign substances as water, table salt,

---

Proposed Actions, 69 Fed. Reg. 68,831, 68,835-36 (Nov. 26, 2004).

[110] Bailey, Knight, & Balcombe, *supra* note 68, at 105 (citing FDA Report, *supra* note 109, at 69,823).

[111] *Id.* at 110 (analyzing FDA Report, *supra* note 109, at 69,823). The analysis also showed little agreement between the negative predictive value and positive predictive value for a single species. *Id.* at 105 (analyzing FDA Report, *supra* note 109, at 69,823).

[112] Bailey, Knight, & Balcombe, *supra* note 68, at 110.

[113] *Id.*

[114] *Id.* at 105.

[115] *Id.* at 113.

[116] Bailey, Knight, & Balcombe, *supra* note 68, at 110 (discussing FDA Report, *supra* note 109, at 69,823).

[117] Bailey, Knight, & Balcombe, *supra* note 68, at 110.

and sugar have been found to cause birth defects in animals using such methods.[118] Besides, retrospective finding of birth defects in animals after they have already been documented in humans does not validate extrapolation in the relevant direction, from animals to humans.[119]

The tragedy of thalidomide demonstrates why extrapolation from animals to humans (as opposed to extrapolation from humans to animals) is significant.[120] Thalidomide is a sedative that doctors prescribed to pregnant women, for the purposes of controlling nervousness and nausea, in the 1950s.[121] When women used the drug during the fifth and sixth weeks of pregnancy, many of their children were born with birth defects, mostly missing or shortened limbs.[122] Later testing on pregnant animals, performed in the early 1960's on pregnant mice, rats and guinea pigs, revealed no birth defects in offspring.[123]

Subsequent testing of thalidomide on other animals demonstrated extreme variability between species; thalidomide caused birth defects in some but not in others.[124] Despite the failure of animal tests to predict human thalidomide birth defects, it is widely believed that the thalidomide tragedy prompted regulatory agencies such as the FDA to direct that new drugs be tested on animals prior to approval for marketing.[125]

4. Need for Human Data in Order to Prove Causation of Birth Defects

Although extrapolation from animals to humans is the goal of birth-defects animal testing, virtually every substance currently recognized as a human teratogen was initially identified because of human data.[126] Scientists would understandably prefer not to rely upon human birth-defects data to derive an "after the event" classification.[127] However, human data is still the most powerful and reliable way to determine the teratogenic potential of substances, despite the large amount of animal-based information generally available.[128]

---

[118] *Id.* at 138.

[119] *Id.* at 110; *see also* James, *supra* note 9, at 30 ("To know whether it is valid to extrapolate from a particular animal species to human beings requires prior knowledge of both outcomes.").

[120] *See* Krages, *supra* note 80, at 235-36.

[121] Bailey, Knight, & Balcombe, *supra* note 68, at 124.

[122] *Id.* at 125.

[123] *Id.*

[124] *Id.*

[125] *Id.* at 98.

[126] Polifka & Friedman, *supra* note 87, at 416.

[127] Bailey, Knight, & Balcombe, *supra* note 68, at 126.

[128] *Id.*; *see also* Brent, *supra* note 75, at 987.

Human data is obtained primarily through epidemiological studies.[129] Epidemiology is the study of the distribution of disease in human populations and the factors that influence or cause this distribution.[130] Epidemiologists observe the differences (if any) between people who have had a particular environmental exposure with those who have not.[131] By studying data obtained from such observations, epidemiologists can discover associations between environmental exposures and diseases or other adverse health effects.[132] Epidemiologists employ statistical analysis to evaluate the significance of observed associations.[133]

Although epidemiological studies are widely recognized as the best way to determine human health effects,[134] they are not without drawbacks.[135] Designing and conducting sound epidemiological studies is difficult, costly, and time-consuming.[136] In addition, human exposures can occur to many agents simultaneously, making it difficult to isolate the increased risk due to any one substance.[137] Some commentators further criticize epidemiological studies because they are not controlled experiments.[138] Despite these limitations, epidemiological studies are much preferable to animal studies, since "[t]he uncertainty stemming from interspecies extrapolation is far larger than the uncertainty resulting from uncontrolled bias or errors in exposure information in epidemiological studies."[139]

Credited with the initial unearthing of almost all known human teratogens, epidemiology has been the critical factor in the identification and characterization of agents that cause birth defects in humans.[140] The

---

[129] *Cf.* Landau & O'Riordan, *supra* note 79, at 530 (comparing clinical studies and case reports, other sources of human data, with epidemiological studies in toxics torts context).

[130] Gordis, *supra* note 97, at 3.

[131] *Id.* at 159.

[132] *Id.*

[133] *Cf. id.* at 160 (calculation of relative risk).

[134] *See, e.g.*, Brent, *supra* note 75, at 984 (deeming epidemiological studies "the best method for determining human risk and the effects of environmental toxicants"); Bernstein, *supra* note 85, at 2166 (touting epidemiological data as "by far the best evidence that can be presented on the issue of whether a substance causes human health effects").

[135] *See, e.g.*, REFERENCE MANUAL ON SCI. EVIDENCE, *supra* note 86, at 346; Polifka & Friedman, *supra* note 87, at 413.

[136] Beecher-Monas, *supra* note 99, at 1065 (1999); REFERENCE MANUAL ON SCI. EVIDENCE, *supra* note 86, at 346.

[137] Polifka & Friedman, *supra* note 87, at 413; *see also* REFERENCE MANUAL ON SCI. EVIDENCE, *supra* note 86, at 405.

[138] *See, e.g.*, Cranor, *supra* note 93, at S124.

[139] Hertz-Picciotto, *supra* note 96, at 485.

