

ARTICLE

SCIENCE AND TOXIC TORTS: IS THERE A RATIONAL SOLUTION TO THE PROBLEM OF CAUSATION?

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I. INTRODUCTION

Recent controversies over the safety of breast implants,¹ electrical power transmission lines,² and even cellular phones³ portend yet another period of protracted litigation in which the courts will confront issues of what constitutes admissible and sufficient evidence⁴ of causation in toxic torts.⁵ Questions have surfaced regarding the safety of each product, but there is no clearly established causal link between chronic exposure to any of them and disease or injury. News reports indicate that while anecdotal reports abound regarding breast implants, little if any systematic testing has been done to confirm suspicions of harmful effects.⁶ Concerns about cellular phones were prompted by an even sparser array of anecdotal reports and studies.⁷ Electromagnetic radiation from electrical power lines has been studied more extensively, but many scientists remain unconvinced of the purported link between such

1. See, e.g., Philip J. Hilts, *Experts Suggest U.S. Sharply Limit Breast Implants*, N.Y. TIMES, Feb. 21, 1992, at A1.

2. See Bill Richards, *Elusive Threat: Electric Utilities Brace for Cancer Lawsuits Though Risk Is Unclear*, WALL ST. J., Feb. 5, 1993, at A1.

3. See Natalie Angier, *Cellular Phone Scare Discounted*, N.Y. TIMES, Feb. 2, 1993, at C1.

4. The United States Supreme Court recently granted the plaintiffs' petition for certiorari in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 951 F.2d 1128 (9th Cir. 1991), cert. granted, 113 S. Ct. 320 (1992). In *Daubert*, the Ninth Circuit held that animal testing and chemical studies provided insufficient foundation for expert testimony that Bendectin causes limb reduction defects. 951 F.2d at 1131. The court also held that unpublished reanalyses of epidemiologic studies which had not been peer reviewed and which were generated solely for use in litigation were inadmissible on the issue of causation. *Id.*

5. This article uses the term "toxic tort" for cases, including products liability and environmental exposure cases, in which disease or injury is alleged to have resulted from exposure to harmful substances (i.e., chemicals) See 1 MICHAEL DORE, *THE LAW OF TOXIC TORTS* § 2.02 (1992). The toxic tort rubric also applies to cases involving radiation exposure. See, e.g., *Allen v. United States*, 588 F. Supp. 247 (D. Utah 1984), rev'd, 816 F.2d 1417 (10th Cir. 1987), cert. denied, 484 U.S. 1004 (1988). For discussion of the characteristics of toxic torts cases, see *infra* notes 43-49 and accompanying text.

6. This statement is intended to apply to the issue of whether breast implants or their constituents pose systemic risks. There are, of course, cases in which the implants have ruptured or produced localized effects, where the injuries and the causal role of breast implants is not subject to the same level of doubt.

As the breast implant controversy came to a head, *Chemical & Engineering News* reported:

After 30 years of silicone gel breast implant use, the biological, physiological, physical, and chemical reactions of silicones in the human body are likely, finally, to be systematically studied. A major goal of these studies will be determining how often the devices rupture, and what happens when they do.

Lois Ember, *Breast Implants: Silicone Effects in Body to Be Probed*, CHEMICAL & ENGINEERING NEWS, Mar. 2, 1992, at 4. Almost a year later, the *Wall Street Journal* reported that some researchers have identified diseases that they believe are unique to or more common in breast implant recipients. Joan Rigdon, *Breast Implants Raise More Safety Issues: Saline Implants Appear to Carry Hazard as Well*, WALL ST. J., Feb. 4, 1993, at B1.

7. See *infra* notes 10-13 and accompanying text.

exposure and disease.⁸ Nonetheless, all three exposures are the subject of recently filed, and in some cases adjudicated, lawsuits.⁹

The current scare over cellular phones is instructive. The primary "evidence" of a causal link between the phones and brain cancer is the fact that a number of cellular phone users have been diagnosed with brain cancer, several with the cancer located near the location of the phone's antenna in use. Using newspaper estimates of over three million users of hand held portable cellular phones in the United States¹⁰ and 11,000 expected deaths from brain cancer this year,¹¹ it is hardly surprising that several cases of brain cancer in cellular phone users have been reported. One reported laboratory study which reported that radio-frequency radiation increased the growth rate of tumor cells is consistent with the possibility that such radiation could increase the growth rate of preexisting cancers,¹² but it does not prove that there is any effect in humans from cellular phone use.¹³

8. See Richards, *supra* note 2.

9. *Plaintiffs in Georgia, Texas Sue Makers, Contending Devices Caused Various Ailments*, Current Report, Toxics L. Rep. (BNA) 937 (Jan. 8, 1992) (breast implants). On February 4, 1993, the *Wall Street Journal* reported a plaintiffs' lawyer's estimate that 2000 breast implant cases have been or soon will be filed in consolidated court proceedings in Birmingham, Alabama. Rigdon, *supra* note 6. At least one California case produced a verdict for the plaintiff. *Federal Court Upholds \$7.3 Million Award, Says Verdict Supported, Punitives Proper*, Toxics L. Rep. (BNA) 1480 (May 6, 1992). Regarding radiation from electrical power transmission lines, see *Suit Seeks to Hold Two Utilities Liable for Injuries to Family Living Near Substation*, Toxics L. Rep. (BNA) 927 (Jan. 8, 1992). See also Richards, *supra* note 2, at A1 (describing a "nationwide group of law firms eager to turn [electromagnetic field radiation] into a legal battleground").

Cellular phones are at issue in at least one lawsuit. See Angier, *supra* note 3.

10. See Stephen Nohlgren et al., *A Lethal Connection?*, ST. PETERSBURG TIMES, Jan. 10, 1993, at 1A (reporting estimates of 10 million owners of cellular phones, approximately one third of which are hand-held portables).

11. See Mary Lu Carnevale, *Scientists Doubt Phones Cause Brain Tumors*, WALL ST. J., Feb. 3, 1993, at B1. Richard Adamson, a researcher at the National Cancer Institute, was quoted as predicting 11,800 deaths from brain cancer in the U.S. this year. *Id.* Estimating the population of the U.S. at 250 million, the brain cancer death rate would then be approximately 47 per million, leading to an expected mortality of approximately 140 cases per year among the 3 million hand-held cellular phone users. Even if the age-adjusted cancer rates are lower for the age groups who use cellular phones, it is not unexpected that there would be a number of cases of brain cancer among cellular phone users each year. Further, incidence of brain cancer in the United States is undoubtedly somewhat higher than mortality from the disease.

12. See *supra* note 11.

13. Even the study's author, Stephen Cleary, a physiology and biophysics professor at the Medical College of Virginia, was quoted by the *Wall Street Journal* as stating that he does not believe that portable cellular phones cause cancer. Carnevale, *supra* note 11, at B1. The *Journal* cited scientists from the National Cancer Institute, the Food and Drug Administration, the Environmental Protection Agency, and the Federal Communications Commission as stating that they do not believe that phone use causes brain cancer, but they might pose a small risk of increasing the growth rate of existing cancers. *Id.*

Despite the obvious lack of evidence to prove that cellular phone use causes brain cancer given the current state of knowledge, the evidence available today on cellular phones does not differ substantially in quantity or quality from the evidence that courts have found admissible and sufficient in other recent toxic tort cases. Those problematic cases are likely to be supported only by a combination of anecdotal evidence that amounts to no more than coincidence, speculation in the guise of scientific explanation, and testing based on unvalidated methodology or studies that have limited predictive value for human disease. Sometimes, as in the Bendectin litigation, such evidence is urged upon and accepted by courts in the face of overwhelming scientific consensus, supported by evidence, that a substance is unlikely to be a cause of injury. In other cases, very tenuous evidence is deemed sufficient where more probative positive or negative evidence is unavailable. Such unprobative and insufficient evidence and testimony, termed "junk science" by some observers,¹⁴ has been the subject of increasing commentary and criticism.¹⁵

Erroneous plaintiffs' verdicts and the corresponding overcompensation and overdeterrence are not just academic concerns. The prospect of useful products being driven from the market or of economic resources being diverted from productive uses is real, as the cases of vaccines¹⁶ and

14. The term "junk science" has been popularized by Huber. See PETER HUBER, *GALILEO'S REVENGE: JUNK SCIENCE IN THE COURTROOM* (1991). At least one court has used the term in a toxic tort case as of this writing. *Landrigan v. Celotex Corp.*, 605 A.2d 1079, 1086 (N.J. 1992).

15. See generally Bert Black, *A Unified Theory of Scientific Evidence*, 56 *FORDHAM L. REV.* 595 (1988); Jude P. Dougherty, *Accountability Without Causality: Tort Litigation Reaches Fairy Tale Levels*, 41 *CATH. U. L. REV.* 1 (1991); Peter Huber, *Junk Science in the Courtroom*, 26 *VAL. U. L. REV.* 723 (1992). For commentary on the courts' tendency to ignore probative evidence in favor of unproven mechanistic explanations and medical testimony, see Troyen A. Brennan, *Causal Chains and Statistical Links: The Role of Scientific Uncertainty in Hazardous Substance Litigation*, 73 *CORNELL L. REV.* 469 (1988).

16. The cost of litigation and the threat of liability have discouraged research and development of new vaccines, as well as production of existing vaccines, activities that are already of marginal interest to pharmaceutical companies because of high production costs and low return on investment. Louis Lasagna, *The Chilling Effect of Product Liability on New Drug Development*, in *THE LIABILITY MAZE* 335, 341-45 (Peter W. Huber & Robert E. Litan eds., 1991). In 1991, there was only one U.S. manufacturer of vaccines for measles, mumps, rubella, and polio, down from three to six for each. *Id.* at 344. The high price of vaccines for childhood diseases has recently become the focus of public health concerns about low immunization rates among children in the United States. See Richard L. Berke, *President Assails "Shocking" Prices of Drug Industry*, *N.Y. TIMES*, Feb. 13, 1993, § 1, at 1. Those prices are attributable in part to liability concerns. See Lasagna, *supra* note 16 at 344; James V. Aquavella, *Profits Don't Explain High Drug Costs*, *N.Y. TIMES*, Feb. 23, 1993, at A20 (letter to the editor) (attributing high costs to product liability insurance and limited life of patent protection).

Bendectin¹⁷ illustrate. Submission of a case to the jury may result in a plaintiff's verdict where even the most cursory examination of the evidence reveals its deficiencies.¹⁸ Verdicts may be very large,¹⁹ and an occasional plaintiff's verdict may even encourage other suits and increase the settlement value of other cases.²⁰ The social and economic significance of breast implants, electrical transmission lines and cellular phones varies considerably, but clearly the costs to society of an erroneous conclusion that any of them causes harm are significant, potentially even catastrophic.

To deal with the problems of junk science in court, several commentators have suggested that courts regularize the standard for admissibility of scientific evidence. One frequent suggestion is that courts reinstate or continue to apply the standard announced in *Frye v. United States*,²¹ which requires that novel scientific evidence have general acceptance within the relevant scientific discipline,²² an issue that the United States Supreme Court is expected to address this year in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*²³ As will be demonstrated in this article, however, many of the issues that arise are more properly viewed as questions about the sufficiency of relevant evidence to meet the more probable than not standard of proof. Thus, solutions that depend on tightening the criteria for admissibility will either require distortion of the

17. Bendectin was eventually withdrawn from the market despite defense verdicts in the overwhelming majority of cases. Lasagna, *supra* note 16, at 340; *see also* Joseph Sanders, *The Bendectin Litigation: A Case Study in the Life Cycle of Mass Torts*, 43 HASTINGS L.J. 301, 357 (1992).

18. *See, e.g., Ferebee v. Chevron Chem. Co.*, 736 F.2d 1529 (D.C. Cir.), *cert. denied*, 469 U.S. 1062 (1984). Obviously, no plaintiff's verdict can result where a case is not submitted for a decision on the merits. It is understood among plaintiffs' lawyers that the objective is to get to trial. Thus, plaintiffs often propose to fully try a few "bellwether" cases, while defendants move for exclusion of evidence and summary judgment on causation issues. *See, e.g., Renaud v. Martin Marietta Corp.*, 749 F. Supp. 1545, 1547 (D. Colo. 1990), *aff'd*, 972 F.2d 304 (10th Cir. 1992).

19. In *Ealy v. Richardson-Merrell, Inc.*, Civ. A. No. 83-3504, 1987 WL 18743 (D.D.C. Oct. 1, 1987), *rev'd*, 897 F.2d 1159 (D.C. Cir.), *cert. denied*, 498 U.S. 950 (1990), the jury awarded compensatory damages of \$20 million and punitive damages of \$75 million to a boy born with limb reduction defects attributed to Bendectin. The district court allowed the compensatory verdict to stand, but granted remittitur as to the punitive verdict. The compensatory verdict was reversed on appeal.

20. *See Sanders, supra* note 17, at 357.

21. 293 F. 1013 (D.C. Cir. 1923).

22. *See, e.g., Black, supra* note 15, at 637-38; Huber, *supra* note 15, at 742-47. The *Frye* rule is still followed in many jurisdictions. *See, e.g., Christopherson v. Allied-Signal Corp.*, 939 F.2d 1106, 1110 (5th Cir. 1991) (en banc), *cert. denied*, 112 S. Ct. 1280 (1992). *See generally* Black, *supra* note 15, at 601 & n.23. *Frye* was also the basis of rejection of certain of plaintiffs' evidence in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 951 F.2d 1128 (9th Cir. 1991), *cert. granted*, 113 S. Ct. 320 (1992). *See* discussion of *Frye* *infra* notes 55-61 and accompanying text.

23. 951 F.2d 1128 (9th Cir. 1991), *cert. granted*, 113 S. Ct. 320 (1992).

admissibility inquiry to encompass sufficiency issues, or will address only part of the problem. Similar concerns are raised by proposals to change the rules of evidence to limit the use of expert testimony.²⁴

The problem of determining the sufficiency of evidence of causation is more directly addressed by proposals that courts use science boards, science panels or court-appointed experts to assist in resolving scientific issues.²⁵ Such proposals, however, except for the use of court-appointed experts, depart substantially from existing notions of civil jurisprudence because they involve delegation to experts of the traditional fact-finding functions of the lay trier of fact.

The thesis of this article is that measures such as the return to the *Frye* rule, or the use of science panels or science courts are unnecessary, because common law courts already possess the authority under the existing rules to "actively review"²⁶ scientific evidence by eliciting and scrutinizing the reasoning underlying scientific evidence and expert testimony and determining its validity and probative worth. As this article will demonstrate, much of the junk science that appears in toxic tort cases is readily apparent or easily uncovered by inquiry of which courts are quite capable.

If active review under the existing rules can uncover bad science, why do a significant number of courts take a lenient posture toward scientific evidence? There appear to be two major reasons for the deferential approach. First, some courts are philosophically indisposed to examine scientific reasoning or methodology, fearing that they are ill-

24. A working group of the Judicial Conference proposed the following amendment of Rule 702 of the Federal Rules of Evidence:

Testimony providing scientific, technical, or other specialized information, in the form of an opinion or otherwise, may be permitted only if (1) the information is reasonably reliable and will substantially assist the trier of fact to understand the evidence or to determine a fact in issue, and (2) the witness is qualified as an expert by knowledge, skill, experience, training, or education to provide such testimony. Except with leave of court for good cause shown, the witness shall not testify on direct examination in any civil action to any opinion or inference, or reason or basis therefor, that has not been seasonably disclosed as required by Rules 26(a)(2) and 26(e)(1) of the Federal Rules of Civil Procedure.

137 F.R.D. 83 (1991). The proposed changes seem more a shift in emphasis than a radical revision of the existing rule. See also Black, *supra* note 15, at 611-13 (proposing a modification of Rule 702 to require the court to determine the validity of reasoning as well as its reliability as a precondition to admitting scientific evidence).

25. See 2 AMERICAN LAW INST. REPORTERS' STUDY, ENTERPRISE RESPONSIBILITY FOR PERSONAL INJURY, APPROACHES TO LEGAL AND INSTITUTIONAL CHANGE 332-51 (1991). The ALI Reporters' Study recommendations were based on Brennan, *supra* note 15, and Troyen Brennan, *Helping Courts with Toxic Torts: Some Proposals Regarding Alternative Methods for Presenting and Assessing Scientific Evidence in Common Law Courts*, 51 U. PITT. L. REV. 1 (1989).

26. For a discussion of "active review," see Black, *supra* note 15, at 674-77.

equipped to delve into scientific disciplines. As will be described below, however, scientific reasoning and legal factfinding employ the same rules of logic. Thus, lay judges need not fear that examination of scientific evidence to determine whether it is soundly reasoned and reliable is beyond their capabilities.

Moreover, the reasons for judicial control of evidence are more compelling where technical evidence is concerned than for non-technical evidence. Judges exhibit no hesitation in barring non-expert testimony based on hearsay and otherwise lacking in foundation even though juries could readily identify the flaws in such testimony with skilled cross-examination and argument by opposing counsel. Juries are less likely to identify the weaknesses in testimony cloaked in technical jargon from an expert with a lengthy list of credentials than in testimony on ordinary factual issues.²⁷ Thus, it is more important for the judge, who understands the legal requirements of proof, to discriminate between reliable and unreliable scientific evidence than between well founded and unfounded evidence on matters within the understanding of ordinary people.²⁸

A second reason for the lenient treatment of scientific evidence in some courts is the apparent desire to compensate for perceived inequities and deficiencies of the tort system. Much of the movement toward the adoption of lenient standards of admissibility and proof of causation in toxic torts has been prompted by the recognition of the difficulties faced by plaintiffs in meeting the traditional requirement that they prove, by a preponderance of the evidence, that their injuries were caused by chronic, low-level chemical or radiation exposures that were remote in time from the manifestation of injury. The paucity of scientific evidence on the causation of diseases such as cancer and birth defects, and the difficulty of distinguishing other identified or background risk factors for the disease, decrease the likelihood that deserving plaintiffs will be compensated. The level of concern about those difficulties was heightened by increasing scientific knowledge of the role of chemicals and radiation in diseases such as cancer and birth defects, as well as scientific speculation about

27. Courts that scrutinize scientific evidence more closely recognize that jurors are likely to be persuaded by the aura of infallibility that surrounds scientific evidence, or by the credentials and certainty expressed by the expert. See *Barefoot v. Estelle*, 463 U.S. 880, 926-28 (1983) (Blackmun, J., dissenting).

28. Courts' abandonment of the *Frye* standard increases the need for judicial scrutiny of scientific evidence because the *Frye* general acceptance standard assures that some evaluation of methods or theories other than that of the expert witness has occurred. Once courts unhinge the admissibility of scientific evidence from scientists' standards, it is incumbent on them to see that other safeguards are in place. See Steven M. Egesdal, Note, *The Frye Doctrine and Relevancy Approach Controversy*, 74 GEO. L.J. 1769, 1787 (1986) (suggesting the need to increase jurors' understanding of novel scientific techniques under the relevancy approach).

potential effects of the greatly accelerated dissemination of untested new chemicals in consumer products and the environment.²⁹ Taking their cue from the scientists,³⁰ legal scholars began to address the difficulties faced by plaintiffs in proving that exposure to toxic substances or chemicals caused their diseases or injuries,³¹ difficulties that can result in uncompensated injuries and the failure to adequately deter harmful activity.³² Lenient standards of admissibility and proof certainly facilitate plaintiffs' recoveries; further, they are consistent with courts' suspicions that mainstream scientists are too demanding in their requirements of proof, and that the unconventional scientists who testify that an exposure caused a plaintiff's disease may be correct.