[140] Bailey, Knight, & Balcombe, *supra* note 68, at 126; Brent & Beckman, *supra* note 74, at

importance of human data is recognized in the Teratology Society Public Affairs Committee's recently released position paper on Causation in Teratology-Related Litigation, which asserts, "[h]uman data are required for conclusions that there is a causal relationship between an exposure and an outcome in humans."[141] Moreover, according to a prominent teratologist, "human epidemiologic surveillance by various methods is and will be our most powerful tool for discovering human reproductive toxins and teratogens."[142]

II. ANALYSIS/DISCUSSION

A. THE MAJORITY OF *DAUBERT* COURTS HOLD BIRTH DEFECTS CAUSATION TESTIMONY BASED ON ANIMAL STUDIES INADMISSIBLE

A survey of federal and state courts shows that the *Daubert* two-prong test compels exclusion of expert opinions based on animal studies from causation determinations in birth-defects cases.[143] Post-*Daubert*, the majority of federal courts have kept animal tests out of the courtroom in birth-defects cases,[144] as has the one state court following *Daubert* that has published an opinion addressing the admissibility of opinions based on animal tests in a birth-defects case.[145]

Some *Daubert* courts have explicitly applied the *Daubert* factors, discussed *supra*, and determined that animal studies are unreliable[146] and

741; *see also* Oxendine v. Merrell Dow Pharms., Inc., Civ. No. 82-1245, 1996 WL 680992, at *7 (D.C. Super. Ct. Oct. 24, 1996) ("The overriding significance of epidemiological studies (human data) in determining human teratogenicity has been accepted judicially and scientifically.").

[141] Public Affairs Committee of the Teratology Society, *Teratology Society Public Affairs Committee Position Paper: Causation in Teratology-Related Litigation*, 73 BIRTH DEFECTS RES. (PART A) 421, 423 (2005); *see also* Gordis, *supra* note 97, at 185 (stating observations in human populations are needed to draw a conclusion as to whether a substance causes disease in humans).

[142] Brent, *supra* note 75, at 987.

[143] Raynor v. Merrell Pharms. Inc., 104 F.3d 1371, 1377 (D.C. Cir.1997); Lust v. Merrell Dow Pharms., Inc., 89 F.3d 594, 598 (9th Cir.1996); Daubert v. Merrell Dow Pharms., Inc., 43 F.3d 1311, 1322 (9th Cir. 1995) [hereinafter *Daubert II*, in short form]; Sorensen v. Shaklee Corp., 31 F.3d 638, 650 (8th Cir.1994); Elkins v. Richardson-Merrell, Inc., 8 F.3d 1068, 1073 (6th Cir. 1993); Bourne v. E.I. du Pont de Nemours & Co., 189 F. Supp. 2d 482, 501 (S.D. W.Va. 2002), *aff'd*, 85 F. App'x 964 (4th Cir. 2004); National Bank of Commerce v. Dow Chem. Co., 965 F. Supp. 1490, 1530 (E.D. Ark. 1996), *aff'd*, 133 F.3d 1132 (8th Cir. 1998); Wade-Greaux v. Whitehall Labs., Inc., 874 F. Supp. 1441, 1482 (D.V.I. 1994), *aff'd*, 46 F.3d 1120 (3d Cir. 1994) (table); Merrell Dow Pharms., Inc. v. Havner, 953 S.W.2d 706, 730 (Tex. 1997).

[144] *Raynor*, 104 F.3d at 1377; *Lust*, 89 F.3d at 598; *Daubert II*, 43 F.3d at 1322; *Sorensen*, 31 F.3d at 650; *Elkins*, 8 F.3d at 1073; *Bourne*, 189 F. Supp. 2d at 501; *National Bank of Commerce*, 965 F. Supp. at 1530; *Wade-Greaux*, 874 F. Supp. at 1482.

[145] *Havner*, 953 S.W.2d at 730.

[146] *E.g.*, *Lust*, 89 F.3d at 597 (not peer reviewed or generally acceptable); *Sorensen*, 31 F.3d at

a poor fit[147] to show causation of human birth defects. Other courts have made the same determinations without explicit discussion of the *Daubert* factors.[148] *Daubert* courts have also used insufficiency of evidence as a basis to exclude animal experiments.[149]

These courts have properly recognized the problems, discussed *supra*, with using animal studies to prove causation of human birth defects.[150] The meager statistical predictability of such animal tests substantiates that these courts have correctly excluded opinions based on animal studies.[151] It is thus unsurprising that only a small minority of federal courts since *Daubert* have admitted expert opinions based on animal studies to prove human causation in birth-defects cases.[152]

Some *Daubert* courts, although excluding opinions based on animal tests because of unreliability or poor fit, qualified their exclusions with comments regarding the paucity of corroborating epidemiological data.[153] Whether this qualification is sound will be examined *infra*.

1. Under Daubert, Courts Find Animal Studies Unreliable

Numerous *Daubert* courts, recognizing the inherent unreliability of extrapolation from animal studies to humans, have excluded expert opinions on that basis.[154] *Wade-Greaux v. Whitehall Laboratories, Inc.*,

649 (not tested or subject to peer review; no evidence of general acceptability in the relevant scientific community); *Wade-Greaux*, 874 F. Supp. at 1478-80 (high rate of error, not peer reviewed, and not generally acceptable).

[147] *Daubert II*, 43 F.3d at 1314, 1318 (plaintiff experts' opinions not peer reviewed nor published, and not reflective of consensus in scientific community).

[148] *Bourne*, 189 F. Supp. 2d at 499; *National Bank of Commerce*, 965 F. Supp. at 1527. While courts religiously applied the *Daubert* factors in the first few years after *Daubert*, judges are increasingly moving away from that practice, instead addressing the "broader, bottomline question of the reliability of the evidence." Edward J. Imwinkelried, *Expert Witness: A 'Daubert' Checklist*, NAT'L L.J., Sept. 12, 2005, at 12.

[149] *Sorensen*, 31 F.3d at 651; *Wade-Greaux*, 874 F. Supp. at 1485; *Havner*, 953 S.W.2d at 730; *accord Elkins*, 8 F.3d at 1073.

[150] *See supra* notes 85-125 and accompanying text.

[151] *See supra* notes 101-115 and accompanying text.

[152] Ambrosini v. Labarraque, 101 F.3d 129, 136-37 (D.C. Cir.1996); Dyson v. Winfield, 113 F. Supp. 2d 44, 51 (D. D.C. 2000).