More than a decade of scientific research into cancer incidence and causation, however, has failed to bear out the fears that prompted deferential review of causation evidence. Many of the assumptions that underlay the shift to more lenient standards for causation evidence in toxic torts are still unproven or are even contrary to current scientific thinking. The contribution of toxic synthetic chemicals and other hazards of the industrial age to cancer and other diseases and injuries is still an open question, but it appears unlikely that such substances cause anything approaching a majority of human cancer and birth defects.

As for the possibility that the unconventional expert may be right, even a superficial examination of much of the disputed evidence reveals that it amounts to speculation about possibilities that have not been tested or that fall far short of meeting the more probable than not standard of proof. Speculation about possibilities forms the beginning, not the endpoint, of factual inquiry, in either the scientific or legal realm. A causal explanation of disease or injury can be said to be probable only when it is supported by observations or data that distinguish between it and other possible explanations. When courts authorize or approve plaintiffs' verdicts without a factual basis for causal inference, they undermine traditional tort requirements for rational factfinding and the "more probable than not" standard of proof. The case for the abrogation of those standards has not been made, nor have courts given full consideration to the implications of such a radical change in the law.

29. See Bruce N. Ames, *Identifying Environmental Chemicals Causing Mutations and Cancer*, 204 *SCIENCE* 587, 588-89 (1979).

30. See, e.g., *id.* at 592 (recommending short-term mutagenicity testing to expedite identification of environmental mutagens and carcinogens).

31. See, e.g., Jeffrey Trauberman, *Statutory Reform of "Toxic Torts": Relieving Legal, Scientific and Economic Burdens on the Chemical Victim*, 7 *HARV. ENVTL. L. REV.* 177, 188 n.48 (1983) (citing law review articles and other writings).

32. See generally David Rosenberg, *The Causal Connection in Mass Exposure Cases: A "Public Law" Vision of the Tort System*, 97 *HARV. L. REV.* 849 (1984).

The purpose of this Article is to demonstrate that courts can and should actively review scientific evidence of causation in toxic tort cases. The next Part describes how courts have loosened the standards for expert testimony in an effort to compensate for the perceived problems faced by toxic tort plaintiffs. Part III then discusses active review and its relation to the rules of evidence and civil procedure and attempts to allay courts' fears that they are ill equipped to evaluate the basis of scientific opinion testimony. Part IV then describes the criteria against which the reliability of scientific evidence can be evaluated and then applies those criteria to the kinds of evidence offered on causation in toxic tort suits. Part V examines a sampling of recent cases that illustrate inadequate judicial scrutiny of scientific evidence, as well as cases that skillfully distinguish probative from nonprobative or insufficient evidence. Lastly, Part VI discusses in depth the factors that underlie courts' failure to examine adequately scientific evidence and shows that many of those concerns are unjustified or that, even where justified, the remedy of authorizing plaintiffs' verdicts that are unsupported by a factual foundation goes too far.

II. HARD CASES MAKE BAD LAW

In the 1960s and 1970s, mounting evidence on the harmful effects of chemicals such as asbestos, vinyl chloride, dioxin and many others, together with the dramatic increase in the use of new chemicals in products ranging from foods, to drugs and medical devices, to many other consumer products, raised concerns that chronic, low level exposures to those substances would lead, or might already have led, to widespread illness and injury.³³ As evidence mounted that exposure to substances such as asbestos and vinyl chloride could cause cancer and other debilitating or fatal conditions, the courts began to see an increasing number of toxic tort suits—tort actions seeking to recover for injuries attributed to toxic substances.

As numerous commentators have explained, proof of causation³⁴ has been the biggest stumbling block to recovery in toxic torts cases.³⁵

33. See R. Jeffrey Smith, *Government Says Cancer Rate Is Increasing*, 209 *SCIENCE* 998 (1980); Mostafa K. Tolba, *Chemicals in the Environment*, 1979 *NAT'L PARKS & CONSERVATION MAG.* 16. The controversy continues, as indicated by more recent publications. See Eliot Marshall, *Experts Clash over Cancer Data*, 250 *SCIENCE* 900 (1990); see also *infra* notes 332-38 and accompanying text.

34. This Article is addressed to issues of causation in fact, by which is meant the issue of whether there is an empirical linkage between the causative event and the claimed injury.

35. See Brennan, *supra* note 25, at 2; Daniel A. Farber, *Toxic Causation*, 71 *MINN. L. REV.* 1219, 1219-20 (1987); Jean M. Eggen, *Toxic Reproductive and Genetic Hazards in the Workplace: Challenging the Myths of the Tort and Worker's Compensation System*, 60 *FORDHAM L. REV.* 843, 861-64 (1992) (discussing causation problems in the worker's compensation system);

Both negligence and strict liability require the plaintiff to prove that the substance in question³⁶ caused the plaintiff's disease or injury.³⁷ That inquiry often involves a number of subissues,³⁸ including whether: (1) the toxic substance is capable of causing the harm complained of³⁹; (2) the plaintiff was exposed to the toxic substance in quantity sufficient to cause disease,⁴⁰ and (3) the toxic substance exposure caused the particular plaintiff's injury or disease.⁴¹ Proof of any of these propositions is likely to require expert testimony on scientific evidence.⁴²

Palma J. Strand, Note, *The Inapplicability of Traditional Tort Analysis to Environmental Risks: The Example of Toxic Waste Pollution Victim Compensation*, 35 STAN. L. REV. 575, 583-84 (1983); Note, *Tort Actions for Cancer: Deterrence, Compensation, and Environmental Carcinogenesis*, 90 YALE L.J. 840 (1981) (hereinafter Note, *Tort Actions for Cancer*).

36. Disputes over who produced the offending substance have also been cast as causation questions. These "indeterminate defendant" cases have arisen frequently in asbestos and DES litigation where the plaintiff may have difficulty identifying the producer of the substance to which the plaintiff was exposed, even where the causal connection between the substance and the injury is established. See Richard Delgado, *Beyond Sindell: Relaxation of Cause-in-Fact Rules for Indeterminate Plaintiffs*, 70 CAL. L. REV. 881 (1982); Eggen, *supra* note 35, at 890-91 & n.258.

37. Most courts require proof of causation to meet a "more likely than not" standard. See, e.g., *Renaud v. Martin Marietta Corp.*, 749 F. Supp. 1545, 1553 (D. Colo. 1990), *aff'd*, 972 F.2d 304 (10th Cir. 1992). See generally Bert Black & David E. Lilienfeld, *Epidemiologic Proof in Toxic Tort Litigation*, 52 FORDHAM L. REV. 732, 749-50 (1984). But see Black, *supra* note 15, at 659-69 (discussing the meaning of "reasonable medical certainty"). Additionally, most jurisdictions require the plaintiff to prove that her injuries would not have occurred "but for" the exposure to the toxic substance. Brennan, *supra* note 15, at 493-94. Where there are two or more contributing causes to a single harm, some courts will require proof only that the exposure was a "substantial factor" in causing the plaintiff's injury or that it "contributed to" the plaintiff's injury. See *Renaud v. Martin Marietta Corp.*, 749 F. Supp. at 1551 (plaintiff must prove that "the exposure caused, or contributed to, plaintiff's injuries"). Proof under the substantial-or-contributing-factor test nonetheless requires establishment of a "but for" causal relationship between the substance and the plaintiff's disease. See Bert Black et al., *Unravelling Causation: Back to the Basics*, 7 TOXICS L. REP. (BNA) 1061, 1063 (1993). A somewhat different formulation, perhaps more suited to the realities of toxic torts, is Calabresi's "causal linkage," that is, the belief that the causative event makes the occurrence of the injury result more likely. See Guido Calabresi, *Concerning Cause and the Law of Torts: An Essay for Harry Kalven, Jr.*, 43 U. CHI. L. REV. 69, 71 (1975).

38. See Black & Lilienfeld, *supra* note 37, at 737-38.

39. See Black, *supra* note 15, at 689. Although this framing of the question seems implicit, plaintiffs sometimes argue that evidence of causation of one type of harm is evidence of causation of other types of harm. *Id.*; see also *Christopherson v. Allied-Signal Corp.*, 939 F.2d 1106, 1115 (5th Cir. 1991) (en banc) (association of nickel and cadmium with small-cell carcinoma of the lung asserted as probative of causation of small-cell colon cancer), *cert. denied*, 112 S. Ct. 1280 (1992).

40. See Black & Lilienfeld, *supra* note 37, at 737-38. Courts sometimes frame the question more simply as whether the plaintiff was exposed to the toxic substance, and there is some divergence in the case law as to the specificity with which exposure must be proved. See *infra* notes 219-20 and accompanying text.

41. This statement, which appears all-inclusive, is intended to cover those aspects of causation-in-fact that remain after exposure and capability of the substance to cause harm ("general causation") are established, including primarily the issue of whether plaintiff's

Several characteristics of the typical toxic tort case diminish the prospects of recovery by deserving plaintiffs.⁴³ The long latency period between exposure and disease manifestation⁴⁴ decreases the likelihood that the plaintiff will even suspect the causal connection, as well as decreasing the likelihood that the plaintiff will be able to marshal the facts on issues such as exposure necessary to prove her case.⁴⁵ Typically there is no clinical evidence capable of linking the substance to the disease.⁴⁶ The situation is further complicated by the fact that exposure to the toxic

injury was the result of the toxic substance exposure or other causes. This issue is sometimes referred to as one of "individual causation" or "medical causation." *Renaud v. Martin Marietta Corp.*, 972 F.2d 304, 306 (10th Cir. 1992) (discussing medical causation); see also *Rosenberg*, *supra* note 32, at 855-56 (discussing "specific causation").

42. See, e.g., *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829 (3d Cir. 1990) (plaintiff's case depended upon expert testimony relating to exposure and causation), *cert. denied*, 111 S. Ct. 1584 (1991); *Renaud v. Martin Marietta Corp.*, 749 F. Supp. 1545 (D. Colo. 1990) (expert testimony on exposure and individual causation), *aff'd*, 972 F.2d 304 (10th Cir. 1992). As a definitional matter, this Article will use the terms science and scientific evidence to encompass both science, in the sense of discovery of new factual information, and technology, which can be defined as application of established scientific principles to a particular problem. See Howard T. Markey, *Needed: A Judicial Welcome for Technology—Star Wars or Stare Decisis?*, 79 F.R.D. 209, 210-12 (1978). An additional assumption will be made that scientific evidence will be presented by expert witnesses, because that is most often the case.

43. See generally *Brennan*, *supra* note 25, at 20-26 (discussing cancer causation); *Strand*, *supra* note 35, at 578-86.

44. See *Strand*, *supra* note 35 at 580-81. More precisely, the lapse of time between exposure and the appearance of clinical symptoms may comprise both an induction period, the period of time between the exposure and disease initiation, and a latency period, the interval between disease occurrence and detection. See KENNETH J. ROTHMAN, *MODERN EPIDEMIOLOGY* 14-15 (1986). The period between first exposure and clinically detectable disease for many cancers is 20 to 30 years. *Ames*, *supra* note 29, at 587. Birth defects that are manifest at birth or soon thereafter would not exemplify this problem to nearly as great a degree.

45. Delay may, however, increase the chance that epidemiologic evidence will be available. Nonetheless, latency also gives rise to problems under some formulations of statutes of limitation, although many jurisdictions employ the discovery rule to determine when the statute of limitations begins to run. See *Black & Lilienfeld*, *supra* note 37, at 780; *Strand*, *supra* note 35, at 580-81.

46. In cases involving "signature diseases," diseases that are almost exclusively associated with a toxic substance, the presence of the condition is highly probative of the causative agent. Examples of signature diseases are mesothelioma, associated almost entirely with asbestos exposure, and clear cell adenocarcinoma of the vagina, associated almost exclusively with diethylstilbestrol (DES) exposure in utero. See *Brennan*, *supra* note 25, at 21 & n.96. In most cases, however, either the toxic substance is no longer present when the disease manifests itself, as is the case with benzene and leukemia, or its presence, if persistent, is not the only or even most probable explanation of disease. See *Brennan*, *supra* note 15, at 502. An example of the latter is the almost ubiquitous presence of PCBs in human adipose tissue, apparently without effect in most cases. See *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829, 843 (3d Cir. 1990) (discussing ATSDR studies), *cert. denied*, 111 S. Ct. 1584 (1991). But see *Landrigan v. Celotex Corp.*, 605 A.2d 1079, 1087 (N.J. 1992) (discussing the presence of asbestos near the tumor as probative of colon cancer causation).

substance, even at relatively high levels, may not result in disease in most persons.⁴⁷ Moreover, many of the diseases caused by toxic chemicals, particularly cancers and birth defects, occur in the general population.⁴⁸ The absence of any unequivocal linkage between the disease and the toxin, together with the absence of clinical tests that could establish a linkage, means that proof of causation, if it can be made out at all, must be made indirectly, from comparisons between exposed and unexposed groups, or from studies where surrogates such as animals or single-celled organisms are used. Further, there may be other known risk factors for the claimed injury, whose role in the disease process must be considered.⁴⁹

The obvious difficulties of proof in toxic tort cases provoked a flood of commentary and proposals for reform.⁵⁰ A number of commentators have focused specifically on limitations placed by courts on the kinds of

47. Occupational asbestos exposure in nonsmokers increases the risk of lung cancer by about a factor of five, from about 11 per 100,000, for nonsmoking industrial workers not exposed to asbestos, to about 58 per 100,000 for nonsmoking asbestos workers. See U.S. SURGEON GEN., U.S. DEP'T OF HEALTH & HUMAN SERVS., PUB. NO. 85-50207, HEALTH CONSEQUENCES OF SMOKING: CANCER AND CHRONIC LUNG DISEASE IN THE WORKPLACE 216 (1985); see also Rodolfo Saracci, *The Interactions of Tobacco Smoking and Other Agents in Cancer Etiology*, EPIDEMIOLOGIC REVS. 175, 181-83 (1987).

48. See, e.g., *Rubanick v. Witco Chem. Corp.*, 593 A.2d 733, 745 (N.J. 1991) (involving contention that PCB exposure caused colon cancer). Colorectal cancer is the second most common cancer in the United States. *Colonoscopy Recommended*, AM. MED. NEWS, Sept. 16, 1991, at 39, cited in *Landrigan*, 605 A.2d at 1082).

49. For example, although asbestos is recognized as a cause of lung cancer, see *supra* note 47, other causative factors such as smoking are well known. That fact often leads to contentions that the plaintiff's disease was caused by factors other than the toxic chemical exposure. For discussion of attributable risk and the problems of distinguishing among causes, see *infra* notes 206-18 and accompanying text.

50. Some commentators have proposed modification of the tort system's rules of liability, suggesting, for example, that courts recognize causes of action for tortiously created risk. See, e.g., Glen O. Robinson, *Probabilistic Causation and Compensation for Tortious Risk*, 14 J. LEGAL STUD. 779 (1985) [hereinafter Robinson, *Probabilistic Causation*]. Others have suggested that all victims of a disease attributable in part to toxic chemical exposure recover the fraction of their damages that corresponds to the proportion of disease incidence attributable to the toxic exposure. See, e.g., Delgado, *supra* note 36, at 892; Glen O. Robinson, *Multiple Causation in Tort Law: Reflections on the DES Cases*, 68 VA. L. REV. 713, 759 (1982); Rosenberg, *supra* note 32; cf. Farber, *supra* note 35, at 1221 (proposing compensation for the "most likely victim"). A number of courts have redefined damages or injury to include exposure, presumed subclinical injury, medical monitoring costs, or fear of cancer where clinically manifest disease or injury is absent. See 2 DORE, *supra* note 5, §2.02.

Other commentators have recommended the shifting burden of proving causation to defendants, once a threshold showing is made of the possibility of harm. See Note, *Tort Actions for Cancer*, *supra* note 35, at 855-62. Still others have suggested administrative compensation systems with reduced requirements for proof of causation. See Black & Lilienfeld, *supra* note 37, at 734 & nn.3-5 (discussing the Superfund Study Group's proposal for an administrative compensation scheme); see also E. Donald Elliott, *Why Courts? Comment on Robinson*, 14 J. LEGAL STUD. 799, 801 (1985).

evidence deemed admissible or sufficient to prove causation. One set of problems has been courts' reluctance to accept statistical evidence, such as epidemiologic studies, because statistical evidence does not provide mechanistic explanations of cause and because statistics do not provide a basis for distinguishing between persons in an exposed group whose disease was caused by the exposure from those whose disease was caused by background or other risk factors.⁵¹ Recognizing that epidemiologic evidence is often the best if not the only evidence linking a toxic substance exposure to disease, however, recent cases have been more accepting of epidemiologic evidence,⁵² in some cases evidencing quite a sophisticated understanding of epidemiologic evidence.⁵³

Other commentators have urged courts to liberalize the standards for admissibility of scientific evidence in general.⁵⁴ They have suggested that the traditional requirement under *United States v. Frye* that limits the admission of scientific evidence to that generally accepted in the relevant scientific discipline⁵⁵ may preclude recovery by deserving plaintiffs who

51. See, e.g., Black & Lilienfeld, *supra* note 37, at 767; Brennan, *supra* note 15, at 491-501.

52. See, e.g., Brock v. Merrell Dow Pharmaceuticals, Inc., 874 F.2d 307, 313 (5th Cir.) (holding absence of "conclusive" epidemiologic evidence fatal to plaintiffs' case), *modified*, 884 F.2d 166, 167 (5th Cir. 1989), *cert. denied*, 494 U.S. 1046 (1990). The Fifth Circuit subsequently modified Brock, stating that the plaintiffs' case was fatally flawed because of their failure to present "statistically significant" epidemiologic evidence. Brock v. Merrell Dow Pharmaceuticals, Inc., 884 F.2d 166, 167 (5th Cir. 1989) (denying plaintiffs' motion for rehearing en banc and modifying prior opinion), *cert. denied*, 494 U.S. 1046 (1990). Courts willing to accept statistical evidence as probative of the capability of a substance to cause harm have sometimes balked at accepting such evidence on the question of whether the substance caused the *plaintiff's* injury, on the basis the epidemiologic evidence cannot prove individual causation. See, e.g., Landrigan v. Celotex Corp., 605 A.2d 1079, 1087 (N.J. 1992) (discussing the trial court's refusal to allow an epidemiologist to testify on individual causation). In *Landrigan*, the New Jersey Supreme Court, however, set forth a detailed summary of how epidemiologic reasoning could be applied to the question of individual causation and concluded that an epidemiologist could offer an opinion on that issue, provided the expert's qualifications and methodology withstood the trial court's scrutiny. *Id.* at 1087-89.

53. See, e.g., DeLuca v. Merrell Dow Pharmaceuticals, Inc., 911 F.2d 941, 946-49 (3d Cir. 1990) (discussing statistical significance); *Landrigan*, 605 A.2d at 1087 (discussing the concept of attributable risk derived from epidemiologic studies). Several courts have announced that epidemiologic evidence is the only sufficient evidence on the question of whether Bendectin causes human birth defects. See, e.g., Brock, 874 F.2d at 313-15.

54. Anne S. Toker, *Admitting Scientific Evidence in Toxic Tort Litigation*, 15 HARV. ENVTL. L. REV. 165 *passim* (1991); see also citations in *Rubanick v. Witco Chem. Corp.*, 593 A.2d 733, 740 (N.J. 1991).