[153] *E.g., Bourne*, 189 F. Supp. 2d at 496; *Wade-Greaux*, 874 F. Supp. at 1480. One *Frye* court has also qualified exclusion of animal studies in a similar manner. DePyper v. Navarro, No. 83-303467-NM, 1995 WL 788828, at *32 (Mich. Cir. Ct. Nov. 27, 1995), *aff'd*, No. 191949, 1998 WL 1988927 (Mich. Ct. App. Nov. 6, 1998).

[154] *E.g., Sorensen*, 31 F.3d at 650 (plaintiffs' testimony not derived from a reliable methodology); National Bank of Commerce v. Dow Chem. Co., 965 F. Supp. 1490, 1527 (E.D. Ark. 1996), *aff'd*, 133 F.3d 1132 (8th Cir. 1998) (noting that with 1200 teratogens identified in various animal species but only 40 in humans, a prediction based on animal studies would be erroneous 96% of the time); *Havner*, 953 S.W.2d at 729 (predictability of experts' animal studies unreliable).

provides a good example of this reasoning.[155] Plaintiffs offered expert opinions to prove that the nasal decongestant Primatene Mist caused limb defects.[156] Their opinions were based in part on rabbit tests that had resulted in some malformations in rabbit offspring.[157] The *Wade-Greaux* court found that it was scientifically invalid to extrapolate observations in animal experiments directly to human beings to determine human teratogenicity, and the court declined to admit the opinions.[158] Observing that there are a large number of agents that have been shown to be teratogenic in some animal species, but very few proven human teratogens, the court remarked that even "sugar and table salt have been shown to be teratogenic in some animal species."[159]

Noting that the rabbits were administered doses of Primatene Mist that were two to five times what a human would normally take based on body weight,[160] the *Wade-Greaux* court found that high-dosage animal tests were not reliable to determine whether a substance causes birth defects in humans at therapeutic doses.[161] Other *Daubert* courts have similarly found that extrapolations from high-dose animal studies to humans are unreliable.[162] However, replacing high-dose animal studies with low-dose animal studies would not make extrapolations to humans any more reliable. Courts have recognized that other factors besides high dosages make extrapolation unreliable. For example, courts have noted that inter-species differences in maternal metabolism can affect whether a substance causes birth defects, as can the stress of animal tests.[163]

Extrapolation from single-species animal experiments to humans has also troubled courts, and they have held this practice to be unreliable.[164] However, using more animal species to test a substance for birth defects is not the answer. Courts have found that extrapolation

---

[155] *Wade-Greaux*, 874 F. Supp. at 1453.

[156] *Id.* at 1448.

[157] *Id.* at 1460.

[158] *Id.* at 1453.

[159] *Id.*

[160] *Id.* at 1471.

[161] Wade-Greaux v. Whitehall Labs., Inc., 874 F. Supp. 1441, 1454 (D.V.I. 1994) (acknowledging Karnofsky's Law, a principle of teratology that recognizes that at a high enough dose, any substance can be teratogenic), *aff'd*, 46 F.3d 1120 (3d Cir. 1994) (table).

[162] *E.g.*, National Bank of Commerce v. Dow Chem. Co., 965 F. Supp. 1490, 1527 (E.D. Ark. 1996) (large doses used in animal tests ordinarily preclude extrapolation to humans), *aff'd*, 133 F.3d 1132 (8th Cir. 1998).

[163] *See id.*; *Wade-Greaux*, 874 F. Supp. at 1454.

[164] *E.g.*, Bourne v. E.I. du Pont de Nemours & Co., 189 F. Supp. 2d 482, 496 (S.D. W.Va. 2002) (holding extrapolations from high-dosage, single-species testing neither reliable nor relevant to determine if pesticide Benlate causes human birth defects), *aff'd*, 85 F. App'x 964, 967 (4th Cir. 2004).

from multi-species tests is no less troubling and have excluded opinions based on multi-species tests as unreliable as well.[165] Multi-species tests were evidently no more persuasive than their single-species counterparts in overcoming the inherent problems with extrapolation to humans, such as inter-species, physiological, and metabolic differences, discussed *supra*.[166]

2. *Under Daubert, Courts Find Animal Studies Are a Poor Fit*

In addition to requiring that scientific evidence be reliable, the *Daubert* Court stated that it must also "fit" the facts at issue in a case.[167] Expert opinions based on animal studies fail this prong of the *Daubert* test too. Federal and state courts have not only found opinions based on animal experiments to be unreliable; they have also excluded opinions based on animal tests because they do not fit the issue of causation in birth-defects cases.[168]

In particular, courts have pointed out that the dosages and routes of administration used in animal studies lead to a poor fit between such studies and human birth-defects cases.[169] For example, the court in *Bourne v. E. I. du Pont de Nemours & Co.* observed that although plaintiffs claimed dermal exposure to low levels of a pesticide caused birth defects, the rat tests on which that claim was based involved administration of high doses of the pesticide via stomach tube.[170] The court found the analytical gap between the rat experiments relied upon and the inferences the experts drew to be too wide, "rendering the extrapolation a poor 'fit' for the facts of the case."[171]

The court in *National Bank of Commerce v. Dow Chemical Co.* similarly excluded animal studies because they did not fit the plaintiffs' case.[172] The court noted that the method of administration in the animal

---

[165] *See* Lust v. Merrell Dow Pharms., Inc., 89 F.3d 594, 596, 598 (9th Cir.1996) (excluding expert opinion partly based on animal studies reporting fertility drug to be teratogenic in four species of animals); Sorensen v. Shaklee Corp., 31 F.3d 638, 644 (8th Cir.1994) (rejecting plaintiff expert opinion based on animal studies showing sterilant caused teratogenic effects in mice, rats, rabbits, and monkeys).

[166] *See supra* notes 85-92 and accompanying text.

[167] Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 591 (1993).

[168] *See* Daubert v. Merrell Dow Pharms., Inc., 43 F.3d 1311, 1322 (9th Cir. 1995) (bypassing reliability inquiry because case began under *Frye* and finding poor fit under second prong); *Sorensen*, 31 F.3d at 648; *Bourne*, 189 F. Supp. 2d at 498-99; *National Bank of Commerce*, 965 F. Supp. at 1527.

[169] *See Bourne*, 189 F. Supp. 2d at 499.

[170] *Id.* at 498.

[171] *Id.* at 499.

[172] *National Bank of Commerce*, 965 F. Supp. at 1527. Plaintiffs were the guardian of the

studies did not fit with the method of exposure alleged by the plaintiffs.[173] Whereas rabbits were fed and therefore orally ingested the substance,[174] the child's mother claimed she was exposed to it through inhalation and dermal contact.[175] The *National Bank of Commerce* court also found a poor fit between the dosages used in the animal tests and those alleged by plaintiffs, finding that the doses used in the animal studies did not fit with any dose the mother or fetus could have conceivably received.[176]

3. *Daubert Decisions Admitting Expert Opinions Based in Part on Animal Studies Have Not Entailed Explicit Analysis of their Admissibility*

Only two *Daubert* courts have admitted expert opinions, based in part on animal studies, in birth-defects cases.[177] Neither of those courts specifically discussed the admissibility of animal experiments; at most, they mentioned animal tests only in passing.[178] More importantly, neither of the courts expressly stated that such studies were reliable or a good fit to prove causation in human birth-defects cases.[179] Furthermore, these courts' opinions have questionable bases.

Without expressly discussing animal studies, the majority in *Ambrosini v. Labarraque* nevertheless held admissible expert testimony from a teratologist that derived in part from such studies.[180] The majority ruled that the expert should have been allowed to testify even though none of the studies he relied upon, animal or otherwise, specifically concluded that the agent in question caused the type of birth defects found in the plaintiff child.[181] As noted by the dissent in *Ambrosini*, the majority also accepted the expert teratologist's conclusory, self-serving proclamation that he used generally accepted methods, without further

---

deceased infant's estate and the infant's father. *Id.* at 1132.

[173] *Id.* at 1527.

[174] *Id.* at 1528.

[175] *Id.* at 1492.

[176] *Id.* at 1527. The defendants calculated that the smallest dose given to the animals exceeded the mother's worst-case dose by a factor of 1,000,000. National Bank of Commerce v. Dow Chem. Co., 965 F. Supp. 1490, 1549 (E.D. Ark. 1996), *aff'd*, 133 F.3d 1132 (8th Cir. 1998).

[177] Ambrosini v. Labarraque, 101 F.3d 129, 137-140 (D.C. Cir.1996); Dyson v. Winfield, 113 F. Supp. 2d 44, 50-51 (D. D.C. 2000).

[178] *Ambrosini*, 101 F.3d at 137-140; *Dyson*, 113 F. Supp. 2d at 50-51. The cases either involved Depo Provera or Provera (the acetate derivative of Depo Provera). *Ambrosini*, 101 F.3d at 131; *Dyson*, 113 F. Supp. 2d at 45.

[179] *Ambrosini*, 101 F.3d at 137-140; *Dyson*, 113 F. Supp. 2d at 50-51.

[180] *Ambrosini*, 101 F.3d at 137.

[181] *Id.*

inquiry.[182]

In addition, the majority in *Ambrosini* explicitly approved of the methodology of plaintiffs' epidemiological expert, as did another court in *Dyson v. Winfield* (the expert was the same in both cases).[183] This approval occurred despite the expert forming his own opinions based on published epidemiological data and discounting other studies,[184] a methodology found wanting in *Daubert II*.[185] Moreover, the *Dyson* court summarily approved of the expert with an opinion based in part on animal studies, finding his methods acceptable merely because they were similar to those approved of by the *Ambrosini* court.[186]

The *Ambrosini* and *Dyson* opinions are problematic, as demonstrated above; in fact, the *Dyson* court seemed to be piggybacking on the *Ambrosini* court's opinion, having cited it with approval throughout the case.[187] Furthermore, with the short shrift given the evaluation of animal studies, these anomalous cases do not present a compelling case for admitting expert opinions based on animal tests to prove causation of human birth defects.

B. POST-*DAUBERT*, BETTER-REASONED *FRYE* COURTS EXCLUDE BIRTH DEFECTS CAUSATION OPINIONS BASED ON ANIMAL STUDIES

Post-*Daubert* birth-defects court opinions in states that follow the *Frye* "generally acceptable" standard are mixed.[188] Three courts in states that follow *Frye* have excluded expert testimony based on animal studies proffered to demonstrate teratogenicity in humans,[189] whereas three courts have admitted such testimony.[190]

---

[182] *Id.* at 143 (Henderson, J., dissenting).

[183] *Id.* at 136 (majority opinion); *Dyson*, 113 F. Supp. 2d at 49. The court in *Dyson* deemed *Ambrosini* to be the leading case in the District of Columbia Circuit on expert testimony. *Dyson*, 113 F. Supp. 2d at 47.

[184] *Ambrosini*, 101 F.3d at 140 (Henderson, J., dissenting).

[185] Daubert v. Merrell Dow Pharms., Inc., 43 F.3d 1311, 1314 (9th Cir. 1995) (on remand from Supreme Court).

[186] *Dyson*, 113 F. Supp. 2d at 51.

[187] *Id.* at 47-51.

[188] Oxendine v. Merrell Dow Pharms., Inc., Civ. No. 82-1245, 1996 WL 680992, at *34 (D.C. Super. Ct. Oct. 24, 1996); DePyper v. Navarro, No. 83-303467-NM, 1995 WL 788828, at *34 (Mich. Cir. Ct. Nov. 27, 1995), *aff'd*, No. 191949, 1998 WL 1988927 (Mich. Ct. App. Nov. 6, 1998); Blum v. Merrell Dow Pharms., Inc., 764 A.2d 1, 5 (Pa. 2000); (excluding expert opinions); Castillo v. E.I. du Pont de Nemours & Co., 854 So. 2d 1264, 1276 (Fla. 2003); Rodriguez v. Feinstein, 793 So. 2d 1057, 1061 (Fla. Dist. Ct. App. 2001); Duran v. Cullinan, 677 N.E.2d 999, 1004 (Ill. App. Ct. 1997); (admitting expert opinions).

[189] *Oxendine*, 1996 WL 680992, at *34; *DePyper*, 1995 WL 788828, at *34; *Blum*, 764 A.2d at 5.