55. The traditional standard for determining the admissibility of novel scientific evidence was set forth in *Frye v. United States*, 293 F. 1013 (D.C. Cir. 1923). The *Frye* court stated, in regard to evidence based on a forerunner of modern polygraph testing, that "the thing from which the deduction is made must be sufficiently established to have gained general acceptance in the particular field to which it belongs." *Id.* at 1014. The *Frye* test is most appropriately applied to the expert's methodology or reasoning, including but not limited to devices or techniques such as the breathalyzer or polygraph. See Black, *supra* note 15, at 627-29. It is sometimes applied to the expert's opinion or conclusions, however,

must rely on novel, yet valid and reliable evidence.⁵⁶ That line of reasoning was accepted in *Ferebee v. Chevron Chemical Company*,⁵⁷ in which the Court of Appeals for the District of Columbia Circuit upheld a jury verdict of liability based on expert opinion testimony on causation that did not enjoy general acceptance in the scientific community.⁵⁸

Ferebee coincided with a general move away from the *Frye* standard under the Federal Rules of Evidence toward the relevancy or reliability test articulated in *United States v. Downing*.⁵⁹ In *Downing*, the Third Circuit stated that the admissibility of scientific evidence should focus on the soundness and reliability of the expert's methodology, the strength of the connection between the evidence and the issues in the case, and the possibility of confusing or misleading the jury.⁶⁰ Acceptance of the

in such cases being stated to require that the expert's opinion or theory be generally accepted by the relevant scientific community. See, e.g., *Rubanick v. Witco Chem. Corp.*, 542 A.2d 975, 982 (N.J. Super. Ct. Law Div. 1988) (applying *Frye* analysis to scientific principle on which expert's opinion was based), *rev'd*, 576 A.2d 4 (N.J. Super. Ct. 1990), *modified*, 593 A.2d 733 (N.J. 1991); see also Black, *supra* note 15, at 629-38. Contrarily, some commentators have taken the position *Frye's* general acceptance test should not be applied to an expert's reasoning or methodology, but only to particular techniques or devices. See, e.g., *Christopherson v. Allied-Signal Corp.*, 939 F.2d 1106, 1131-33 (5th Cir. 1991) (Rawley, J., dissenting), *cert. denied*, 112 S. Ct. 1280 (1992). Many jurisdictions still follow *Frye*. See, e.g., *Christopherson*, 939 F.2d 1106.

56. *Frye* has proven to be a significant barrier to novel scientific theories and methodologies. Edward J. Imwinkelreid, *The Standard for Admitting Scientific Evidence: A Critique from the Perspective of Juror Psychology*, 28 VILL. L. REV. 554, 555-56 (1982-83). As Huber has pointed out, however, when the *Frye* inquiry is directed to the methodology and reasoning underlying scientific opinion, a novel opinion on causation will easily pass muster if it is based on well-established and properly conducted methods, such as epidemiologic studies. Huber, *supra* note 15, at 744.

57. See *Ferebee v. Chevron Chem. Co.*, 736 F.2d 1529 (D.C. Cir.), *cert. denied*, 469 U.S. 1062 (1984).

58. *Id.* at 1535-36. The *Ferebee* court did not reject *Frye* out of hand, however, but construed it as applicable only to novel techniques or methodologies, not scientific opinion testimony. *Id.* at 1535.

59. 753 F.2d 1224 (3d Cir. 1985); see also *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829, 856-60 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991); *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223, 1242 (E.D.N.Y. 1985), *aff'd*, 818 F.2d 187 (2d Cir. 1987), *cert. denied*, 487 U.S. 1234 (1988); *Rubanick v. Witco Chem. Corp.*, 593 A.2d 733, 746 (N.J. 1991).

60. In *Downing*, the Third Circuit articulated the proper test as follows:

In our view, Rule 702 [of the Federal Rules of Evidence] requires that a district court ruling upon the admission of (novel) scientific evidence . . . conduct a preliminary inquiry focusing on (1) the soundness and reliability of the process or technique used in generating the evidence, (2) the possibility that admitting the evidence would overwhelmingly confuse or mislead the jury, and (3) the proffered connection between the scientific research or test result to be presented and the particular disputed factual issues in the case.

Downing, 753 F.2d at 1238. The *Downing* reliability standard is inherently more flexible than *Frye* because it is not tied to "general acceptance." Nonetheless, courts recognize that acceptance in the expert community is an important indicium of reliability. See, e.g., *id.*

expert's techniques or methodology in the relevant scientific community is evidence of soundness, but need not be the sole basis for that determination.

Although *Frye* has been justifiably criticized as too simplistic and inflexible,⁶¹ the *Downing* standard is equally problematic when it is used to justify such minimal scrutiny of the reliability of scientific evidence, particularly of expert opinion testimony, that it amounts to no standard at all. The troublesome, deferential application of the reliability standard adopts the approach that if "qualified" experts are willing to testify that a causal relationship exists, the court is willing to uphold a plaintiff's verdict without examining whether a reasoned basis exists for the expert's opinion.⁶² This approach is undoubtedly the result of some courts' reluctance to delve into the reasoning underlying scientific evidence, a reluctance that results in deference to the expert with seemingly impressive credentials. The crucial determination then becomes whether the expert is qualified, a particularly weak screening device given the lenient standards for determining expert qualifications.⁶³

Deferential review is the gateway for the admission of junk science into the courts. When courts do not examine the reasoning of expert testimony, they are likely to accept medical opinion based on the facts in the case at hand, or supported by perhaps a few other case reports, facts

Thus, the *Frye* standard is related to reliability, though more limiting. See generally Imwinkelried, *supra* note 56.

61. Part of the difficulty with the *Frye* rule is the lack of consensus regarding the subject matter to which it applies. For example, is it the expert's opinion, the reasoning or methodology that underlies the opinion, or both that must be generally accepted? See *supra* note 55. The better rule would seem to be that the *Frye* general acceptance test applies to the expert's reasoning and methodology, but not to the opinion or conclusion derived from that methodology. Otherwise, the *Frye* rule effectively delegates part of the admissibility determination to the scientific discipline, obviating the need for the court to evaluate the expert's reasoning or methodology. On the other hand, as Black has pointed out, the general acceptance test of *Frye* is not an appropriate standard to apply to the uncertainty or accuracy (i.e., the reliability) of scientific methodology. See Black, *supra* note 15, at 629-57. The Ninth Circuit's opinion in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 951 F.2d 1128 (9th Cir. 1991), *cert. granted*, 113 S. Ct. 320 (1992), appears to commit this error, when it frames the admissibility standard regarding an unpublished, un-peer-reviewed reanalysis of epidemiologic data as follows: "Expert opinion based on a scientific technique 'is admissible if it is generally accepted as a reliable technique among the scientific community.'" *Id.* at 1129 (quoting *United States v. Solomon*, 753 F.2d 1522, 1526 (9th Cir. 1985)).

62. *Ferebee v. Chevron Chem. Co.*, 736 F.2d 1529 (D.C. Cir.), *cert. denied*, 429 U.S. 1062 (1984), is the leading case following this approach and is often cited by other courts taking similar approaches. In *Ferebee*, the Court of Appeals for the District of Columbia Circuit upheld a jury verdict for the plaintiff where testimony of causation was based on "tissue samples, standard tests, and patient examination." *Id.* at 1536. There is nothing in the opinion to suggest that the cited tests and examinations were capable of indicating the cause of the lung disease complained of, however.

63. FED. R. EVID. 702 provides that a witness may be qualified as an expert "by knowledge, skill, experience or training."

that cannot establish causation because the coincidence of exposure and disease may be the result of chance.⁶⁴ In some cases, courts accept as sufficient medical or similar opinions supplemented by reference to animal studies, chemical structure-activity analyses, mutagenicity testing, or other similar lines of reasoning that are subject to a large degree of uncertainty.⁶⁵ Affirmative epidemiologic evidence of a statistically significant association between the alleged causative agent and human disease is absent.⁶⁶ As a practical matter, only those cases based on studies in human populations of the association of suspected toxic substances and disease—e.g., epidemiologic studies or highly unusual disease clusters—have proven to be sound as new scientific information developed.⁶⁷

A reliability analysis should not result in uncritical acceptance of junk science.⁶⁸ Tort jurisprudence requires that there be a rational basis

64. See, e.g., *Ferebee*, 736 F.2d at 1535.

65. See, e.g., *Rubanick v. Witco Chem. Corp.*, 593 A.2d 733, 735-36 (N.J. 1991) (expert based opinion that PCBs caused plaintiff's colon cancer on animal test reports and other cancer cases at Witco). The Bendectin litigation has been characterized by plaintiffs' cases based on animal testing, structure-activity relationships, *in vitro* testing, and reanalysis of data from epidemiologic studies that failed to show statistically significant increased risks. See, e.g., *Brock v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307 (5th Cir.), *modified*, 884 F.2d 166 (5th Cir. 1989), *cert. denied*, 494 U.S. 1046 (1990). See generally *Sanders*, *supra* note 17. Brennan in particular has urged courts to admit animal studies and other methods used in cancer and other medical research. Brennan, *supra* note 25, at 41-57; see also Michael D. Green, *Expert Witnesses and Sufficiency of the Evidence in Toxic Substances Litigation: The Legacy of Agent Orange and the Bendectin Litigation*, 86 NW. U. L. REV. 643, 680-81 (1992).

66. Occasionally, plaintiffs may offer a "reanalysis" of existing epidemiologic data. See *infra* notes 350-58.

67. It may be tempting to characterize the argument made herein as establishing a threshold requirement of epidemiologic evidence to support a toxic tort case. A number of commentators have characterized *Brock v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307 (5th Cir.), *modified*, 884 F.2d 166 (5th Cir. 1989), *cert. denied*, 494 U.S. 1046 (1990), and cases that have followed it as creating such a threshold in Bendectin cases. See, e.g., Green, *supra* note 65, at 679-82. The intent of this Article, however, is to show why, given the present state of toxicological science, anecdotal evidence, animal test results, and other evidence offered when positive human evidence is missing are generally unreliable and insufficiently probative in the typical toxic torts case. The kind of analysis proposed herein can be applied to new information as it develops, without the rigidity of a per se rule about specific kinds of evidence.

68. In *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223 (E.D.N.Y. 1985), *aff'd*, 818 F.2d 187 (2d Cir. 1987), *cert. denied*, 487 U.S. 1234 (1988), Judge Weinstein excluded the causation opinion testimony of several of plaintiffs' witnesses because he concluded that their testimony, which relied on animal tests and studies of industrial exposures, and which failed to consider and eliminate other causal explanations, was "insufficiently grounded in any reliable evidence." *Id.* at 1248-51. Although Judge Weinstein cited Rule 703 as the basis of his ruling, see *id.* at 1243-55, it is clear that he recognized the uncertainty associated with causal inferences derived from animal studies or human studies where exposures differed widely from plaintiffs', particularly where the experts ignored more relevant studies and alternative causal explanations. See *id.* at 1250. Under the analysis proposed in this Article, the factors cited by Judge Weinstein would be part of a reliability

for judicial findings of fact.⁶⁹ The relevancy or reliability standard's "soundness and reliability" inquiries bear directly on whether there is a rational basis for findings of fact and whether the evidence is sufficient to meet the more probable than not standard of proof.⁷⁰ Active review facilitates the inquiries necessary to decide those issues, while deferential review avoids them. Courts cannot and should not avoid those responsibilities by deferring to "qualified" experts.

III. ACTIVE REVIEW OF SCIENTIFIC EVIDENCE

A. Active Review and the Rules of Evidence

The active review contemplated by this article and being conducted by some courts is a process in which the court conducts two inquiries. First, the court examines the evidentiary basis and reasoning of scientific opinion testimony and determines whether there is a rational basis for the opinion. The evidentiary basis of the opinion, as well as the expert's reasoning, can be probed by the proponent of the testimony, the opponent, or the court,⁷¹ and will often be assisted by the defendants' experts.

The second inquiry focuses on the sufficiency of the admissible evidence to meet the plaintiff's burden of proof. This inquiry goes to the reliability or accuracy of the evidence and requires that the plaintiff present admissible evidence from which a reasonable juror could find that it is more probable than not that the defendant caused the plaintiff's

analysis. See *infra* notes 310-14 and accompanying text; see also Black, *supra* note 15, at 674-76.

69. See, e.g., *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. at 1250.

70. FED. R. EVID. 104 requires the court to determine questions of admissibility of evidence. See, e.g., *Eggar v. Burlington N.R.R.*, No. CV89-159-BLG-JFB, 1991 U.S. Dist. LEXIS 19240 (D. Mont. Dec. 18, 1991). Generally, the proponent of evidence must demonstrate by a preponderance of the evidence that the evidence in question is admissible. *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. at 1239. Under FED. R. CIV. P. 50, 56, the court must determine the sufficiency of the evidence on a motion for summary judgment, a motion for a directed verdict, or a motion for judgment notwithstanding the verdict. Generally the standard for granting any of the foregoing (for defendant) is that no reasonable juror could find or have found for the plaintiff. See, e.g., *Renaud v. Martin Marietta Corp.*, 749 F. Supp. 1545, 1555 (D. Colo. 1990) (granting summary judgment to defendants), *aff'd*, 972 F.2d 304 (10th Cir. 1992).

71. FED. R. EVID. 705 provides: "The expert may testify in terms of opinion or inference and give his reasons therefor without prior disclosure of the underlying facts or data, unless the court requires otherwise. The expert may in any event be required to disclose the underlying facts or data on cross-examination."

As a practical matter, the court may have to do some translation of the language of the scientific field or of legal expressions into commonly understood terms. The court may also be guided by court-appointed experts who serve as witnesses or advisors. For an example of court-appointed experts serving as advisors to the judge, see *Renaud*, 749 F. Supp. 1545.

disease or injury. The same tools used to probe the underlying reasoning of the evidence can be used to inquire into its accuracy, but the question of whether the evidence is sufficiently accurate to satisfy legal standards is, of course, a legal question.

It is important to note that active review is not strict scrutiny.⁷² The plaintiff need not show that her evidence is stronger than the defendant's or that it meets some high level of certainty. The plaintiff's scientific evidence need only be such that a rational factfinder could conclude from the testimony that it is more likely than not that the defendant caused the plaintiff's injury.⁷³ Only when the factual basis and reasoning underlying the expert's opinion on causation do not meet that minimum level of rationality and accuracy should the evidence be excluded.

Active review is not tied to any particular formulation of the standards for admissibility of expert testimony. It is, however, more easily related to the "reliability" determination embraced by a number of courts⁷⁴ than it is to the general acceptance rule of *United States v. Frye*.⁷⁵ The *Frye* rule forecloses the occasion for the court to examine the reasoning underlying the expert's method; however, it leaves questions such as the applicability of a generally accepted method to a particular case, the way in which a generally accepted method was carried out in a particular case,⁷⁶ and the sufficiency of the evidence to be addressed under other criteria. Thus, even if the United States Supreme Court upholds the application of the *Frye* rule in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*,⁷⁷ it will not eliminate the need for courts to actively review scientific expert testimony.⁷⁸

72. *But see, e.g.*, Peter A. Bell, *Strict Scrutiny of Scientific Evidence: A Bad Idea Whose Time Has Come*, *Toxics L. Rep.* (BNA) 1014 (1992). A more apt comparison would be to the "hard look" doctrine of administrative law, that is, the view articulated by Judge Leventhal that courts reviewing the decisions of a technical agency, such as the Environmental Protection Agency, should review the evidence on which the agency's decision is based to determine "whether the agency decision was rational and based on consideration of the relevant factors." *Ethyl Corp. v. EPA*, 541 F.2d 1, 34-36 (D.C. Cir.) (en banc), *cert. denied*, 426 U.S. 941 (1976). Judge Leventhal's views are not without detractors. *See id.* at 66-67 (Bazelon, C.J.). A non-technical, lay jury's decisions would seem to justify greater scrutiny than those of a regulatory agency with technical expertise.

73. *See, e.g., Renaud*, 749 F. Supp. 1545.

74. *See supra* notes 59-60.

75. *See supra* note 55.

76. *Cf., e.g., United States v. Jacobetz*, 955 F.2d 787 (2d Cir. 1992) (the value of DNA testing depends on whether accepted protocols were followed in the specific case), *cert. denied*, 113 S. Ct. 104 (1992).

77. 951 F.2d 1129 (9th Cir. 1991), *cert. granted*, 113 S. Ct. 320 (1992).

78. The *Frye* rule at least creates a threshold for evaluation of the evidence that may serve to curb courts' tendencies to uncritically admit all arguably relevant evidence. The reliability standard nonetheless can serve an appropriate screening function if the court actually conducts a reliability analysis.

B. Active Review and Scientific Reasoning

One of the factors that seems to dissuade courts from scrutinizing scientific evidence more carefully is the belief that the differences between scientific and legal inquiries into causation are such that courts are poorly equipped to examine and evaluate science.⁷⁹ Actually, in determining whether there is a link between an event and a later harm, law and science use identical reasoning processes. Differences between scientific and legal institutions, goals and policies, however, obscure that commonality.

Judge Markey has succinctly stated an essential distinction between science and technology on the one hand, and law on the other:

The differences between the judicial and scientific-technological processes are profound and pervasive. Failure to recognize that difference has led to judicial expressions of frustration and an unfortunate tendency to rest judicial decisions on current, often transient, "truths" and "facts" of science and technology. The purpose of science is to learn physical facts. The purpose and function of technology is to provide a means of using that learning. All that is important and necessary, but that's all it is—learning and using physical facts.

The purpose and function of law is to resolve disputes and to facilitate a structure for the organization of a just society—in a word, to provide justice.⁸⁰

As Markey suggests, science and law do differ in important ways. The culture, institutions and processes by which scientific knowledge is developed and refined are very different from those of law.⁸¹ The development of scientific knowledge involves observation, hypothesis

79. See, e.g., *Ferebee v. Chevron Chem. Co.*, 736 F.2d 1529 (D.C. Cir.), cert. denied, 469 U.S. 1062 (1984). The *Ferebee* court stated:

Judges, both trial and appellate, have no special competence to resolve the complex and refractory causal issues raised by the attempt to link low-level exposure to toxic chemicals with human disease. On questions such as these, which stand at the frontier of current medical and epidemiologic inquiry, if experts are willing to testify that such a link exists, it is for the jury to decide whether to credit such testimony.

Id. at 1534.

80. Markey, *supra* note 42, at 210, quoted in *Rubanick v. Witco Chem. Corp.*, 593 A.2d 733, 741 (N.J. 1991).

81. See Sheila Jasanoff, *What Judges Should Know About the Sociology of Science*, 32 JURIMETRICS J. 345 (1992); David Kaye, *Proof in Law and Science*, 32 JURIMETRICS J. 313, 317-18 (1992). The discomfort many scientist-experts experience in the adversarial setting of legal adjudication is largely due to scientists' perception that the law requires unequivocal statements on matters that are not clear cut from the scientist's perspective. Further, they are uncomfortable with the legal system's insistence on decisions, often before adequate evidence is available from a scientific perspective. For further discussion of the differences between the processes of legal and scientific inquiry, see Huber, *supra* note 15, at 739-42 (1992).

building, testing, generalizing, and consensus building.⁸² Legal fact-finding, on the other hand, is adversarial, confrontational, and directed toward a definitive result in the case at hand. Concern for consistency from case to case plays a lesser role in law⁸³ than in science.⁸⁴

Unfortunately, these institutional and methodological differences obscure the reality that factfinding, that is, science in its broadest sense, is a necessary part of legal decisionmaking. Legal decisionmaking has additional policy components beyond the purely factual, so that it may attach different consequences to the same facts than would a scientist. Thus, the starting point for the analysis of the relationship between science and law on the issue of causation is a delineation of the factual and nonfactual components of legal concepts of cause.