[190] Castillo v. E.I. du Pont de Nemours & Co., 854 So. 2d 1264, 1268, 1275 (Fla. 2003);

1. *Frye Decisions Excluding Animal Studies Are Supported by Daubert Not Generally Acceptable Findings*

Courts in the District of Columbia, Michigan, and Pennsylvania have held expert opinions based on animal tests to be inadmissible under *Frye*.[191] The analysis of other courts analyzing birth defects cases post-*Daubert* supports these decisions. Federal courts applying the "generally acceptable" factor as a consideration in birth-defects cases have found that extrapolation of animal experiments to humans is not generally acceptable in the relevant scientific community.[192] Thus, a strong argument exists that such extrapolations are therefore inadmissible under the *Frye* "general acceptability" test.[193]

2. *Frye Cases Admitting Animal Studies in Human Birth-Defects Cases Post-Daubert Can Be Distinguished*

Three *Frye* courts have admitted expert opinions, based at least in part on animal studies, in birth-defects cases.[194] These cases are distinguishable from those excluding expert opinions based on animal studies and do not present a convincing argument for their admission.

The Florida Supreme Court in *Castillo v. E. I. du Pont de Nemours & Co.* upheld the admission of the plaintiffs' expert testimony based primarily on extrapolation from animal studies.[195] This decision appears to be out of line with opinions in similar cases.[196] *Bourne* (discussed *supra*) and *Bowen v. E. I. du Pont de Nemours & Co.* both involved the

---

Rodriguez v. Feinstein, 793 So. 2d 1057, 1061 (Fla. Dist. Ct. App. 2001); Duran v. Cullinan, 677 N.E.2d 999, 1004 (Ill. App. Ct. 1997).

[191] *Oxendine*, 1996 WL 680992, at *34; *DePyper*, 1995 WL 788828, at *34; *Blum*, 764 A.2d at 5. In fact, the Pennsylvania court in *Blum* held that the plaintiff's causal link between animal studies and human teratogenicity was unreliable under both *Frye* and *Daubert*. *Blum*, 764 A.2d at 4.

[192] *See, e.g.*, Raynor v. Merrell Pharms. Inc., 104 F.3d 1371, 1376 (D.C. Cir.1997) (plaintiff's methodology does not enjoy "general acceptance"); Lust v. Merrell Dow Pharms., Inc., 89 F.3d 594, 597 (9th Cir.1996) (expert failed to demonstrate method was generally accepted); Sorensen v. Shaklee Corp., 31 F.3d 638, 649 (8th Cir.1994) (no evidence of general acceptance); Wade-Greaux v. Whitehall Labs., Inc., 874 F. Supp. 1441, 1478 (D.V.I. 1994) (plaintiff experts' methodology contrary to generally accepted methodology employed by relevant scientific community), *aff'd*, 46 F.3d 1120 (3d Cir. 1994) (table).

[193] *See DePyper*, 1995 WL 788828, at *32 (methodology of experts relying on animal studies not generally acceptable).

[194] *Castillo*, 854 So. 2d at 1268; *Rodriguez*, 793 So. 2d at 1061; *Duran*, 677 N.E.2d at 1004.

[195] *Castillo*, 854 So. 2d at 1267-68.

[196] Bourne v. E.I. du Pont de Nemours & Co., 189 F. Supp. 2d 482, 496 (S.D. W.Va. 2002), *aff'd*, 85 F. App'x 964 (4th Cir. 2004); Bowen v. E.I. du Pont de Nemours & Co., No. Civ. A. 97C-06-194 CH, 2005 WL 1952859, at *11 (Del. Super. Ct. 2005), *appeal dismissed*, 879 A.2d 920 (Del. 2005).

same purported teratogen[197] as *Castillo,* and the same expert testified in all three cases.[198] As discussed *supra,*[199] the *Bourne* court deemed the high-dose, stomach-injected rat study relied upon by the expert to be a poor fit to prove causation of human birth defects; the court additionally found numerous other issues with the expert's proffered testimony.[200] The *Bowen* court likewise found the expert to be unreliable.[201] The *Bourne* and *Bowen* courts ultimately rejected the plaintiffs' expert's methodology, yet the *Castillo* majority found it to be "generally acceptable."[202]

Other aspects of majority's analysis in *Castillo* are problematic. In response to the defendant's argument that the dosages in rat tests could not be extrapolated to humans, the majority said that the expert's underlying scientific methodology was undisputedly accepted in the scientific community.[203] However, the majority addressed this remark to the dosing of the rats and not the extrapolation,[204] which is what the court there should have analyzed for general acceptability under *Frye.*[205] In addition, the majority seemed to misunderstand the *Daubert* and *Frye* rules, asserting at one point that *Frye* was the first prong of the *Daubert* test.[206]

The other two *Frye* birth defects cases admitting expert testimony based partly on animal studies are also not convincing. Neither of these cases explicitly discussed, let alone made a strong case for, the admissibility of expert opinions based on animal tests in birth-defects cases. Plaintiffs' expert opinions in *Duran v. Cullinan* were submitted in the form of essays and were based primarily on extrapolation from forty-

---

[197] The pesticide Benlate.

[198] *Bourne*, 189 F. Supp. 2d at 485; *Bowen*, 2005 WL 1952859, at *4; *Castillo*, 854 So. 2d at 1267.

[199] *See supra* notes 170-171 and accompanying text.

[200] *Bourne*, 189 F. Supp. 2d at 496, 499, 501 (expert used purely speculative figure to determine percentage of body exposed to pesticide; expert improperly back-calculated concentration of pesticide metabolite).

[201] *Id.* at 496; *Bowen*, 2005 WL 1952859, at *11.

[202] *Bourne*, 189 F. Supp. 2d at 501; *Bowen*, 2005 WL 1952859, at *13; *Castillo*, 854 So. 2d at 1273.

[203] *Castillo*, 854 So. 2d at 1273.

[204] *Id.*

[205] *See, e.g.,* DePyper v. Navarro, No. 83-303467-NM, 1995 WL 788828, at *31-32 (Mich. Cir. Ct. Nov. 27, 1995), *aff'd*, No. 191949, 1998 WL 1988927 (Mich. Ct. App. Nov. 6, 1998). *Cf.* Landau & O'Riordan, *supra* note 79, at 557 (stating that the appropriate question under *Frye* is whether the scientific community accepts use of animal studies as a basis for determining human causation). The *Castillo* majority even criticized the lower court for analyzing the methodology of extrapolating from animal studies to humans for general acceptance. *Castillo*, 854 So. 2d at 1276.