To be sure, causation issues in tort law have nonfactual, policy-laden elements, as exemplified by the legal concept of proximate cause.⁸⁵ All tort theories include some notion of "cause-in-fact" as a prerequisite to liability,⁸⁶ however, and where cause-in-fact is concerned, science and law are attempting to answer the same questions. Further, law, like science, accepts only rational or reasoned findings of fact.⁸⁷ Most importantly, scientific and legal factfinding employ the same logic.⁸⁸

82. See Black, *supra* note 15, at 615-27.

83. In *Wells v. Ortho Pharmaceutical Corp.*, 615 F. Supp. 262 (D. Ga. 1985), *aff'd in part, modified on other grounds*, 788 F.2d 741 (11th Cir.) (modifying damage award), *cert. denied*, 479 U.S. 950 (1986), the court held that plaintiff had proved that her daughter's birth defects were caused by the mother's prenatal use of a spermicide, despite FDA approval and scientific consensus that spermicides do not cause birth defects. See *id.* at 266. But see *Brock v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307, 315 (5th Cir.), *modified*, 884 F.2d 166 (5th Cir. 1989), *cert. denied*, 494 U.S. 1046 (1990). In *Brock*, the court expressed the hope that its ruling would have "a precedential effect on other cases pending in this circuit which allege Bendectin as the cause of birth defects." *Id.* at 315.

84. That is not to say that science is fixed and unchangeable. Scientific knowledge is always open to revision as new information comes to light that is inconsistent with previously understanding. The point, however, is that scientific reasoning requires that a scientific explanation accommodate and be consistent with all the available data at any point in time.

85. The concept of proximate cause is generally recognized as encompassing policy questions of how closely the defendant's tortious conduct must be related to the plaintiff's injury for the defendant to be held liable. See, e.g., Richard W. Wright, *Responsibility, Risk, Probability, Causation, Naked Statistics and Proof: Pruning the Bramble Bush by Clarifying the Concepts*, 73 IOWA L. REV. 1001, 1011-12 (1988). Viewed in that light, the proximate cause requirement is a limitation on liability where defendant's conduct was the actual cause of plaintiff's injury. *Id.*

86. See *id.* Of course, the way in which the factual question is framed, as well as the burden of proof and evidentiary standards has policy overtones. See Eggen, *supra* note 35, at 899-904 (suggesting shift of burden of proving causation); Nancy L. Firak, *The Developing Policy Characteristics of Cause-in-Fact: Alternative Forms of Liability, Epidemiologic Proof and Trans-Scientific Issues*, 63 TEMP. L. REV. 311, 313 (1990) (arguing that courts' acceptance of epidemiologic evidence is a policy choice rather than a factual conclusion).

87. See Wright, *supra* note 85, at 1011-12; see also *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223, 1250 (E.D.N.Y. 1985), *aff'd*, 818 F.2d 187 (2d Cir. 1987), *cert. denied*, 487

Much of the early commentary about the differences between science and law in toxic torts concerned courts' discomfort with statistical evidence of causation. Commentators have attributed that discomfort in part to courts' preferences for mechanistic causal explanations and their reluctance to rely heavily or entirely on statistical evidence.⁸⁹ Courts and lay persons typically think about causal issues in terms of *how* things happen and statistical evidence does not explain how events occur.⁹⁰

When mechanistic thinking about cause is extended to the area of toxic substance disease causation, it immediately encounters a large, perhaps insurmountable, stumbling block. Scientists know very little about how, in a mechanistic sense, toxic substances cause diseases such as

U.S. 1234 (1988). The ubiquitous legal requirement that there exist a rational or reasonable basis for findings of fact evidences the underlying assumption that reasoning and logic must connect evidence to conclusions.

88. David Kaye has demonstrated that science and law use the same logical rules in proving facts. See Kaye, *supra* note 81. He concludes: "[W]hen it comes to proving facts, the logic of law and that of science are one and the same. At an abstract level, the rules of inference can be given the same formal representation." *Id.* at 317; see also Lee Loevinger, *Standards of Proof in Science and Law*, 32 JURIMETRICS J. 323, 328 (1992).

In regard to the role of social science in overturning *Plessy v. Ferguson*, Kenneth B. Clark has stated:

The development of science as an approach to the determination of truth involved the development of methods for the control of errors in human observation, judgment, biases, and vested interests. These were the factors which seemed to have distorted man's concept of, or blocked his contact with, the "truth" or "facts" of experience. When they are operative, man's "common knowledge" becomes inconsistent with "scientific knowledge." When they are controlled or for some other reason non-operative, "common knowledge" and "scientific knowledge" are coincident—both reflecting the nature of reality, truth, or facts, as these are knowable to the human senses and intelligence.

Science is essentially a method of controlled observation and verification for the purpose of reducing human errors of observation, judgment, or logic. Science begins with observation and ends by testing its assumptions against experience. It is not a creation of another order of reality. In a very basic sense there cannot be a "legal fact" or a "fact of common knowledge" which is not at the same time a "scientific fact." Whenever this appears to be true, one or the other type of "fact" is not a fact.

Kenneth B. Clark, *The Desegregation Cases: Criticism of the Social Scientist's Role*, 5 VILL. L. REV. 224, 233 (1959).

89. See e.g., Brennan, *supra* note 15, at 478-91. Brennan refers to mechanistic conceptions of cause as "corpuscularianism," after the writings of various philosophers of science. See *id.* at 478-79.

90. The understanding of how a cause produces an effect makes us more comfortable with the conclusion that causation occurred. Richard Wright puts it this way:

Usually, the issue [of proving causation] is what has happened—including how it happened and who did it—although sometimes the issue is what is expected to happen—for example, the expected reduction in future income as an element of damages. That is, proof generally involves either causal explanation or causal prediction.

Wright, *supra* note 86, at 1049.

cancer or injuries such as birth defects.⁹¹ Nonetheless, they may know a considerable amount about *whether* toxic substances cause disease or injury through inferences drawn from statistical associations and other indirect means.⁹² Thus, the shift in thinking required for courts to come to grips with current scientific knowledge had more to do with abandoning a felt need for an explanatory process that increases comfort with the causal inference than it did with redefining causation.

Courts' discomfort with statistical evidence has gone beyond the absence of mechanistic explanations, however.⁹³ Statistical evidence by definition provides information only about the incidence of disease in groups. Where there are other possible causes of disease, statistical evidence cannot determine which individuals' diseases within the exposed group were caused by background or other factors.⁹⁴ It can only

91. Brennan, *supra* note 25, at 20-25 (discussing scientific evidence of cancer causation).

92. *Id.*

93. See Black & Lilienfeld, *supra* note 37, at 744-50; Brennan, *supra* note 15, at 483-93. Brennan states that courts' refusal to consider and accept statistical evidence reflects and is consistent with courts' traditional reliance on mechanistic causal explanations. See Brennan, *id.* at 491-92.

94. Extensive or complete reliance on epidemiologic proof and other statistical evidence is not without its detractors. See, e.g., Michael Dore, *A Commentary on the Use of Epidemiologic Evidence in Demonstrating Cause-in-Fact*, 7 HARV. ENVTL. L. REV. 429 (1983); Wright, *supra* note 86, at 1049-67 (arguing that particularistic evidence is required to prove actual causation). Dore reiterates the commonly held view that epidemiologic evidence is proof not of actual, individual causation, but only of risk. See Dore, *supra*, at 435. Regarding the use of epidemiology in proving risk (apparently meant as the ability of a substance to cause harm), Dore states:

Within the limitations just discussed, epidemiologic evidence can demonstrate the relative level of risk to which the defendant's activities exposed the members of the plaintiff's group. This risk, of course, does relate to the individual plaintiff. Courts that fail to distinguish the issue of risk from that of actual causation may accordingly, but erroneously, permit the evidence of risk to establish causation. Epidemiologists do not design their studies to resolve issues of individual biological causation, however, and the courts must strictly limit the use of such studies for this purpose.

The limitations on epidemiology's ability to prove individual causation stem from its general and statistical nature. Epidemiologic studies are general in that they deal with sources of disease in groups of people rather than particular individuals. Being statistical, they quantify the probabilities, or risks, that members of a group will contract certain diseases under certain conditions. The only individual cause-and-effect relationship that epidemiologic evidence can show is that the defendant's conduct increased the plaintiff's risk of injury to some statistically measurable extent. *It cannot answer the critical question whether the defendant's conduct actually injured the plaintiff.*

Id. at 436 (citations omitted). Dore and other detractors of statistical evidence frame the question incorrectly, however. The issue in toxic torts is whether there is evidence from which an inference can be made that it is more probable than not that the exposure caused the plaintiff's disease. As others have pointed out, the statistical evidence provided by epidemiology is probative of that issue. See Black & Lilienfeld, *supra* note 37, at 764-69 (combining relative risk with more-probable-than-not standard of proof); Kristina L. Hall

provide an estimate of the likelihood that an individual's disease was caused by the toxic substance in question.⁹⁵ Thus, courts' concerns are not unreasonable. The more likely than not standard of proof, however, implicitly contemplates the marshaling of facts that ultimately prove liability in terms of probabilities.

Uncomfortable with factual indeterminacy, some courts rejected statistical evidence entirely, demanding evidence that is particular to the plaintiff.⁹⁶ Other courts have accepted statistical evidence on issues such as whether a toxic substance is capable of causing harm, but not on the question of whether it caused the plaintiff's harm.⁹⁷ A number of recent cases, however, have recognized the necessarily statistical nature of proof at all levels in toxic torts, and accepted statistical evidence as probative of individual causation, at least where there is evidence indicating a greater than 50% likelihood that the toxic substance caused the plaintiff's disease.⁹⁸ A number of recent decisions evidence a sophisticated understanding of epidemiologic evidence and its relation to legal standards of proof.⁹⁹

The remaining areas where science seems to fit poorly with legal problems are largely the result of failure to distinguish legal standards of proof from factual issues. Courts are concerned that they must decide cases based on the information available, which may not be complete enough to satisfy the requirements of a particular scientific discipline.¹⁰⁰ Some courts perceive scientists as generally requiring higher levels of certainty than does the law.¹⁰¹ That perception may be correct in some instances, particularly in areas such as epidemiology, where standard

& Ellen K. Silbergeld, *Reappraising Epidemiology: A Response to Mr. Dore*, 7 HARV. ENVTL. L. REV. 441, 445-46 (1983). Indeed, signature diseases, which are usually not perceived as presenting difficult individual causation issues, are simply cases in which the statistical evidence is very persuasive because the background incidence of disease is very low compared to the incidence in the exposed population.

95. See *supra* notes 94 and accompanying text.

96. See Brennan, *supra* note 15, at 492 & nn.114-15.

97. See, e.g., *Landrigan v. Celotex Corp.*, 605 A.2d 1079 (N.J. 1992) (reversing the trial court's rejection of opinion testimony on individual causation based on epidemiology).

98. See, e.g., *id.* at 1087.

99. See, e.g., *DeLuca v. Merrell Dow Pharmaceuticals, Inc.*, 911 F.2d 941, 946-56 (3d Cir. 1990) (discussing the statistical significance of epidemiologic data); *Landrigan*, 605 A.2d at 1085-87 (discussing the significance of relative risk and attributable fraction).

100. See, e.g., *Ferebee v. Chevron Chem. Corp.*, 736 F.2d 1529 (D.C. Cir.), *cert. denied*, 469 U.S. 1062 (1984). The *Ferebee* court held that a treating physician could testify to his opinion that a cause and effect relationship existed between the insecticide paraquat and Ferebee's pulmonary fibrosis even if such a relationship had not been "clearly established" by animal or epidemiologic studies. *Id.* at 1535.

101. In *Rubanick v. Witco Chem. Corp.*, 593 A.2d 733, 737, 740-41 (N.J. 1991), the New Jersey Supreme Court made several references to the "extraordinarily high level of proof" required by the scientific method. Defendant's witness apparently played into that concern, however unwittingly. See *id.* at 737.

protocols for statistical analysis of relative risk data typically require a 95% level of certainty that an observed increase in risk is not due to chance.¹⁰² Scientists do not require a high degree of certainty for all purposes, however. Risk assessment for purposes of regulation is based on highly uncertain risk estimates. Additionally, scientists often use highly tenuous or uncertain assumptions in making decisions about further research.¹⁰³

The issue of how much uncertainty is acceptable is a legal requirement to be applied to the evidence once the uncertainty attending the scientific evidence is established.¹⁰⁴ Where the law requires the plaintiff to prove her case by a preponderance of the evidence, current standards permit the plaintiff to win if sufficient evidence is available, but not prevail if it is not available.¹⁰⁵ Scientific evidence can be evaluated against those standards, irrespective of whether the scientific discipline would be satisfied or not with the available level of certainty.¹⁰⁶ Moreover, the fact that scientists may require a different level of certainty is not a good reason to dispense with science's requirement of a reasoned analysis, a requirement common to law and science. Unfortunately, some courts throw the baby out with the bathwater by rejecting scientific reasoning altogether when they perceive scientists' requirements for certainty to be too stringent.¹⁰⁷

102. Black & Lilienfeld, *supra* note 37, at 757 n.104; *see infra* notes 364-67 and accompanying text; *see also* DeLuca, 911 F.2d at 946-49 (discussing statistical significance in epidemiology).

103. For example, as discussed in *Wells v. Ortho Pharmaceutical Corp.*, 615 F. Supp. 262 (D. Ga. 1985), *aff'd in part, modified on other grounds*, 788 F.2d 741 (11th Cir.) (modifying damages), *cert. denied*, 479 U.S. 950 (1986), the "Oeschli study" raised suspicions about the possibility of an association between spermicides and birth defects and recommended further study. *Id.* at 284. Further studies with greater statistical power failed to confirm that suspicion. *See id.*

104. *See* Black, *supra* note 15, at 600 (discussing reliability as a legal question).

105. From that perspective, science and law seem to have parallel requirements because each refuses to reach an affirmative conclusion that causation exists until an acceptable level of certainty is attained, even though the law and the scientific discipline may require different levels of certainty. The relationship between legal and scientific notions of sufficiency of proof is perhaps less clear, however, than is the identity of the logic employed by each. *See* David Kaye, *On Standards and Sociology*, 32 JURIMETRICS J. 535 (1992); Lee Loevinger, *On Logic and Sociology*, 32 JURIMETRICS J. 527 (1992). *Compare* Kaye, *supra* note 81, *with* Loevinger, *supra* note 88.

106. That is not to say that scientists' perceptions of the appropriate level of certainty should be ignored. Requirements such as epidemiologists' practice of requiring a 95% confidence level often have their roots in years of experience in the discipline. With epidemiologic studies in particular, there may be undetected systematic bias in selection of the comparison groups, including the possibility of undetected confounding factors, that are not taken into account in the statistical analysis. *See* ROTHMAN, *supra* note 44, at 89-96; Black & Lilienfeld, *supra* note 37, at 737-38; *infra* text accompanying notes 346-49.

107. *See, e.g.,* *Rubanick v. Witco Chem. Corp.*, 593 A.2d 733 (N.J. 1991), *discussed infra* notes 287-300 and accompanying text.

Courts can and should evaluate the underlying reasoning of scientific evidence and measure its reliability or uncertainty against legal standards of sufficiency to meet the applicable burden of proof. The following part of this article attempts to facilitate that process by explicating the bases on which courts can recognize and reject invalid or unreliable evidence, matters on which the differences between science and law are a matter of degree, not kind. Thus, courts need not fear that delving into science and technology will be entirely a foray into alien territory.

IV. ACTIVE REVIEW OF CAUSATION EVIDENCE IN TOXIC TORTS

A. Validity, Reliability, and the Determination of Probative Value

Whether courts operate under the *Frye* rule, the "reliability" standard of *United States v. Downing*,¹⁰⁸ or some other formulation of the rules governing scientific expert testimony, the question courts must answer when they evaluate scientific evidence is, "How probative is it?"¹⁰⁹ That question includes two subissues, however: validity and reliability.¹¹⁰ Validity is the issue of whether the evidence is capable of producing the kind of information sought; thus, it is essentially equivalent to the concept of relevance as used in the rules of evidence.¹¹¹ Reliability connotes the likelihood of a correct or accurate result,¹¹² and thus encompasses notions of certainty or accuracy.¹¹³ Reliability is

108. 753 F.2d 1224 (3d Cir. 1985).

109. So framed, that question corresponds to the determination of "reliability" under *United States v. Downing*. See *supra* notes 59-63 and accompanying text.

110. See Black, *supra* note 15, at 599-600 (discussing validity as part of the reliability determination).

111. FED. R. EVID. 401.

112. See *supra* note 110.

113. This Article thus adopts and expands on the analytical framework proposed by Black, although it uses the terms validity and reliability in a slightly different way. See generally Black, *supra* note 15.

Black defines validity as "that which results from sound and cogent reasoning," and reliability as meaning "that a successful outcome, or correct answer, is sufficiently probable for a given situation." *Id.* at 599-600. Thus, he frames validity as a scientific question, and reliability as a legal one. *Id.* at 600. Validity is to be determined largely by reference to widespread acceptance in the scientific community of the underlying reasoning. *Id.* at 637-38. Black also recognizes, however, that some aspects of the validity analysis relate to the specifics of a particular case that must be examined apart from the test of general acceptance. See *id.* at 657-58 (discussing *Downing* court's evaluation on remand of the applicability of research on eyewitness identification to the facts at hand).

As defined by Black and as used herein, validity is a subissue of reliability, rather than a separate and independent factor, since invalid reasoning or methodology cannot

therefore the ultimate indicator of the probative value and sufficiency of evidence, either alone or in combination with other evidence, to meet the more probable than not standard of proof.

Consider, for example, a diagnostic blood test for a viral blood disease. Without the blood test, the disease can be diagnosed only by elaborate procedures. A simple test is desired for screening large numbers of blood samples for the presence of the virus. A virologist might speculate about any number of parameters that might be indicative of the presence of the virus. None of the possible indicators could be used as a diagnostic test, however, until validated by testing that demonstrates a correspondence between the indicator (a "positive" test) and the presence of the virus. This example illustrates the more general principle that where the physical connections between observed and inferred facts are hidden from direct observation, it is necessary for the inferred connection (e.g., between the indicator and the virus) to be validated through trials or tests that independently measure the properties or characteristics that are ostensibly connected.¹¹⁴

A valid method may nonetheless be insufficiently reliable for evidentiary purposes; that is, the method may be incapable of producing the desired information to an acceptable level of certainty. Using again the example of a test for an asymptomatic virus, the test might have a high rate of false positives or false negatives, or both. Thus, although persons who are test positive are more likely than those who test negative to actually have the virus in their blood, the test may be too inaccurate or unreliable for the purpose for which it is administered.¹¹⁵ Similarly, if the question of whether someone is infected with the virus were a factual

produce reliable or accurate results. *See id.* at 599-606, 613. Reliability is the criterion that courts tend to apply to expert scientific evidence; thus, the proposed analysis fits within recognized criteria for evaluating scientific evidence. *See supra* notes 59-60 and accompanying text.

The definitional structure used herein departs, however, from the usage of the terms validity and reliability in social science research. In social science disciplines, reliability describes the reproducibility of the results and validity describes the degree to which the phenomenon measured corresponds to the phenomenon sought to be measured. Thus, this Article's use of reliability to encompass the accuracy as well as the reproducibility of an outcome encompasses some issues that would be characterized as validity issues under the social science rubric.

114. In toxic torts, validity issues are present when a physician or other expert witness testifies on causation based on patient examination even though there is no clinical basis for linking individual cases to a particular causative agent. *See infra* text accompanying notes 197-205.

115. If, for example, the test were used to determine whether donated blood is safe for transfusions, a significant rate of false negatives would be of much greater concern than a correspondingly high rate of false positives.

question in a legal setting, our hypothetical test might be insufficiently reliable to satisfy the legal standard of proof.¹¹⁶

Validity or reliability questions may arise when methodology that has proved valid and reliable is applied in new circumstances. Invalid application of valid methodology may result from extending a method or line of reasoning to purposes for which it has not been validated.¹¹⁷ In toxic torts, this question arises in connection with whether the conclusions derived from toxicological research on animals or single-celled organisms are applicable to humans.¹¹⁸

Uncertainty or reliability questions may also result from the improper application of valid and reliable methodology. Failure to properly calibrate an instrument such as a breathalyzer, or other concerns related to how a method is applied in a particular case, may increase the likelihood of erroneous results.¹¹⁹ Assume, for example, that in the hypothetical virus test, the incidence of false negatives increases with the length of time that the patient's blood samples are stored before the laboratory test is run. The inferences drawn from a test run by a laboratory that stores its blood samples longer than the optimum time for the test would be subject to a greater variation and uncertainty than results from a laboratory that runs its tests promptly.

A subset of questions regarding "reliability as applied," particularly where the methodology involves calculations from raw data, concerns the quality and quantity of the underlying data. In toxic torts, the data on which estimates of exposure to a toxic substance are based are often sketchy or subject to large uncertainties. Those uncertainties make the inferences of causation that depend on the exposure data similarly uncertain and unreliable.

116. If the question whether someone is infected with a virus were part of the prosecution's proof in a criminal action, that fact would have to be proven beyond a reasonable doubt, so that any significant rate of false positives would likely render it "unreliable" for that purpose. Proof in a civil action would have to satisfy a more probable than not standard, so that a somewhat higher level of false positives, possibly up to 49%, could be tolerated. Courts sometimes refuse to admit evidence that nominally satisfies the applicable standard of proof, however.

117. The issue of the generalizability of a study is characterized as one of external validity. See ROTHMAN, *supra* note 44, at 95-96 (epidemiologic studies).

118. See, e.g., *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223, 1273 (E.D.N.Y. 1985) (questioning the use of human epidemiologic studies of workplace dioxin exposures and animal studies as evidence of effects in Vietnam veterans), *aff'd*, 818 F.2d 187 (2d Cir. 1987), *cert. denied*, 487 U.S. 1234 (1988).

119. See MCCORMICK ON EVIDENCE § 209, at 513 (Edward W. Cleary ed., 3d ed. 1972) (discussing factual predicate for admitting chemical testing for alcohol intoxication). Courts differ, however, in their approach to whether the manner in which a method is applied goes to the weight of the evidence rather than its admissibility, and is therefore a jury question. See, e.g., *United States v. Jakobetz*, 955 F.2d 786 (2d Cir.) (DNA testing), *cert. denied*, 113 S. Ct. 104 (1992).

B. Validity and Reliability of Causation Evidence in Toxic Torts

Analysis of the kinds of evidence at issue in the typical toxic torts case illuminates many of the problems with such evidence that tend to be obscured when cases are considered as a whole. The following discussion is intended to suggest some ways of looking at such evidence to distinguish probative evidence from junk science; thus, the discussion deals separately with the subissues of the ability of the toxic substance to cause disease (general causation), exposure, and the causation of the plaintiff's disease (individual causation). It would be well to keep in mind, however, that the ultimate question on causation is whether the evidence allows a reasoned conclusion that exposure to the toxic substance in question, rather than other known or unknown factors that also cause such disease, caused the plaintiff's condition.

As noted previously, the characteristics of toxic tort cases impose limitations on the ability to establish causal connections between exposure and disease. The latency periods typical of toxic tort injuries, the absence in most cases of a unique signature injury associated with a toxic substance, the fact that injury does not occur in every instance of exposure, and the absence of clinical indicators that discriminate among causes of a particular individual's disease all tend to obscure toxic injury causation.¹²⁰ In simple terms, the typical toxic tort case looks something like this: The plaintiff believes she has been exposed to a toxic chemical. She has a disease that is commonplace, or at least not unknown, in the general population. The current progress of the disease bears no relation to the continuation of exposure, and the exposure may have long since terminated. There is no diagnostic or clinical test that can determine what caused her disease.

How can such a plaintiff prove that a toxic substance caused her disease? Because of the absence of clinical indicia of cause, the plaintiff must always make out her case indirectly. First, she needs evidence that the substance can cause the condition from which she suffers and of the circumstances under which disease causation is reasonably likely to occur. The coincidence of exposure and disease in the same individual, while necessary, can never be sufficient to prove the capability of the substance to cause disease. Similar problems attend the use of anecdotal case reports or evidence of clusters of disease that have not been subjected to statistical analysis because a certain amount of coincidence and toxic chemical exposure or even clustering of a disease can occur as the result of random chance.¹²¹

120. See *supra* notes 43-49 and accompanying text.

121. Chance may lead to disease clusters rather than disease uniformly distributed throughout a large population. Anecdotal reports and clusters of disease are important in

Second, she needs to establish that she is within the class of persons to which inferences from the general causation evidence should be applied. This second, particularistic causation component of proof, which is discussed later in this article, usually involves two parts: proof of sufficient exposure to permit the inference that the general causation evidence is applicable to her and a demonstration that other causal explanations, including background causes, are less likely causes than the toxic substance exposure.¹²²

1. ABILITY OF THE TOXIC SUBSTANCE TO CAUSE DISEASE
(GENERAL CAUSATION)

a. Causal Inferences from Human Disease

On the issue of general causation, systematic studies that can account for the effects of chance are necessary to allow a causal inference to be drawn from data on exposure and disease incidence in humans. Epidemiologic studies, which involve comparisons of disease incidence in exposed and unexposed human populations,¹²³ are based on this line of reasoning. A higher incidence of disease in the exposed population, if parameters of the study are such that the differential rates of disease are unlikely to be due to chance or other confounding factors,¹²⁴ may be indicative of a causal relationship between exposure to the toxic substance and disease.¹²⁵ Scientists have long accepted epidemiologic studies as indicative of causal relationships and courts have more recently begun to do so. Epidemiologic studies are the basis of causation findings

the identification of possible causal links that should be investigated further, however. See Brennan, *supra* note 25, at 21.

122. The issue of whether other causal explanations are less likely is referred to herein as the issue of individual causation.

123. Other commentators have described epidemiologic studies and their relation to proof of causation of human disease. See Black & Lilienfeld, *supra* note 37. See generally 2 DORE, *supra* note 5, §§ 25.01-.05. Epidemiologic studies will be described in more detail in the discussion of distinguishing among causes. See *infra* notes 180-90 and accompanying text; see also *infra* notes 342-58, 364-76 and accompanying text (discussing limitations of epidemiology and statistical significance).

124. See 2 DORE, *supra* note 5, §§ 25.02[4], 25.03.

125. Cause is an inference drawn from epidemiologic studies; the studies themselves can only directly prove an association between exposure and disease incidence. Epidemiologists use the Henle-Koch-Evans postulates or other similar premises as criteria for arriving at biological inferences of causation from epidemiologic studies. Black & Lilienfeld, *supra* note 37, at 762-64. The Henle-Koch-Evans postulates are addressed to the magnitude of the risk elevation in the exposed group and other factors tending to increase the plausibility of a biological relationship between the exposure and disease. See *id.*

in asbestos injury claims, and have served as important evidence of the lack of causation in the Bendectin cases.¹²⁶

Epidemiologic studies are expensive to conduct and are subject to a number of limitations on the size of the effect they can detect.¹²⁷ Thus, it is sometimes argued that case reports and clusters of disease constitute sufficient evidence of the capability of a substance to cause toxic injury.¹²⁸ Case reports and disease clusters are sometimes sufficient to raise suspicions and stimulate investigation of toxic chemicals as causative agents.¹²⁹ Benzene was identified as a leukemogenic agent through clinical studies of case reports beginning in the late 1800s,¹³⁰ and vinyl chloride was more recently recognized as carcinogenic through the appearance of clusters of angiosarcoma of the liver in plant workers in the early 1970s.¹³¹ Those examples, however, are typified, in the case of benzene, by very high exposures and the accumulation of evidence over decades,¹³² or by the unexpected appearance of an otherwise very unusual disease.¹³³ Such identifications through case reports and clusters, however, depend on at least a rough sense that the incidence of the disease in the exposed group exceeds the background rates,¹³⁴ even if the reports of unusually high incidence are not initially subjected to the same rigorous statistical analysis as is typical of an epidemiologic study.¹³⁵ Moreover, those initial clusters or unusual case reports will often suggest other places to look for additional evidence, such as workplace exposures involving the same substance, or other users or consumers of the suspect chemical.¹³⁶ The absence of similarly affected individuals among other

126. See, e.g., *Brock v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307, 313 (5th Cir.) (plaintiffs could not succeed without epidemiologic evidence), *modified*, 884 F.2d 166 (5th Cir. 1989), *cert. denied*, 494 U.S. 1046 (1990).

127. See Brennan, *supra* note 25, at 53 & n.228; Green, *supra* note 65, at 653.

128. See Rubanick v. Witco Chem. Corp., 542 A.2d 975 (N.J. Super. Ct. Law Div. 1988), *rev'd*, 576 A.2d 4 (N.J. Super. Ct. App. Div. 1990), *modified*, 593 A.2d 733 (N.J. 1991); Ferebee v. Chevron Chem. Co, 736 F.2d 1529 (D.C. Cir.), *cert. denied*, 469 U.S. 1062 (1984).

129. See Brennan, *supra* note 25, at 502.

130. JOHN GRAHAM ET AL., IN SEARCH OF SAFETY: CHEMICALS AND CANCER RISK 119-23 (1988).

131. See David D. Doniger, *Federal Regulation of Vinyl Chloride: A Short Course in the Law and Policy of Toxic Substances Control*, 7 *ECOLOGY L.Q.* 497, 500 (1978).

132. See *supra* text accompanying note 130.

133. Doniger, *supra* note 131, at 500.

134. See GRAHAM ET AL., *supra* note 130, at 119-23 (discussing relative risk estimates derived from clinical studies and epidemiologic studies of disease in benzene-exposed workers).

135. A causal argument based on observation of an otherwise unknown group of symptoms in breast implant recipients may be possible if recent reports of such symptoms are borne out. See Rigdon, *supra* note 6, at B1.

136. The suspicions aroused by the initial reports of angiosarcoma of the liver in B.F. Goodrich's vinyl chloride plant were quickly confirmed by reports from other companies. See Doniger, *supra* note 131, at 500.

populations with similar exposures would suggest that the cluster is a statistical accident rather than a true cluster.

Case reports and apparent disease clusters are likely to be argued in toxic tort cases in circumstances where they do not have even minimal indicia of reliability. In *Renaud v. Martin Marietta Corp.*,¹³⁷ the plaintiffs argued that the existence of four cases of childhood cancer in Friendly Hills, an area in which only two would have been expected, was evidence that the substances allegedly in their water supply had caused their cancers.¹³⁸ Plaintiffs' experts agreed, however, that the Friendly Hills population was too small to yield meaningful results. Moreover, another expert's opinion was that four cases of childhood cancer was within the expected range for the community.¹³⁹

b. Animal Studies¹⁴⁰

Animal studies, other biological assay methods and chemical structure-activity relationships, all of which are used by toxicologists to estimate human risk from toxic chemicals,¹⁴¹ are much more problematic than epidemiologic studies in the toxic tort context. The use of such methods in risk regulation is based on unproven assumptions about the applicability of the results of such studies to humans, assumptions that are subject to a large degree of uncertainty and in some cases skepticism in the scientific community.¹⁴²

Animal studies are based on the theory that substances that cause harmful effects in animals are likely to cause similar harmful effects in humans.¹⁴³ That thesis is supported by observations that many substances that cause harmful effects in one species also cause harmful effects in other species.¹⁴⁴ All but one of the chemicals identified by epide-

137. 749 F. Supp. 1545 (D. Colo. 1990), *aff'd*, 972 F.2d 304 (10th Cir. 1992).

138. *Id.* at 1554-55.

139. *Id.* at 1551. Dr. Steven Piantidosi's epidemiological study on the incidence of cancer in children in Friendly Hills indicated that the difference between expected and observed incidence rates was not statistically significant. *Id.*

140. Animal testing has been treated as either admissible or inadmissible. See 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 (1988-89). As is discussed *infra* notes 151-68 and accompanying text, the issue of animal testing should be addressed as one of how probative is animal testing of causation of human disease, that is, as a question of sufficiency rather than of relevance.

141. Brennan, *supra* note 25, at 21-23, 44. See generally Chemical Carcinogens: A Review of the Science and Its Associated Principles, 50 Fed. Reg. 10,371 (Office of Science & Technology Policy 1985) [hereinafter OS&TP, Chemical Carcinogens].

142. Brennan calls these issues "trans-scientific." See Brennan, *supra* note 25, at 23. Such issues are not always inherently unprovable, although it may be impractical to do so.

143. See Brennan, *supra* note 15, at 504-06.

144. See, e.g., James E. Huff & Joseph K. Haseman, *Exposure to Certain Pesticides May Pose Real Carcinogenic Risk*, CHEMICAL & ENGINEERING NEWS, Jan. 7, 1991, at 33, 34

miologic studies as causing cancer in humans have also proven to be carcinogenic in one or more animal species.¹⁴⁵ Thus, there appears to be some correlation between carcinogenicity in animals and carcinogenicity in humans. Similar observations and findings have been made with respect to other kinds of toxic effects, including teratogenic effects.¹⁴⁶

As any observer of the popular media knows, however, animal testing for diseases such as cancer, which has a long latency periods, and for which even low incidence rates are of concern, are conducted under conditions that are very different from the usual human exposure scenario.¹⁴⁷ Animal studies of carcinogenicity typically utilize doses at or near the maximum level tolerated by the animal.¹⁴⁸ That practice is necessitated by the need to detect effects in relatively small groups of test subjects, in a relatively short period of time. Those same concerns also have led to protocols using animal strains bred for their susceptibility for tumor formation.¹⁴⁹ Additionally, the route of administration may differ from the likely human exposure route.¹⁵⁰

The prediction of effects in humans from animal testing involves a number of extrapolations—from animal species to humans, from one route of administration to another, and most acutely, from a high-dose exposure in which the animals are typically subjected to the maximum dose they can tolerate (the MTD),¹⁵¹ to a low-dose chronic exposure.¹⁵² Each of those extrapolations introduces uncertainty into the predictive value of animal testing in proving causation of human disease.¹⁵³

(reporting that information on carcinogenicity of 8 of 54 known carcinogens was first obtained in animal studies).

145. OS&TP, *Chemical Carcinogens*, *supra* note 141, at 10,411; J.F. Robens et al., *Methods of Testing Carcinogenicity*, in *PRINCIPLES AND METHODS OF TOXICOLOGY* 251, 253 (A. Wallace Hayes ed., 2d ed. 1989).

146. See Jeanne M. Manson & L. David Wise, *Teratogens*, in *CASARETT AND DOULL'S TOXICOLOGY* 226, 240 (Mary O. Amdur et al. eds., 4th ed. 1991) [hereinafter *CASARETT & DOULL*].

147. Ames, *supra* note 29, at 589; see Landau & O'Riordan, *supra* note 140, at 545.

148. OS&TP, *Chemical Carcinogens*, *supra* note 141, at 10,377; Bruce N. Ames & Lois S. Gold, *Cancer Prevention Strategies Greatly Exaggerate Risks*, *CHEMICAL & ENGINEERING NEWS*, Jan. 7, 1991, at 28, 29; see also Kent R. Stevens & Michael A. Gallo, *Chronic Toxicity Studies*, in *PRINCIPLES AND METHODS OF TOXICOLOGY*, *supra* note 145, at 237, 238-39.

149. See OS&TP, *Chemical Carcinogens*, *supra* note 141, at 10,377.

150. Animal testing may involve skin application, oral gavaging or injection, see *id.* at 10,413-14, rather than the usual human exposure routes of inhalation, ingestion or dermal contact. See *id.*

151. See Ames & Gold, *supra* note 148, at 29. Test animals such as rodents live only one to two years, though they may receive test doses throughout the majority of their lifespans. See OS&TP, *Chemical Carcinogens*, *supra* note 141, at 10,413, 10,414.

152. See Landau & O'Riordan, *supra* note 140, at 543-48.

153. The use of animal test results as proof of toxic effects in humans can be regarded as raising validity issues, because it is questionable whether results in one species can be extrapolated to another at all. See Black, *supra* note 15, at 677-79; Green, *supra* note 65, at 654-56. This issue is treated here as one of uncertainty or inaccuracy, however, because

Differences in species can have a dramatic impact on the effects of a toxic substance,¹⁵⁴ as can routes of administration.¹⁵⁵

The high dose exposure scenario of typical animal testing protocols raises several concerns. One concern relates to the model used to extrapolate the results of high dose exposures to the much lower doses encountered by humans. The lack of a complete mechanistic understanding of cancer causation precludes the adoption of any particular extrapolation model with a high degree of certainty.¹⁵⁶ For example, one

even if validity is assumed, the uncertainty attending extrapolation of results from animal studies to humans will usually render them insufficiently probative to support a plaintiff's verdict. Additionally, most scientists regard animal studies as having some validity in predicting human disease, and such studies are widely used for regulatory purposes. See OS&TP, *Chemical Carcinogens*, *supra* note 141. Animal studies vary in their predictive value for humans, however, depending on the nature of the effects being studied and the number of species in which toxic effects of a substance have been confirmed. Models that may improve predictive capabilities are being developed for quantitative interspecies extrapolations. See Robert A. Scala, *Risk Assessment*, in CASARETT & DOULL, *supra* note 146, at 985, 993 (discussing potency correlations of animal and human carcinogens). Thus, it seems appropriate to address the extrapolation of animal test results to humans as an issue of the degree of certainty that attends that extrapolation in a given instance, rather than to assert as a general proposition that animal tests results can or cannot in any instance be validly extrapolated to humans. *Id.*

154. Animal testing is of limited value in a context where false positives are a concern, as is the case with toxic torts, a generalization that cuts across the various types of effects for which such studies are conducted. For example, Manson and Wise report that of 38 substances with positive teratogenic findings in humans, only one was negative in all animal species studied, thus producing a low rate of "false negatives" for human teratogenicity. Manson & Wise, *supra* note 146, at 240. In contrast, of 165 substances studied with no teratogenic finding in humans, only 47, or 29%, were negative in all laboratory animal test species. *Id.* Similar uncertainties occur in animal testing for carcinogenicity. Although all but a few of the 30 or so known human carcinogens (substances or industrial processes) are also carcinogenic in at least one animal species, there are many more substances that have exhibited carcinogenicity in animals that are not known to be human carcinogens. *Id.* It is not uncommon for a substance to exhibit carcinogenicity in one species and not in another. See Scala, *supra* note 153, at 992. For example, in one study of almost 1000 chemicals, only 76% of rat carcinogens were positive in mice, and 70% of mouse carcinogens were positive in rats. *Id.* Studies of carcinogenic potency of the same substances in animals and humans have yielded good correlations for some substances, but animal data overpredicts human response by as much as a factor of 500 for vinyl chloride. See Landau & O'Riordan, *supra* note 140, at 536 (citing Michael D. Hogan and David G. Hoel, *Extrapolation to Man*, in PRINCIPLES AND METHODS OF TOXICOLOGY, *supra* note 145, at 879). That difference may be due to incomplete data on human cancer, but it cannot be ignored.