[206] *Castillo*, 854 So. 2d at 1276.

three epidemiological studies showing contraceptives generally to have teratogenic effects; a single essay noted that animal tests indicated oral contraceptives had significant birth-defects potential.[207] Neither the defendants' arguments nor the *Duran* court's opinion focused on the general acceptance of animal experiments or the admissibility of expert opinions based on such experiments.[208]

Like that in *Duran*, the short opinion in *Rodriguez v. Feinstein* did not include a discussion of the admissibility of opinions based on animal studies.[209] Furthermore, the *Rodriguez* court relied on the problematic *Castillo* opinion.[210] Like the anomalous federal cases discussed *supra*, these three cases do not present a compelling case for admission of opinions based on animal studies to prove causation of human birth defects, either because of questionable reasoning, lack of explicit discussion of animal studies, or both.

C. THE COINCIDENTAL EXISTENCE OF CORROBORATING HUMAN DATA DOES NOT WARRANT ADMISSIBILITY OF OTHERWISE UNRELIABLE AND NOT GENERALLY ACCEPTABLE ANIMAL STUDIES

Some courts excluding animal studies under *Daubert* implied that when reliable epidemiological evidence that demonstrates causation of birth defects is available, animal tests could be helpful to corroborate the epidemiological evidence.[211] Several courts seemed to qualify their rejection of animal experiments by noting the absence of supportive epidemiological studies,[212] implying that the admissibility of expert opinions based on such experiments might change if positive epidemiological evidence were available. In addition, some courts suggested that animal models could help confirm positive

---

[207] Duran v. Cullinan, 677 N.E.2d 999, 1002, 1012 (Ill. App. Ct. 1997).

[208] *Id.* at 1002-04. Moreover, the court admitted plaintiffs' expert opinions alleging an oral contraceptive caused birth defects despite plaintiff mother having previously given birth to two children with birth defects. *Id.* at 1000.

[209] Rodriguez v. Feinstein, 793 So. 2d 1057, 1061 (Fla. Dist. Ct. App. 2001).

[210] *Id.* at 1060.

[211] *See, e.g.*, Raynor v. Merrell Pharms. Inc., 104 F.3d 1371, 1375 (D.C. Cir.1997); Bourne v. E.I. du Pont de Nemours & Co., 189 F. Supp. 2d 482, 496 (S.D. W.Va. 2002) *aff'd*, 85 F. App'x 964 (4th Cir. 2004); National Bank of Commerce v. Dow Chem. Co., 965 F. Supp. 1490, 1528 (E.D. Ark. 1996), *aff'd*, 133 F.3d 1132 (8th Cir. 1998); Wade-Greaux v. Whitehall Labs., Inc., 874 F. Supp. 1441, 1455, 1480 (D.V.I. 1994), *aff'd*, 46 F.3d 1120 (3d Cir. 1994) (table).

[212] *See Bourne*, 189 F. Supp. 2d at 496; *Wade-Greaux*, 874 F. Supp. at 1480. One *Frye* court made a similar qualification. DePyper v. Navarro, No. 83-303467-NM, 1995 WL 788828, at *32 (Mich. Cir. Ct. Nov. 27, 1995), *aff'd*, No. 191949, 1998 WL 1988927 (Mich. Ct. App. Nov. 6, 1998).

epidemiological studies.[213] These comments are surprising, given these courts' opinions that extrapolation from animal studies to humans is unreliable.[214]

It is odd for courts to exclude animal tests when epidemiological studies either do not exist or disagree with the animal tests, yet claim that the animal tests can be useful when they agree with the epidemiological evidence.[215] This undercuts *Daubert*. Whether a methodology or technique is reliable should be determined separately from a particular case.[216] Otherwise, the reliability of a methodology would be determined on a case-by-case basis, based on other evidence available in an individual case. The admissibility of opinions based on a particular methodology would then merely turn on the cumulative force of the other evidence available in a case; the more other evidence available, the more likely the methodology would be found reliable, regardless of its true merit.

Courts may be misinterpreting the application of the testing and error rate factors elucidated in *Daubert*.[217] The *Daubert* Court observed that whether a theory or technique can be or has been tested, and the known or potential error rate of such theory or technique, could bear on the reliability or helpfulness and hence admissibility of expert testimony based on the theory or technique.[218] A sensible interpretation of these factors is that the testing and rate of error of a methodology are to be determined generally, rather than on the facts of a particular case.[219]

In fact, the Supreme Court in *Daubert* counseled that "[t]he focus,

---

[213] *See National Bank of Commerce*, 965 F. Supp. at 1528; *Wade-Greaux*, 874 F. Supp. at 1455; *see also* Bernstein, *supra* note 85, at 2177.

[214] *See, e.g., Bourne*, 189 F. Supp. 2d at 496 (extrapolations from animal studies to humans neither reliable nor relevant); *National Bank of Commerce*, 965 F. Supp. at 1527 (animal studies unreliable predictors of causation in humans); *Wade-Greaux*, 874 F. Supp. at 1482 (experts' methodology scientifically invalid and unreliable).

[215] In a similar vein, isolated commentators have opined that courts have excluded animal studies from certain cases because of contrary or extensive epidemiological evidence in those cases. *See, e.g.*, Howard Marks, *Electromagnetic Forces from Overhead High-Voltage Transmission of Electricity: Establishing Causation Using Toxicological and Epidemiological Evidence Under a Post-Daubert Standard*, 13 J. ENVTL. L. & LITIG. 163, 183 (1998); REFERENCE MANUAL ON SCI. EVIDENCE, *supra* note 86 at 347 n. 39.

[216] *Cf.* D.H. Kaye, *The Dynamics of Daubert: Methodology, Conclusions, and Fit in Statistical and Econometric Studies*, 87 J. VA. L. REV. 1933, 1975 (2001) (heightened scrutiny of scientific evidence pertains to methodology rather than case-specific facts).