155. For example, EPA's "level of regulatory concern" for inhalation of chromium has been stated as 1.9×10^{-6} mg/day, as compared to 0.1 mg/day for exposure by ingestion. See, e.g., Final Exclusion, 53 Fed. Reg. 29,038, 29,040-41 (EPA 1988) (tbls. 1 & 2) (evaluating petition for delisting of hazardous waste). The inhalation level of regulatory concern was thus set 50,000 times lower than the ingestion level, apparently due to demonstrated respiratory tract carcinogenicity of inhaled chromium as compared to lower risks through other routes of exposure. See Robert A. Goyer, *Regulatory Toxicology*, in CASARETT & DOULL, *supra* note 146, at 623, 639.

156. See generally Robert A. Scala, *Risk Assessment*, in CASARETT & DOULL, *supra* note 153, at 985, 990-91.

possible set of assumptions is that no dose of a carcinogen is completely risk free and that the disease incidence rate will be directly proportional to the dose. Those assumptions lead to a linear extrapolation model.¹⁵⁷ Another possibility, which apparently applies to some carcinogens, is that at very low levels, a toxic chemical exerts no adverse effects and that such effects appear only when a threshold level of exposure is exceeded.¹⁵⁸ The set of assumptions adopted in a particular instance can lead to vastly different predictions of the effects of low dosage exposures, sometimes as much as several factors of ten.¹⁵⁹

The accuracy of risk extrapolations from exposure of animals to the MTD has recently been called into further question by prominent researchers in the field of carcinogenesis.¹⁶⁰ Bruce Ames, the developer of the "Ames test" for mutagenicity,¹⁶¹ now argues that risk estimates obtained under such circumstances are largely due to toxic effects of the test chemical, rather than factors that might operate at lower doses in human.¹⁶² Thus, the results from animal studies may not be predictive of human carcinogenicity under the usual exposure scenario.

Despite the sparse knowledge of mechanisms of cancer causation, toxicologists have identified a number of steps in the carcinogenesis process, including DNA alteration, DNA expression, and promotion and progression to neoplastic or cancerous tumors. They have also identified two general classes of carcinogens. See Gary M. Williams & John H. Weisburger, *Chemical Carcinogenesis*, in CASARETT & DOULL, *supra* note 146, at 127, 129-31, 170-85. DNA-reactive carcinogens are those that appear to initiate cancer through chemical alteration of DNA. *Id.* at 170. Epigenetic carcinogens, on the other hand, do not necessarily react with DNA and exert carcinogenic effects through other pathways such as by promoting the growth of dormant cancer cells. *Id.* at 185.

157. See Scala, *supra* note 153, at 990-91 (discussing a linearized, multi-stage, nonthreshold model); see also OS&TP, *Chemical Carcinogens*, *supra* note 141, at 10,438-39. This model assumes that there is no threshold dose below which cancer does not occur, but recognizes the multi-step nature of carcinogenesis. See *id.* Threshold doses are common for acute effects of toxins, i.e., those that occur within a short time after exposure. See Curtis D. Klaassen & David L. Eaton, *Principles of Toxicology*, in CASARETT & DOULL, *supra* note 146, at 12, 38. However, whether carcinogens are subject to thresholds is an unresolved issue. See Scala, *supra* note 153, at 990-91. The choice of model can make a difference of several orders of magnitude in risk levels. As a matter of policy, the conservative linearized multi-stage extrapolation model is often used to estimate the upper bound on risk. See OS&TP, *Chemical Carcinogens*, *supra* note 141, at 10,438-39.

158. See Williams & Weisburger, *supra* note 156, at 154. This assumption appears a likely model for carcinogens classed as promoters rather than as initiators. See David J. Hanson, *Dioxin Toxicity: New Studies Prompt Debate, Regulatory Action*, CHEMICAL & ENGINEERING NEWS, Aug. 12, 1991, at 7, 13 (EPA reconsidering model for dioxin carcinogenicity low-dose extrapolation to allow for threshold).

159. See *supra* note 158; see also OS&TP, *Chemical Carcinogens*, *supra* note 141, at 10,439.

160. Ames & Gold, *supra* note 148, at 29.

161. See *supra* note 6 and accompanying text.

162. See *supra* note 139 and accompanying text; see also Bruce N. Ames et al., *Ranking Possible Carcinogenic Hazards*, 236 SCIENCE 271 (1987). The authors believe the toxicity effect to be particularly true for carcinogens that are not DNA reactive. See Bruce N. Ames & Lois S. Gold, *Too Many Rodent Carcinogens: Mitogenesis Increases Mutagenesis*, 249 SCIENCE

Quite a number of toxic torts plaintiffs have offered animal studies in support of their contentions that the substances in question can cause harm in humans.¹⁶³ In some cases courts have been willing to entertain such evidence,¹⁶⁴ while other have found it inadmissible¹⁶⁵ or insufficient.¹⁶⁶ The closer examination of the assumptions and methodologies involved in animal testing, however, reveals that the extrapolation of animal test results to humans is too uncertain—the potential for error is too high—for animal testing alone to support an inference that it is more probable than not that a substance causes cancer or birth defects in humans at a specified level of exposure.¹⁶⁷ There is considerable doubt about the inference that an animal carcinogen is a human carcinogen at all. Even if that hurdle is assumed away, however, the uncertainties that attend the interspecies and high-dose to low-dose extrapolations necessary to extend animal test results to human exposure scenarios are simply too large. Policy considerations in the regulatory arena dictate or at least support the use of models that overpredict rather than underpredict risks levels.¹⁶⁸ Risk estimates based on unproven dose-response models, where the choice of model may alter results by a thousand times or more, however, are not consistent with a more likely than not standard of proof.

c. Biological Screening Methods

Even greater problems attend the application of biological screening methods such as short term assays. Short term assays are designed to detect mutagenic effects and cancer-initiating or promoting properties of

970 (1990). Ames and coworkers direct their argument to the allocation of scarce resources for cancer prevention purposes. Their concern about the predictive value of animal testing and other protocols for determining carcinogenicity bears on the general causation issue in toxic torts, however.

163. See, e.g., *Brock v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307 (5th Cir.), modified, 884 F.2d 166 (5th Cir. 1989), cert. denied, 494 U.S. 1046 (1990); *Renaud v. Martin Marietta Corp.*, 749 F. Supp. 1545 (D.Colo. 1990), aff'd, 972 F.2d 304 (10th Cir. 1992); *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223 (E.D.N.Y. 1985) (*Agent Orange and dioxin*), aff'd, 818 F.2d 187 (2d Cir. 1987), cert. denied, 487 U.S. 1234 (1988).

164. See, e.g., *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829 (3d Cir. 1990), cert. denied, 111 S. Ct. 1584 (1991).

165. See, e.g., *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223 (E.D.N.Y. 1985), aff'd, 818 F.2d 187 (2d Cir. 1987), cert. denied, 487 U.S. 1234 (1988).

166. See, e.g., *Brock*, 874 F.2d 307.

167. In conjunction with positive epidemiologic studies, positive animal results may be relevant. In such instances, however, some would argue that such evidence is cumulative and of such low probative value as to warrant its exclusion. See, e.g., Landau & O'Riordan, *supra* note 67, at 551-54.

168. Douglas G. Camp et al., *Pesticide Regulation Is Sound*, CHEMICAL & ENGINEERING NEWS, Jan. 7, 1991, at 44, 46.

substances.¹⁶⁹ Mutagenicity,¹⁷⁰ for example, is used as a predictor of carcinogenicity because many known carcinogens are also mutagens.¹⁷¹ Mutagenicity is also considered to be an indicator of potential for causing birth defects.¹⁷² Short term assays' predictive capabilities have been validated by reference to animal carcinogenesis,¹⁷³ however, so they are subject to all of the uncertainties of animal testing, as well as additional uncertainties introduced by the procedure itself.¹⁷⁴ Moreover, because such tests involve single-celled organisms, they are less likely than *in vivo* testing in animals to represent the response of humans.

Another kind of evidence, typically offered as evidence of causation of birth defects or other noncancerous disease or injury, is *in vitro* testing, tests involving exposure of isolated groups of cells or organs¹⁷⁵ to suspect chemicals. To test for teratogenesis (birth defects), fetal cells or embryos may be used. These tests are fraught with uncertainties, however, related to whether and to what degree the chemical in question would reach or react with the sensitive cells or organs in a whole organism.¹⁷⁶ They are also fraught with the same uncertainties relating to interspecies extrapolation as is animal testing generally.

d. Chemical Structure-Activity Analysis

Chemical structure-activity analysis is a kind of scientific reasoning by analogy that is based on the recognition that similarities in chemical structure sometimes correspond to similarities in biological activity.

169. See OS&TP, *Chemical Carcinogens*, *supra* note 141, at 10,403.

170. Mutagenicity refers to the alteration of the genetic material of a cell.

171. Ames, *supra* note 29, at 589.

172. *Id.* at 587.

173. *Id.* at 588.

174. Single-celled organisms are, of course, farther removed biologically from humans than are mammals such as mice and rats which are typically used in animal testing. See OS&TP, *Chemical Carcinogens*, *supra* note 141, at 10,404 (listing commonly used assays). Short-term assays are utilized to select substances for chronic (i.e., long-term) animal testing. See *id.* at 10,408. The OS&TR review states the utility of short-term assays succinctly:

Short-term tests are presently limited in their ability to predict the presence or absence of carcinogenicity and cannot supplant data from long-term animal studies or epidemiologic data since the tests do not necessarily screen for all potential means of cancer induction and do not necessarily mimic all reactions that would occur *in vivo*.

Id. at 10,376.

175. In *Brock v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307 (5th Cir.), *modified*, 884 F.2d 166 (5th Cir. 1989), *cert. denied*, 494 U.S. 1046 (1990), the plaintiff's evidence included limb bud tests as evidence of teratogenicity of doxylamine, the active ingredient of Bendectin.

176. See *id.* at 314 (discussing the possibility that doxylamine breaks down in the human body and does not reach limb buds in unaltered form).

Observations based on such reasoning are the impetus of much drug research, as well as research on the hazardous effects of chemicals.¹⁷⁷ The relation of chemical structure to biological activity is highly uncertain, however, at least where the effects of only one or two compounds similar to the one in question are known.¹⁷⁸ No two chemicals have the same structure, so the question is always whether the similarities are more important than the differences in predicting toxicological properties. Structure-activity analysis is used primarily to select candidates for additional study. In most cases, reasoning based on structure-activity relationships will fall far short of the reliability required to satisfy a more probable than not standard of proof.

- e. The Insufficiency of Animal Test Results, Short-term Assays, *In Vitro* Testing and Structure-Activity Relationships to Prove General Causation.

As can be seen from the foregoing discussion, animal test results, biological screening methods and chemical structure-activity relationships are insufficiently reliable, even if arguably valid, to permit inferences to be drawn that it is more probable than not that a substance can cause a disease in humans. It is also important to understand that even when all such indicators are positive, they are still insufficient for that purpose, given the present state of science.

Toxicological research into the causes of human disease, when direct evidence in humans is unavailable, proceeds according to a hierarchy of reasoning, from the least costly and time-consuming, and least predictive methods, to the most costly, time-consuming methods

177. See Williams & Weisburger, *supra* note 156, at 156-57 (discussing chemical structure-activity analysis as the first step in carcinogenicity assessment).

178. Saffiotti summed up the state of predictions from structure-activity analysis as follows:

There is a moderately substantial base of empirical data that permits conclusions about carcinogenic potential on the basis of molecular structure, *at least on the basis that* certain groupings of atoms (functional groups) in some molecules may impart carcinogenic properties. *The predictive power of such correlations has, however, been unsatisfactory so far, and the general consensus of the scientific community appears to be that chemical structure has limited value in identifying carcinogens and is to be used in carcinogenic hazard assessment only as corroborative supporting evidence.*

Umberto Saffiotti, *Identification and Definition of Chemical Carcinogens: Review of Criteria and Research Needs*, 6 J. TOXICOLOGY & ENVTL. HEALTH 1029, 1043 (1980).

It is unusual for all chemicals in a class to be carcinogenic, or for all carcinogenic members of a class to be equally potent. When 60 structural analogs of thalidomide were studied for teratogenicity, only three were found to exhibit that property. Manson & Wise, *supra* note 146, at 228. Structure-activity relationships are used in toxicology research primarily to select candidates for short-term assays and other more extensive tests. See, e.g., Williams & Weisburger, *supra* note 156, at 156-67.

that are believed to correspond most closely to human response. Thus, the investigation of the toxicological properties of a chemical is likely to start with the analysis of available information about chemicals with similar structures—chemical structure-activity analysis.¹⁷⁹ The most likely candidates identified by structure-activity analyses are then subjected to biological assays such as mutagenicity testing or *in vitro* testing on cell groups. Lastly, animal testing will likely be conducted on chemicals that exhibit toxic effects in the short-term screening procedures. Structure-activity analysis and short-term screening are not the end points of the evaluation process, even in a regulatory context, because they are recognized as significantly less valid and reliable than animal testing. Whether considered separately or in the aggregate, the methods that do not involve observations of disease in humans are too likely to lead to an erroneous conclusion to satisfy the traditional burden of proof.

2. CAUSATION OF PLAINTIFF'S DISEASE (INDIVIDUAL CAUSATION)

Even where the capability of a substance to cause disease can be shown, the plaintiff will still need to prove that the toxic substance caused his disease. The primary difficulty facing such a plaintiff is the need to differentiate between the exposure and background causes as explanations of the injury. Much speculation masquerading as science appears in connection with this issue.

To understand what kinds of evidence are probative of individual causation, we must first make reference to the kinds of evidence probative of the capability of the substance to cause harm, namely, epidemiologic evidence or possibly other human evidence of sufficient reliability. That evidence will identify one or more diseases that are believed to be causally associated with exposure to a toxic substance. Such studies will also typically be based on or identify certain levels or ranges of exposures. The plaintiff must argue that the association established through the statistical study applies to him and that background and other risk factors are less likely causal explanations.

a. Epidemiologic Reasoning

The best case for the plaintiff is the situation in which an epidemiologic study has identified an association between exposure to a toxic substance and a disease. For example, a number of studies have shown an association between asbestos exposure and lung cancer. The study will produce an estimate of the increased incidence of disease

179. See Williams & Weisburger, *supra* note 156, at 156-57 (describing the decision point approach to carcinogen testing).

associated with the exposure, such as relative risk.¹⁸⁰ Relative risk, illustrated by the formula below, is the ratio of disease incidence in the exposed population to disease incidence in the unexposed population in the study.¹⁸¹

$$\text{Relative Risk} = \frac{\text{incidence in exposed group}}{\text{incidence in unexposed group}}$$

Black provides an example in which the disease rates in exposed and unexposed groups are 50 and 5 per 100,000 population respectively.¹⁸² The relative risk in that case is 50/5 or 10, indicating that the exposure increases the disease rate to ten times that of the background rate.

How can a toxic tort plaintiff use such information? At a minimum, it would seem obvious that the plaintiff must have a disease identified as associated with the toxic chemical exposure. Nonetheless, it is not uncommon for plaintiffs' experts to assert that evidence that a substance causes any cancer is evidence that it can and has caused other cancers.¹⁸³ Although substances that are discovered to cause one type of cancer may cause other types of cancer as well, that possibility does not permit a prediction of what those other cancers, if any, are likely to be.¹⁸⁴ The

180. See Black & Lilienfeld, *supra* note 37, at 758.

181. *Id.* at 758 & n.105. Relative risk estimates can also be generated from case control studies, which compare the incidence of exposure in cases and controls that do not exhibit the disease in question. See ROTHMAN, *supra* note 44, at 63-64.

182. See Black & Lilienfeld, *supra* note 37, at 758 & n.105.

183. In *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223 (E.D.N.Y. 1985), *aff'd*, 818 F.2d 187 (2d Cir. 1987), *cert. denied*, 487 U.S. 1234 (1988), the opt-out plaintiffs alleged, based in part on animal tests, that Agent Orange exposure had caused a number of different kinds of cancer, including Hodgkin's disease and cancer of the ileum, chronic skin rashes, infertility, *id.* at 1239, 1252-54, gastrointestinal disorders, miscarriages and other birth defects, *id.* at 1231, various behavioral disorders, including memory loss, increased irritability, anger, depression and others, weight loss, various liver disorders, including abnormal liver function, hepatitis and cirrhosis, and elevated triglycerides and cholesterol, *id.* at 1235-36. Plaintiffs relied on animal and workplace exposure studies to link Agent Orange or its contaminant, dioxin, to their injuries. *Id.* at 1236. The court noted, however, that plaintiffs' liver injuries differed "substantially" from those reported in the studies. *Id.* at 1236. Plaintiffs' reports of skin rashes or chloracne many years after exposure were also inconsistent with the immediate and transient relationship of chloracne and dioxin exposure. *Id.* at 1260.

Renaud v. Martin Marietta Corp., 749 F. Supp. 1545 (D. Colo. 1990), *aff'd*, 972 F.2d 304 (10th Cir. 1992), also typifies such cases. Plaintiffs alleged that a number of injuries, including childhood cancers (one case of leukemia), kidney cancer, seizure disorders, and congenital heart defects resulted from exposure primarily to hydrazines, also classified as animal carcinogens. *Id.* at 1547. Plaintiff also alleged exposure to several other chemicals. *Id.*

184. Nor does it suggest what the relative risk ratios would be for this possible, but unproven disease. This question is thus one of both general and individual causation.

problem is compounded when the plaintiff's general causation evidence is not based on human evidence, but on animal studies or other less reliable methods that only generally suggest a possible carcinogenic effect;¹⁸⁵ in such cases, the evidence may not allow an identification of any particular disease associated with the substance.

If plaintiff has a disease associated with the toxic substance exposure, demonstrating that it is more likely than not that plaintiff's condition was caused by exposure usually will require the plaintiff to demonstrate that her exposure was in the range found to be associated with an increased risk of disease.¹⁸⁶ Alternatively, plaintiff might be able to show that the results of the study could be extrapolated to lower doses.¹⁸⁷

If the plaintiff can demonstrate sufficient exposure to argue that the relative risk factor in the study applies to him, he still must differentiate background causes where the disease occurs in the background population. Under the traditional more likely than not rule, the plaintiff will prevail if the relative risk identified in the epidemiologic study is greater than two. That is because relative rate greater than two corresponds to more than doubling of the disease rate, permitting the inference that more than half of the cases of the disease in the exposed population were caused by the exposure. When applied to the plaintiff, the inference can be made that it is more likely than not that the exposure caused the

185. Such was the problem in *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991), *discussed infra* text accompanying notes 250-85. *See also* *Rubanick v. Witco Chem. Corp.*, 593 A.2d 733 (N.J. 1991), *discussed infra* text accompanying notes 287-300.

186. Exposures are often at issue. *See, e.g., In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991). Much of the evidence at issue in *Paoli* concerned whether plaintiffs' PCB exposures had exceeded normal background levels in the general population. *See id.* at 860-61; *see also* *Renaud v. Martin Marietta Corp.*, 749 F. Supp. 1545, 1555 (D. Colo. 1990) (dismissing suit because of plaintiffs' inability to present evidence of exposure establishing a prima facie case), *aff'd*, 972 F.2d 304 (10th Cir. 1992). Proof of exposure is discussed *infra* notes 214-49 and accompanying text.

187. It is widely accepted that dose-response relationships exist for toxic substances, that is, that disease incidence increases with increased exposure. The existence of a dose-response relationship is considered to be evidence that the association of toxic substance and disease incidence is causal. *See* Black & Lilienfeld, *supra* note 37, at 762-63 (discussing the Henle-Koch-Evans postulates).

High-dose to low-dose extrapolations based on epidemiologic data are subject to some of the same limitations as those discussed in connection with animal studies. *See supra* notes 151-59 and accompanying text. At some point, the application of epidemiologic studies to persons whose exposure levels were very different from those in the study raises a validity issue. This issue arises in cases where plaintiffs offer epidemiologic evidence based on relatively high occupational exposures as probative of the effects of lower level environmental exposures. *See, e.g., In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223, 1241 (E.D.N.Y. 1985) (rejecting epidemiologic studies based on industrial exposures), *aff'd*, 818 F.2d 187 (2d Cir. 1987), *cert. denied*, 487 U.S. 1234 (1988).

plaintiff's disease.¹⁸⁸ Put another way, when the relative risk is greater than two, the fraction of all disease in the exposed group attributable to the exposure is greater than 50%.¹⁸⁹ The causal connection inferred from the presence of a signature disease represents the application of this principle when the relative risk is very large and the corresponding risk attributable to the exposure may be ninety percent or more.¹⁹⁰

b. Mechanistic Explanation

When the plaintiff's exposure evidence is weak, and when general causation evidence is based on animal studies, *in vitro* testing and the like, experts may attempt to bolster the plaintiff's case through speculation in the guise of a mechanistic explanation of causation.¹⁹¹ For example, an expert may offer testimony about the "one hit" theory of causation, namely, the theory that cancer can be caused by only one molecule of the

188. See Black & Lilienfeld, *supra* note 37, at 767-69. Relative risks greater than two are the basis of causation findings in cases involving claims for lung cancer from asbestos exposure. See *infra* notes 212-15 and accompanying text. The principle has been cited with seeming approval in a number of cases. See, e.g., DeLuca v. Merrell Dow Pharmaceuticals, Inc., 911 F.2d 941, 958-59 (3d Cir. 1990).

189. Attributable risk can be viewed as the proportion of a disease that is statistically attributable to a risk factor. Black & Lilienfeld, *supra* note 37, at 760-61. The attributable risk in an exposed population can be calculated as follows:

$$\text{Attributable Risk} = (\text{Relative Risk} - 1) / (\text{Relative Risk})$$

Where the relative risk is 2.0, attributable risk or attributable fraction is (2.0-1.0)/2.0, or 0.5. See Black & Lilienfeld, *supra* note 37, at 761 & n.123.

The reasoning illustrated in the text accompanying this note can result in recovery by 100% of exposed persons with the disease where the relative risk is greater than two, even though up to 50% would almost certainly have contracted the disease without exposure. Further, when there is a relative risk less than 2.0 but greater than 1.0, no plaintiffs will recover even though the epidemiologic study indicates causation of a group constituting less than half the cases. The unfairness of such results has led commentators to suggest that when an epidemiologic study indicates any increased risk, all exposed individuals with the indicated disease should recover proportionately to the magnitude of the increased risk. See, e.g., David Rosenberg, *supra* note 32; cf. Robinson, *Probabilistic Causation*, *supra* note 50, at 783 (recommending compensation for risk of future disease); Gregory L. Ash, Note, *Toxic Torts and Latent Diseases: The Case for an Increased Risk Cause of Action*, 38 KAN. L. REV. 1087, 1102-03 (1990).

190. For example, the relative risk of mesothelioma for asbestos exposure is on the order of 46, see Brennan, *supra* note 25, at 39 n.166 (citing A.D. McDonald & J.C. McDonald, *Malignant Mesothelioma in North America*, 46 CANCER 1650 (1980)), resulting in an attributable risk of over 97%.

191. In Brock v. Merrell Dow Pharmaceuticals, Inc., 874 F.2d 307 (5th Cir.), *modified*, 884 F.2d 166 (5th Cir. 1989), *cert. denied*, 494 U.S. 1046 (1990), Dr. McBride, one of plaintiff's experts on the issue of whether Bendectin causes limb defects, testified about his theory of how Bendectin could cause such defects. *Id.* at 314-15. The court characterized the doctor's theory of causation as "nothing more than unproven medical speculation lacking any sort of consensus." *Id.*

toxic substance acting on only one cell, which then becomes cancerous.¹⁹² The witness may then explain that cancerous changes are thought to involve chemical alteration of DNA, the genetic material of cells, alterations that can be brought about by interaction with toxic chemicals.¹⁹³ Sometimes the witness expounds on the one hit theory by explaining that even very low concentrations of toxic chemicals involve exposure to trillions of molecules, and thus many opportunities for cancerous or mutagenic changes.¹⁹⁴ This kind of argument has much superficial appeal because it represents a common line of reasoning in cancer research or risk assessment.¹⁹⁵ When offered in proof of the likelihood that a low-level exposure, rather than background factors, caused the plaintiff's disease, however, the one hit theory and its corollaries amount to nothing more than speculation. The validity of the theory in a given case will rarely have been tested. Moreover, unless a mechanistic explanation offers a way to distinguish between causation by the toxic substance and causation by background factors,¹⁹⁶ it adds nothing to the proof of the plaintiff's case. Mechanistic explanations are not a substitute for statistical information such as epidemiologic studies when the background rate of the plaintiff's disease is significant.

192. See, e.g., *Peteet v. Dow Chem. Co.*, 868 F.2d 1428, 1433 (5th Cir.), cert. denied, 493 U.S. 935 (1989). A variant of this line of reasoning, mechanistically related to it, is the assertion that there is no safe level of a carcinogen, that is, that there is no threshold dose below which cancer does not occur. See *supra* notes 157-59 and accompanying text; see also *Sterling v. Velsicol Chem. Corp.*, 647 F. Supp. 303, 482-83 (W.D. Tenn. 1986), *aff'd in part, rev'd in part*, 855 F.2d 1188 (6th Cir. 1988); *Rubanick v. Witco Chem. Corp.*, 576 A.2d 4, 12 (N.J. Super. Ct. App. Div. 1990), *modified*, 593 A.2d 733 (N.J. 1991);. The U.S. Supreme Court discussed the one-hit theory and its relation to the issue of threshold exposures in *Industrial Union Department, AFL-CIO v. American Petroleum Institute*, 488 U.S. 607, 636 & n.41 (1979).

193. See, e.g., 2 Transcript of Hearing at 191-95 (testimony of Dr. Marvin Legator), *Renaud v. Martin Marietta Corp.*, 749 F. Supp. 1545 (D. Colo. 1990) (Civ. A. No. 87-Z-42), *aff'd*, 972 F.2d 304 (10th Cir. 1992); *id.* at 275-79 (testimony of Dr. David Ozonoff).

194. *Id.*

195. See generally OS&TP, *Chemical Carcinogens*, *supra* note 141, at 10,387-88, 10,438; see also *supra* notes 157-59. Cancer researchers recognize that DNA alteration represents only one mode of chemical carcinogenesis. Some carcinogens have been demonstrated not to react with DNA. These are generally grouped under the general heading of epigenetic carcinogens, which include promoters, that is, agents that facilitate the growth of dormant cancer cells into tumors. See *Williams & Weisburger*, *supra* note 156, at 185-86. These carcinogens typically require high doses and sustained exposure to exhibit carcinogenicity. *Id.* at 185.

The "one hit" theory is consistent with the linear extrapolation model or no-threshold model discussed *supra* notes 157-59 and accompanying text. The appeal of this kind of reasoning is also fundamentally related to the desire to understand *how* causation occurs.

196. Nor is even a proven mechanism likely to provide much information on the likelihood that an exposure caused disease unless the mechanistic explanation leads to a clinical test capable of distinguishing toxic chemical exposure from background or other causes.

c. Medical Opinion Evidence

Plaintiffs often offer medical opinion evidence on individual causation; indeed, courts sometimes express a preference for testimony by a treating or examining physician.¹⁹⁷ Such testimony may be essential to establish the diagnosis of the plaintiff's disease, his medical history, and the presence or absence of other possible risk factors for the disease.¹⁹⁸ The problems with medical opinion evidence arise when epidemiologic evidence of general causation is weak or absent¹⁹⁹ and the evidence of the capability of a substance to cause harm consists only of animal studies, mutagenicity testing, *in vitro* studies, or chemical structure-activity relationships.²⁰⁰ Those kinds of evidence are a weak basis for concluding that the toxic substance causes any human disease at all.²⁰¹ They are an extremely uncertain basis for making quantitative predictions that would allow a comparison of exposure risks and background risks. Indeed, the cases that have approved such evidence as sufficient to support a plaintiff's verdict have tended to ignore the absence of evidence²⁰² that would permit the plaintiff to distinguish background risks.

Plaintiffs who lack an epidemiologic basis for their proof of causation nonetheless frequently offer medical testimony from a treating physician or other expert who opines that the plaintiff's disease was caused by toxic substance exposure.²⁰³ This form of opinion is evident in

197. See *Ferebee v. Chevron Chem. Co.*, 736 F.2d 1529 (D.C. Cir.), cert. denied, 469 U.S. 1062 (1984); *Wells v. Ortho Pharmaceutical Corp.*, 615 F. Supp. 262, 272-73 (N.D. Ga. 1985), *aff'd in part, modified in part*, 788 F.2d 741 (11th Cir.), cert. denied, 479 U.S. 950 (1986); *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223, 1235 (E.D.N.Y. 1985), *aff'd*, 818 F.2d 187 (2d Cir. 1987), cert. denied, 487 U.S. 1234 (1988).

198. See *infra* notes 206-12 and accompanying text.

199. See, e.g., *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829, 862 (3d Cir. 1990) (opinion evidence based on, *inter alia*, animal tests and industrial exposures should not have been excluded), cert. denied, 111 S. Ct. 1584 (1991); *Ferebee*, 736 F.2d at 1535 (treating physicians testified).

200. See *supra* note 179 and accompanying text.

201. *Id.*

202. See, e.g., *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d at 862 (approving proffered medical causation evidence). Such evidence is not a valid means of distinguishing other causal explanations when the causes of a majority of background cases are unknown. See *Rubanick v. Witco Chem. Co.*, 593 A.2d 733, 735-36 (N.J. 1991) (animal studies of PCBs, personal history, and higher than expected incidence of cancer at place of work admissible on causation of colon cancer); *infra* notes 264-76, 293-300 and accompanying text.

203. See, e.g., *Eggar v. Burlington N.R.R.*, No. CV89-159-BLG-JFB, 1991 U.S. Dist. LEXIS 19240 (D. Mont. Dec. 18, 1991); *In re Joint E. and S. Dist. Asbestos Litig. (Maiorana)*, 758 F. Supp. 199 (S.D.N.Y. 1991), *rev'd*, 964 F.2d 92 (2d Cir. 1992); *Wells v. Ortho Pharmaceutical Corp.*, 615 F. Supp. 262 (N.D. Ga. 1985), *aff'd in part, modified in part*, 788 F.2d 741 (11th Cir.), cert. denied, 479 U.S. 950 (1986); *Landrigan v. Celotex Corp.*, 605 A.2d 1079 (N.J. 1992).

The problems associated with medical testimony or disease causation have been discussed at length in *Black*, *supra* note 15, at 659-81. Depending on the circumstances, courts or the parties may espouse the view that a physician's testimony is preferred on the

*Renaud v. Martin Marietta Corp.*²⁰⁴ and other recent cases. When there is no clinical test that establishes a cause or distinguishes among possible causes, however, such "intuition" can only be characterized as speculation. This kind of speculation could easily be unmasked by inquiring into the reasoning behind the witness's opinion.²⁰⁵

d. Differential Diagnosis

The problem of distinguishing other causes takes a somewhat different form when there are other known risk factors for the plaintiff's disease. The effort to distinguish and eliminate other known risk factors is sometimes called "differential diagnosis."²⁰⁶ Diseases such as cancer that can result from toxic chemical exposure may also be associated with other identified risk factors, such as smoking, diet, lifestyle, as well as undifferentiated background risk associated with radiation and biological processes. Thus, the obvious question, particularly when the plaintiff does not exhibit other known risk factors such as diet, smoking, or a family history of the same cancer, is whether the absence of other risk factors increases the likelihood that the plaintiff's disease was caused by exposure to the toxic substance.²⁰⁷

issue of causation. The District of Columbia Circuit affirmed a jury's finding of liability in *Ferebee v. Chevron Chem. Co.*, 736 F.2d 1529, 1535-36 (D.C. Cir.), cert. denied, 469 U.S. 1062 (1984), based on the testimony of treating physicians. Plaintiffs often offer such testimony.

Interestingly, defendants sometimes object when a treating physician does not testify on causation. See, e.g., *Landrigan*, 605 A.2d at 1083 (trial court ruled that an epidemiologist could not testify on individual causation, nor could a nontreating physician offer an opinion based on epidemiologic evidence). Medical evidence, including testimony of a treating physician, may provide evidence of diagnosis of plaintiff's disease or injury or of the existence of other risk factors for the disease. See *id.*

204. 749 F. Supp. 1545 (D. Colo. 1990), *aff'd*, 972 F.2d 304 (10th Cir. 1992).

205. See *Ferebee v. Chevron Chem. Corp.*, 736 F.2d 1529 (D.C. Cir.), cert. denied, 469 U.S. 1062 (1984); *Rubanick v. Witco Chem. Corp.*, 593 A.2d 733 (N.J. 1991). The *Ferebee* court based its affirmance of the plaintiff's verdict on the treating physicians' use of "tissue samples, standard tests, and patient examination." 736 F.2d at 1536. The court did not appear to consider whether those tests were in any way indicative of the cause of *Ferebee's* condition.

206. This usage of the term seems to be a misnomer. *STEDMAN'S MEDICAL DICTIONARY* (25th ed. 1990), defines differential diagnosis as "the determination of which of two or more diseases with similar symptoms is the one from which the patient is suffering, by a systematic comparison and contrasting of the clinical findings." *Id.* at 428. In toxic torts, the term is applied to the determination of which of two or more factors caused the plaintiff's disease, the diagnosis of which is not in question.

207. "Differential diagnosis" is an argument that cuts both ways. Plaintiffs are likely to make a differential diagnosis argument that the toxic exposure is the likely cause of the plaintiff's disease because other known risk factors are absent. See, e.g., *Landrigan v. Celotex Corp.*, 605 A.2d 1079 (N.J. 1992) (discussing risk factors for colon cancer). Defendants are likely to point out that plaintiff has failed to eliminate other known risk factors that are applicable to the plaintiff. See, e.g., *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223, 1253 (E.D.N.Y. 1985) (plaintiff's experts "fail to show how the myriad illnesses at issue are more likely to have been caused by Agent Orange than by something

Plaintiffs often argue and courts sometimes accept the notion that the absence of other risk factors increases the likelihood that the plaintiff's disease was caused by the toxic exposure at issue.²⁰⁸ The validity of that kind of reasoning, however, rests on two unstated, and usually untested, assumptions. First, such reasoning treats toxic exposure and the other risks as alternatives. In other words, it assumes that the disease was caused by the toxic exposure *or* some other cause, such as the other identified risk factors.²⁰⁹ Second, it assumes that most causes of the disease in question are known; otherwise, the elimination of other risk factors would not significantly increase the likelihood that the toxic exposure was the cause of the plaintiff's disease.

The assumption that risk factors, including the toxic exposure, represent alternative causes is true only if the various risks are additive. Additivity is only one of several ways in which risk factors for the same disease may relate. The combined effects may be the same, greater, or less than the sum of the effects as measured separately.²¹⁰ Additive effects represent the absence of interaction between risk factors.²¹¹ Thus, each factor adds an incremental level of risk to the background risk that is independent of the presence or absence of other risk factors. Additive

else"), *aff'd*, 818 F.2d 187 (2d Cir. 1987), *cert. denied*, 487 U.S. 1234 (1988). In actuality, the issue of other causes is present in every case that involves a disease with a significant background risk. Almost certainly, there are as yet unidentified risk factors that affect background disease incidence. See ROTHMAN, *supra* note 44, at 12. The assumption of uniform risk factors in the background population reflects ignorance of what those factors are. *Id.* Only with signature diseases such as mesothelioma and clear cell adenocarcinoma that are rare in the absence of exposure to an identified carcinogen can this issue be avoided. See *supra* note 190 and accompanying text.

208. See generally *Landrigan v. Celotex Corp.*, 605 A.2d 1079, 1087-88 (N.J. 1992); *Rubanick v. Witco Chem. Corp.*, 542 A.2d 975 (N.J. Super. Ct. Law Div. 1988), *rev'd*, 576 A.2d 4 (N.J. Super. Ct. App. Div. 1990), *modified*, 593 A.2d 733 (N.J. 1991).

209. Attribution of causation in an illness with several possible causes is often a complex task. As the reader will recall from the discussion at the beginning of this section, the relative risk data from epidemiologic studies can be used to determine the fractions of cases of a disease in an exposed population that are attributable to the exposure and to the background causes. See *supra* notes 187-90 and accompanying text.

210. See ROTHMAN, *supra* note 44, at 311-26. Combined effects that are less than additive are considered antagonistic, while combined risks that are greater than the sum of the separate effects are considered synergistic. *Id.* at 318-20.

211. *Id.* at 313-15. Rothman states that although some epidemiologists treat the foregoing definitional scheme as arbitrary, the use of an additivity assumption for independent action has practical consequences in interpreting and utilizing epidemiologic data. *Id.* at 316-17. For example, the combined relative risks of oral contraceptives and hypertension for thrombotic stroke are greater than the sum of the relative risks of each. *Id.* at 316. When these greater than additive risks are considered to be synergistic, the practical conclusion is that a woman should consider her blood pressure history in deciding whether to use oral contraceptives, a result that seems intuitively correct. *Id.* at 316-17.

risks are properly treated as alternative risks in a causation analysis.²¹² Often, however, the information necessary to support that assumption is not available.