[217] *Cf.* Raynor v. Merrell Pharms. Inc., 104 F.3d 1371, 1375 (D.C. Cir.1997) (experts' conclusions tested by epidemiological data and found wanting).

[218] Daubert v. Merrell Dow Pharms., Inc., 509 U.S. 579, 593-94 (1993).

[219] *Cf.* Hollingsworth & Lasker, *supra* note 89, at 89, 104 (asserting that under *Daubert*, a trial court must consider each category of evidence in light of the scientific method and concluding that each strand in an expert's analysis should be analyzed as to whether it was tested and validated).

of course, must be solely on principles and methodology, not on the conclusions that they generate."[220] Admissibility should therefore not depend on whether a particular conclusion appears accurate because of other evidence in the case. Hence, the admissibility of an opinion based on extrapolation from animal studies should hinge on the overall testing and error rate of this methodology, rather than whether corroborating evidence happens to exist in a particular case.

The existence of epidemiological studies that happen to agree with animal studies should not render the animal studies admissible under the *Frye* evidentiary standard, either. Coincidental evidence does not change the fact that the methodology of extrapolating from animals to humans is not generally accepted in the scientific community. After all, the *Frye* test requires that a methodology be accepted generally, rather than specifically, to be admissible. Its focus is on methodology, not conclusions derived therefrom.[221] Furthermore, under either evidentiary standard, basing admissibility of testimony rooted in a particular methodology on what other evidence is available in a particular case would lead to incongruent court decisions, with the same methodology being found generally acceptable or reliable in some cases but not others.

Moreover, *Daubert* courts have a responsibility under FRE 702, which encompasses the *Daubert* test,[222] to make a preliminary determination of admissibility of an expert opinion.[223] Unlike a lay witness, an expert under FRE 702 is permitted wide latitude to offer opinions, a distinction that merits a gate-keeping role for courts.[224] Since "much of scientific testimony is sophisticated and difficult to comprehend, and . . . analysis of the scientific validity of the methodologies underlying the testimony . . . beyond the capabilities of most lay persons," the gate-keeping role of the court is essential.[225] Otherwise, a scientific expert would be able to testify that "the world is flat [or] the moon is made of green cheese."[226] Hence, FRE 702 requires that prior to admitting expert testimony, a judge must determine its reliability and helpfulness to the case, as discussed *supra*.[227]

---

[220] *Daubert*, 509 U.S. at 595.

[221] *See* Kaye, *supra* note 216, at 1972.

[222] *See* FED. R. EVID. 702 advisory committee's note (2000) (FRE 702 amended in response to *Daubert*).

[223] FED. R. EVID. 702 (Testimony by Experts).

[224] *Daubert*, 509 U.S. at 592. FRE 701 (Opinion Testimony by Lay Witnesses) restricts lay witness testimony to opinions rationally based on the witness' own perceptions. FED. R. EVID. 701.

[225] 3 AM. L. PROD. LIAB. §54:74 (3d ed. 2005).

[226] Merrell Dow Pharms., Inc. v. Havner, 953 S.W.2d 706, 712 (Tex. 1997) (citing E.I. du Pont de Nemours & Co. v. Robinson, 923 S.W.2d 549, 558 (Tex. 1995)).

[227] *See supra* notes 52-61 and accompanying text.

Furthermore, even if a court were to deem expert opinion based on animal studies admissible because of corroborating epidemiological evidence, such opinion would be subject to exclusion under the FRE 403 balancing test. The FRE 403 balancing test, which takes place only after an initial determination of admissibility,[228] allows a judge to exclude otherwise relevant evidence "if its probative value is substantially outweighed by the danger of unfair prejudice, confusion of the issues, or misleading the jury, or by considerations of undue delay, waste of time, or needless presentation of cumulative evidence."[229]

If positive epidemiological evidence is available, any animal studies purporting to support the epidemiological evidence would be less "needed" to prove causation, and hence subject to exclusion under 403 as cumulative evidence.[230] Since the probative value of animal tests would derive entirely from coincidentally corroborative epidemiological studies, presentation of the animal tests in court would be needlessly duplicative.[231]

D. EXCLUSION OF TESTIMONY BASED ON ANIMAL STUDIES HAS POSITIVE ENVIRONMENTAL POLICY IMPLICATIONS

It is crucial to identify those agents with teratogenic potential among the plethora of drugs and other chemicals that human beings come into contact with in their environment.[232] Knowledge of substances that cause birth defects would enable pregnant women to minimize exposure to them and thus avoid teratogenic birth defects in their children.[233] Unfortunately, "[t]he burden of this goal currently rests heavily upon animal-based testing."[234]

1. Exclusion Will Lead to Prioritization of Resources

As the majority of *Daubert* courts have found, extrapolation from animal testing to demonstrate birth-defects causation in humans is not reliable.[235] Admitting data from animal studies in birth-defect cases would promote continuation of these studies, expending valuable

---

[228] *See* FED. R. EVID. 104(a).

[229] FED. R. EVID. 403.

[230] *See* Krages, *supra* note 80, at 252-53.

[231] *See* Landau & O'Riordan, *supra* note 79, at 554; Krages, *supra* note 80, at 252-53.

[232] Bailey, Knight, & Balcombe, *supra* note 68, at 97.

[233] *See id.* at 98.

[234] *Id.*

[235] *See supra* notes 154-166 and accompanying text.

resources on futile efforts. Since "[i]dentification of environmental agents that cause damage to unborn children is absolutely imperative,"[236] resources ought to be spent on reliable means of discovering and evaluating these agents. The refusal of courts to admit expert testimony based on animal tests could lead to the eventual phase-out of these experiments. This would free resources up to be spent on more worthy endeavors, such as epidemiological and *in vitro* studies (discussed *infra*).

A few individual plaintiffs might benefit if courts were to admit animal tests to prove causation of birth defects.[237] Ultimately though, parents, children, and animals would lose out, because fruitless experimentation on animals would continue, depriving vital studies of the diligent pursuit they deserve.

2. *Promising In Vitro Testing Will Further Improve*

In vitro testing[238] shows promise for determining teratogenic causes of human birth defects.[239] Although the teratology community has imposed demanding validation standards on *in vitro* tests (which were never applied to corresponding *in vivo* animal tests), three *in vitro* tests have passed these strict criteria.[240] The embryonic stem-cell, micromass, and whole embryo culture tests were endorsed as scientifically validated by the European Centre for the Validation of Alternative Methods in 2001.[241] Already more reproducible than animal tests, i*n vitro* methods provide easier quantification of biological effects than do animal studies.[242] Moreover, *in vitro* tests do not present problems related to metabolic differences, routes of exposure, and other issues associated with animal tests.[243]

If resources are freed up to pursue these promising alternatives to animal studies, "the technology [will] develop and the tests [will] become more reliable."[244] Focusing resources on alternatives will allow

---

[236] Bailey, Knight, & Balcombe, *supra* note 68, at 137.

[237] If admitted, animal studies can mislead juries with the aura of scientific reliability, because they involve a laboratory setting and mathematical computations. Juries might then be persuaded to find for plaintiffs based on these studies. *See* Krages, *supra* note 80, at 249.

[238] Tests using animal or human cells in a test tube or similar media. *See supra* note 75 and accompanying text.

[239] *See* 49 AM. JUR. 2d *Proof of Facts* 125, Teratogenic Drugs § 8 (2005) ("[*I*]*n vitro* studies may provide the best available direct evidence of teratogenicity.").

[240] Bailey, Knight, & Balcombe, *supra* note 68, at 139.

[241] *Id.*

[242] *Id.*

[243] *Id.*

[244] *Id.*

scientists to establish essential models of how teratogenic action occurs.[245] Furthermore, use of alternatives will reduce the potential for detrimental human impact when unreliable and confusing animal models generate false positive and false negative results.[246] Improvement of human cell culture technology will lead to new *in vitro* methods that approximate the formation of human birth defects even better than they do now.[247]

III. CONCLUSION

Courts should keep animal studies out of the courtroom in birth-defects toxic-torts cases. *Daubert* requires exclusion of opinion testimony based on these unreliable predictors, which are simply not a good fit for determining causation of birth defects in humans.[248] Virtually all human teratogens were established with the use of human data,[249] and the ability of animal tests to predict birth defects in humans is little better than pure chance.[250]

Frye also commands exclusion of testimony based on animal studies from birth-defects cases. The extrapolation from animal experiments to prove causation of birth defects in humans is not generally accepted in the scientific community.[251] Additionally, courts should exclude opinions basing causation on animal studies even when supportive human data happens to be available under either admissibility standard, because the coincidental existence of evidence pointing to the same result does not alter the reliability or general acceptance of the extrapolation from animal studies to humans.

Exclusion of animal studies in birth-defects cases would shift resources from unreliable animal experimentation to vital

---

[245] *Id.*

[246] Bailey, Knight, & Balcombe, *supra* note 68, at 139.

[247] *Id.* Some courts up to now have been reluctant to admit testimony based on *in vitro* studies in birth-defects cases. *See, e.g.*, Wade-Greaux v. Whitehall Labs., Inc., 874 F. Supp.1441, 1484 (D.V.I. 1994), *aff'd*, 46 F.3d 1120 (3d Cir. 1994) (table). However, the proven reliability of these tests (as demonstrated by their recent validation, discussed *supra* at notes 240-241 and accompanying text), combined with increased devotion of resources to these tests as urged here, should lead to increased admissibility.

[248] *See, e.g.*, Bourne v. E.I. du Pont de Nemours & Co., 189 F. Supp. 2d 482, 498 (S.D. W.Va. 2002), *aff'd*, 85 F. App'x 964 (4th Cir. 2004); *Wade-Greaux*, 874 F. Supp. at 1482.

[249] Polifka & Friedman, *supra* note 87, at 416.

[250] Bailey, Knight, & Balcombe, *supra* note 68, at 110.

[251] *See, e.g.*, Daubert v. Merrell Dow Pharms., Inc., 43 F.3d 1311, 1314 (9th Cir. 1995); *Wade-Greaux*, 874 F. Supp. at 1478; DePyper v. Navarro, No. 83-303467-NM, 1995 WL 788828, at *34 (Mich. Cir. Ct. Nov. 27, 1995), *aff'd*, No. 191949, 1998 WL 1988927 (Mich. Ct. App. Nov. 6, 1998).

epidemiological studies and promising *in vitro* tests. Eventually, this would lead to increased knowledge of the environmental causes of birth defects and ultimately reduce both human and animal suffering. Instead of hypothesizing about environmental agents or exposures, for which existing animal data is insufficient, scientists need to initiate new investigative approaches that will obtain the necessary data.[252] Shifting resources from animal experiments to epidemiological studies and *in vitro* tests would help accomplish this goal. Therefore, exclusion of opinion testimony based on animal studies in birth-defects cases would help achieve the dual goals of eliminating teratogenic human birth defects and ending the suffering that lab animals in these experiments endure.

DIJE NDREU*

[252] *Cf.* Robert L. Brent, Susanne Tanski, & Michael Weitzman, *A Pediatric Perspective on the Unique Vulnerability and Resilience of the Embryo and the Child to Environmental Toxicants: The Importance of Rigorous Research Concerning Age and Agent*, 113 PEDIATRICS 935, 942-43 (2004) (remarking on the need for an increase in quality environmental toxicology research).

* J.D., Candidate, 2007, Golden Gate University School of Law, San Francisco, CA; B.S. Chemistry, 1989, University of California at Santa Cruz, Santa Cruz, CA; M.S. Chemistry, 1991, University of California at San Diego, La Jolla, CA. Many thanks to editors Angela Lipanovich and Roger Lin and faculty mentor Althea Kippes for their guidance and encouragement, with special thanks to Angela for her invaluable help in structuring this Comment. Thanks also to journal editor Ida Martinac for her unfailing support, and to Professor Cliff Rechtschaffen for his guest review of this Comment and valuable feedback. Heidi Hofmann and Ruby Steinbrecher provided vital cite-checking assistance, and Professor Michael Daw helped solve some perplexing *Bluebook* quandaries. Lastly, thanks to my husband Jim Dulla for his love and support during this process.