Risk factors whose combined effects are greater than additive are considered interactive or synergistic.²¹³ In this situation, each risk factor enhances the risk contributed by the other factor so that the total incidence of the disease is greater than the sum of the incidence attributable to each factor separately, sometimes approaching a multiplicative effect. Perhaps surprisingly, the presence or absence of other risk factors that are multiplicative does not increase or decrease the fraction of disease attributable to the toxic exposure. Thus, when the causes are synergistic, as with smoking and asbestos and lung cancer,²¹⁴ it is incorrect to pose the question as one of whether the disease was caused by one factor or another.²¹⁵

212. For example, smoking increases the incidence of lung cancer by a factor of about 10 and occupational exposure to asbestos increases risk by about a factor of 5. U.S. SURGEON GEN., *supra* note 47, at 216-17. If the background incidence of lung cancer among nonsmokers who do not have occupational exposures to asbestos is normalized to 1.0, nonsmoking asbestos workers would have a lung cancer incidence of 5.0, while smokers would have a lung cancer rate incidence of 10.0. For smoking asbestos workers, if the risks were noninteractive (and therefore additive), the lung cancer incidence would be about 14, which is the sum of the background case, the four cases added by asbestos exposure, and the nine cases expected to be added as a result of smoking. In this situation, smoking and asbestos would represent alternative causes, since any one plaintiff's case would probably be caused by one factor or the other, not by both acting together. Thus, while a nonsmoking asbestos worker could argue that the probability that asbestos caused his cancer was 80% (4/5), the smoking asbestos worker could point to only a 28% probability (4 cases out of 14 total) that his lung cancer was caused by asbestos (the other 10 cases being the result of background causes or cigarette smoking).

213. ROTHMAN, *supra* note 44 at 315-16.

214. *Id.* at 312.

215. Because the effects of smoking and asbestos are multiplicative for lung cancer, the population of smoking asbestos workers described in *supra* note 212 is expected to have lung cancer incidence of 5 times 10, or 50, rather than the 15 cases predicted by adding the separate risks. See U.S. SURGEON GEN., U.S. DEP'T OF HEALTH & HUMAN SERVS., *supra* note 47, at 216-17. The fraction attributable to asbestos in this case is 40/50 (or 0.8, subtracting the 10 cases that would have occurred as the result of smoking alone or without exposure to either factor from the 50 total cases), the same attributable fraction obtained when the effects of asbestos alone are considered. Counterintuitively, the fraction of lung cancer cases among smoking asbestos workers for which smoking can be considered causative is 45/50 (or 0.9, obtained by subtracting the 5 cases that would have occurred due to asbestos alone or in the absence of either exposure, from the total cases). Those results do not mean, however, that arguments cannot be made that the plaintiff's smoking constituted contributory negligence or an intervening cause that should reduce the asbestos manufacturer's liability or eliminate it altogether.

Defendants sometimes make such arguments. See, e.g., *In re Brooklyn Navy Yard Asbestos Litig.* (Joint E. & S. Dist. Asbestos Litig.), 971 F.2d 831 (2d Cir. 1992); *In re Manguno* (*Acosta v. Babcock & Wilcox*), 961 F.2d 533 (5th Cir. 1992); *Borman v. Raymark Indus.*, 960 F.2d 327 (3d Cir. 1992) (upholding plaintiff's verdict and affirming trial court's refusal to charge the jury on apportionment of damages between smoking and asbestos). In *Manguno*, the jury returned a verdict for defendant asbestos manufacturers. *Id.* at 534.

There are several scenarios under which this issue could arise, but the actual cases tend to be grouped into two extremes. Where epidemiologic data are available that address the contributions of both the toxic substance and other causal factors, the plaintiff's attributable risk and probability of causation by the toxic substance can be determined by calculating attributable fractions, whether the risks are additive, multiplicative or antagonistic. From those calculations, it can be determined whether the plaintiff can satisfy the more likely than not standard of proof on causation.²¹⁶

The other extreme is represented by toxic tort cases where multiple risk factors are treated in a vague or qualitative fashion and data are not available to support a quantitative analysis. The plaintiff's expert may opine that because other known risk factors are absent in plaintiff's case, it is the expert's opinion that plaintiff's disease was caused by the toxic substance exposure.²¹⁷ This argument has superficial appeal. It can only be valid, however, when risk factors that account for most cases of the plaintiff's injury and their interactions are understood. Although some risk factors for cancers and birth defects have been identified, the causes of background incidence of most birth defects and cancers remain unknown. Even if the identified risk factors are alternative, independent causes, as this line of analysis assumes, the expert's opinion distinguishes among factors that make up only a small part of the total picture, while ignoring the probability that the plaintiff's injury may stem from the same unidentified factors that are responsible for most cases of the injury. Whether the differential diagnosis argument is made on behalf of plaintiff or defendant, it adds little to the resolution of the case when it is based on vague, qualitative assumptions about alternative causes.²¹⁸

The defendants argued, and the jury apparently accepted, that plaintiff's smoking cast sufficient doubt on the proposition that asbestos caused the plaintiff's lung cancer. The Fifth Circuit reversed on the basis of improper jury instructions and remanded for a new trial. *Id.* at 535-36.

216. Often there will not be sufficient data to determine whether the risk factors are additive, synergistic, or antagonistic. In such cases the point is arguable, but the better approach would seem to be to ignore other risk factors whose interactions with the toxic substance exposure are unknown and assume that the relative risk associated with the toxic substance exposure applies whether the other risk factors are present or not.

217. *See, e.g., Rubanick v. Witco Chem. Corp.*, 593 A.2d 733, 735-36 (N.J. 1991).

218. The defendant's argument that the existence of known risk factors dilutes the likelihood of causation by the chemical exposure has a point, however, when the plaintiff's general causation evidence is based on medical opinion, animal studies, cellular assays and other such evidence. In *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829, 839-40 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991), the plaintiffs claimed that a variety of commonplace ailments were due to PCB exposure. Available epidemiologic data failed to demonstrate any connection between PCBs and the claimed physical injuries. The defendants' objection that plaintiffs failed to rule out the known causes of such commonplace ailments as high cholesterol and high blood pressure should have been well taken by the court. *See id.* at 861-62.

3. PROOF OF EXPOSURE

a. Inferences from Similar Circumstances.

While the foregoing discussion has focused on proving the harmful effects of exposure, the issues of whether an exposure occurred and if so, of what magnitude, are often present in toxic tort cases.²¹⁹ In several recent cases, the duration and magnitude of the plaintiffs' exposure was subject to a great deal of uncertainty.²²⁰ How can the plaintiff prove exposure? In instances where the plaintiff has a signature disease, the disease itself constitutes strong evidence of exposure because it rarely occurs in the absence of exposure.²²¹ More commonly, however, the plaintiff's injury is not so distinctive that it can be reliably attributed to a toxic substance exposure, even where the substance is known to increase the risk of the condition. Where the claimed injury is one that is not attributable almost solely to a toxic substance, exposure data is meaningful only if it is quantitative. The plaintiff must prove the magnitude of her exposure to a degree of certainty that supports the inference that the evidence linking a toxic chemical to disease is applicable to her.

Some cases, particularly those involving workplace exposures, involve situations that are known to involve exposure to a toxic substance.²²² The severity of the plaintiff's exposure can be inferred from the length of time he was present in the environment. The situation would be similar where there is an ongoing exposure, such as a drinking

219. See, e.g., *Paoli R.R. Yard*, 916 F.2d 829 (evidentiary issue of the degree of plaintiffs' exposure to PCBs), *cert. denied*, 111 S. Ct. 1584 (1991); *Renaud v. Martin Marietta Corp.*, 749 F. Supp. 1545 (D. Colo. 1990) (case dismissed because of plaintiffs' inability to make out a prima facie case of exposure), *aff'd*, 972 F.2d 304 (10th Cir. 1992).

220. See *Christopherson v. Allied-Signal Corp.*, 939 F.2d 1106 (5th Cir. 1991) (en banc), *cert. denied*, 112 S. Ct. 1280 (1992). In *Christopherson*, plaintiff's husband worked in a plant that produced nickel/cadmium batteries. *Id.* at 1108. He did not work in the production area, however, but visited the area intermittently. *Id.* There also appears to have been no direct evidence on the nature of fumes to which Christopherson was exposed during those visits. *Id.* at 1113. Apparently a fellow employee's affidavit alleged that Christopherson was exposed to airborne particles of nickel and cadmium, but it is not clear that the employee could have known the chemical composition of the fumes. See *Christopherson v. Allied-Signal Corp.*, 902 F.2d 362 (5th Cir. 1990), *rev'd*, 939 F.2d 1106 (5th Cir. 1991) (en banc), *cert. denied*, 112 S. Ct. 1280 (1992).

221. In signature disease cases, the existence of the disease may suffice to prove that sufficient exposure occurred and that the exposure caused the plaintiff's injury. Cf. *Renaud*, 749 F. Supp. at 1553 (plaintiffs could have attempted to prove exposure through epidemiologic study).

222. Occupational exposure of insulation installers to asbestos is an example of that situation. See, e.g., *In re Joint E. & S. Dist. Asbestos Litig. (Johns-Manville Corp.)*, 129 B.R. 710, 868 (E.D. & S.D.N.Y. 1991) (Weinstein, J.) (discussing proof of asbestos exposure in occupational and other settings), *vacated*, 982 F.2d 721 (2d Cir. 1992).

water exposure, that can be measured. In such cases, inferences about past conditions can be drawn from the present ones.²²³

Sometimes there is clinical evidence of the toxic substance that will suffice to prove the plaintiff's exposure.²²⁴ Substances such as asbestos²²⁵ and PCBs²²⁶ remain in tissues indefinitely, and can be detected by appropriate analytical tests. Other substances may result in subclinical changes that can be detected through appropriate testing.²²⁷

b. Inferences from Modeling

The reasoning underlying the proofs of exposure outlined above is readily apparent and is of the kind already familiar to courts in other contexts. Cases involving possible past exposures where contemporaneous measurements cannot be taken or inferred, and for which there are no available analytical tests, present a much more difficult case. In such cases, experts may use various models to estimate exposure. Models are mathematical formulas that are designed to provide estimates of facts that cannot be measured directly.²²⁸ They range from simple formulas such as the model discussed below that purports to describe the ratio of blood or serum PCB levels to adipose tissue levels, to complex computer programs used to model groundwater contaminant migration and air pollutant dispersion.

Models, at least conceptually, sometimes begin with theories or hypotheses about how different kinds of data might be related. A scientist would be unlikely to propose a model that was not at least plausible, based on her understanding of how the phenomena in question

223. See, e.g., *Sterling v. Velsicol Chem. Corp.*, 855 F.2d 1188 (6th Cir. 1988) (chlorinated hydrocarbons detected in 12 to 15 drinking water wells).

224. Clinical evidence will not necessarily be sufficient to prove that the exposure caused injury, however, because exposure does not always result in disease. See *supra* note 47 and accompanying text.

225. See, e.g., *Landrigan v. Celotex Corp.*, 605 A.2d 1079 (N.J. 1992) (clinical data, such as asbestos in or near a tumor, may support a finding of specific causation).

226. See, e.g., *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829, 841 & n.10 (3d Cir. 1990), cert. denied, 111 S. Ct. 1584 (1991). Dioxin is also retained in fat. Brennan, *supra* note 25, at 51 (citing Peter C. Kahn et al., *Dioxins and Dibenzofurans in Blood and Adipose Tissue of Agent Orange-Exposed Vietnam Veterans and Matched Controls*, 259 JAMA 1661 (1988)).

227. See Robert R. Lauwerys, *Occupational Toxicology*, in CASARETT & DOULL, *supra* note 148, 947, 954-66; see also OS&TP, *Chemical Carcinogens*, *supra* note 141, at 10,386, 10,441 (discussing DNA alteration and relation to carcinogenesis); Brennan, *supra* note 15, at 502 n.174. Clinical testing for exposure-induced damage may become more important as knowledge accumulates regarding molecular alterations from chemical exposures. See OS&TP, *Chemical Carcinogens*, *supra* note 141, at 10,441.

228. For a discussion of groundwater contaminant migration modeling, see Allen Kezsbom & Alan V. Goldman, *The Boundaries of Groundwater Modeling Under the Law: Standards for Excluding Speculative Expert Testimony*, 27 TORT & INS. L.J. 109 (1991). See also Itzhak E. Kornfeld, *Comment to the Boundaries of Groundwater Modeling Under the Law: Standards for Excluding Speculative Expert Testimony*, 28 TORT & INS. L.J. 59 (1993).

are connected. Plausibility alone, however, like the mechanistic theories of cancer causation, is often insufficient to eliminate other plausible but untested models or theories. Thus, a model must be validated before an expert or a court should assume that it has any probative value.

Validation of a model involves testing the model's predictive capability in circumstances where the expected results can be independently measured.²²⁹ In the case of the blood/adipose tissue partition model or the much more complex groundwater contaminant migration modeling, actual concentrations can be measured and compared with values predicted by the model. From such data, it can be determined whether the model has any predictive value and how accurate or reliable those predictions are. If the model proves valid and reasonably accurate, then it is reasonable to apply it to other situations similar to the one for which the model has been tested.

A number of cases, however, have involved modeling of exposures where the models have not been subjected to the most cursory validation, sometimes in the face of data that contradict the model. In *In re Paoli Railroad Yard PCB Litigation*,²³⁰ one of the ways the plaintiffs attempted to prove exposure to PCBs was by showing that their PCB levels were elevated above background levels. Because PCBs accumulate in fatty tissue and are not quickly eliminated from the body, it is possible to measure PCB levels in blood or tissue samples from individuals and compare them to norms for the general population.²³¹ The Agency for Toxic Substances and Disease Registry (ATSDR) had done a study on blood PCB levels in Paoli residents and concluded that the residents' serum PCB levels did not differ significantly from those of the general population.²³² Plaintiffs contended that the ATSDR study's conclusions regarding background PCB levels in the general population were erroneous. Their experts sought to show that the plaintiffs' adipose or fat PCB levels exceeded norms found in the Environmental Protection Agency's National Human Adipose Tissue Study.²³³ Because most of the plaintiffs' PCB levels were determined by blood tests alone, plaintiffs'

229. See Kezsbom & Goldman, *supra* note 228, at 117 (noting that the plaintiffs in *Sterling v. Velsicol* never verified their model against real-world data). Kornfeld, who has a contrary view of *Sterling v. Velsicol*, states that models must be scrutinized to determine whether they replicate real-world data and have been calibrated. See Kornfeld, *supra* note 228, at 68.

230. 916 F.2d 829 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991).

231. See *id.* at 839-41. PCBs are polychlorinated biphenyls, once commonly used in electrical transformers.

232. Nor did they differ significantly among the residents according to higher soil concentrations in the residents' yards, number of years in the vicinity, or residence in more or less highly contaminated areas. *In re Paoli R.R. Yard PCB Litig.*, 706 F. Supp. 358, 364-65 (E.D. Pa. 1988), *rev'd*, 916 F.2d 829 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991).

233. *Id.* at 371. The study was conducted between 1970 and 1983.

expert used his own formula to calculate their adipose tissue PCB levels, which he then compared with results reported in the national study.²³⁴

As the trial court recognized, however, neither of the plaintiffs' experts on this issue²³⁵ cited any basis for the claimed relationship between PCB concentrations in blood and adipose tissue.²³⁶ Moreover, where blood and adipose tissue PCB levels were measured in the same plaintiffs, the results did not bear out the ratios asserted by plaintiffs' experts.²³⁷ Thus, although a relationship between blood and adipose tissue levels of PCBs is plausible, the direct ratio posited by plaintiffs' witnesses was not validated and was demonstrably inaccurate as indicated by comparison of predicted levels with actual measurements in plaintiffs who had both tests. Conclusions based on models that have not been validated by actual measurement,²³⁸ or worse, which are contradicted by actual measurements, are based on invalid reasoning and should be rejected by the courts.

Use of unvalidated models is not the only concern about models. Models inherently involve approximations—generalizations about physical phenomena and estimations that must be made because the actual situation cannot be studied directly.²³⁹ Those approximations inevitably introduce inaccuracies into the model's predictions. At some point, the uncertainty or inaccuracy may become so large that the model's results are too unreliable to prove the fact on which they are offered.

Modeling of groundwater and surface water contamination was at issue in *Renaud v. Martin Marietta Corp.*,²⁴⁰ in which the plaintiffs claimed that contamination of the public water supply had caused childhood cancers and other diseases.²⁴¹ Plaintiffs' case on exposure involved the issue of whether contaminants released at the Martin Marietta facility had reached their taps through the Denver culinary water distribution system. Because the circumstances that created the discharges at issue had changed in the years preceding the suit, the plaintiffs relied on

234. *Id.* at 370-71. The Third Circuit opinion implies that the NHATS study used the formula that relates blood and adipose tissue levels. See *Paoli*, 916 F.2d at 841 n.10.

235. Dr. Ian C.T. Nesbit, a Ph.D. physicist and consultant, and Dr. Robert K. Simon, an industrial hygienist, toxicologist, and forensic analytical chemist, testified on the same issue. See *Paoli*, 916 F.2d at 840, 847.

236. *Paoli*, 706 F. Supp. at 372..

237. *Id.*

238. In *Paoli*, one of plaintiffs' experts, Dr. Herbert Allen, purported to calculate the levels of airborne PCBs to which plaintiffs had been exposed based on soil PCB concentrations, using a formula, i.e. a model, he had devised. 916 F.2d at 839. Dr. Allen's predictions, however, were higher than the measurements actually taken. See *infra* text accompanying notes 257-59.

239. See Kezsbom & Goldman, *supra* note 228, at 109, 116-19.

240. 749 F. Supp. 1545 (D. Colo. 1990), *aff'd*, 972 F.2d 304 (10th Cir. 1992).

241. *Id.* at 1547.

hydrological modeling of ground and surface water movement as proof that contaminants had reached the water distribution system.²⁴²

Defendants argued that there were serious flaws in the modeling, most notably that plaintiffs had erred by failing to consider all relevant factors when deriving the decay coefficient for the contaminants.²⁴³ Further, the experts had not taken into account the possibility that chlorination at the water intake plant had destroyed or greatly reduced the concentration of contaminants.²⁴⁴ Although the court stated that “[t]he issues of which factors should have been considered and what impact each should have been given” were questions for the jury, it seems clear that the factors that plaintiffs’ experts ignored would have had a large impact on the concentrations predicted by the fate and transport modeling.²⁴⁵ Models are always subject to dispute over the factors that are included or excluded, and thus cannot be judged by too rigorous a standard. Nonetheless, where experts have excluded significant factors that would tend to produce results at odds with their conclusions, the court should exclude the modeling results unless there is some more direct way to demonstrate the model’s validity and accuracy.²⁴⁶

Another concern with modeling is that uncertain input data affect the reliability of the results of all kinds of exposure modeling. If the input data are very limited, there will be uncertainty about how representative those data are, and those uncertainties will produce corresponding uncertainties about the modeling results, no matter how good the model is. The greatest uncertainty about the exposure modeling in *Renaud* resulted from such a scarcity of data.²⁴⁷ In that case, the plaintiffs’ exposure estimate, obtained through the transport modeling described above, was based on a single loading concentration for the contaminants. The court recognized that the single data point on which the modeling was based could not be said to be representative of the 11-year period

242. *Id.* at 1549.

243. *Id.* at 1552. A decay coefficient was necessary because the chemicals at issue were known to undergo degradation in the environment. *See id.* at 1549.

244. *See* Letter from Dr. Hannah Pavlik, Ebasco Environmental, to Judge Zita Weinshienk, U.S. District Court (Aug. 29, 1990). Dr. Pavlik, a geochemist and hydrogeologist, was retained as a court-appointed expert witness. *Renaud*, 749 F. Supp. at 1553. Her report also indicated a number of other methodological and factual flaws in the hydrological modeling. *See* Letter from Dr. Hannah Pavlik, *supra*, at 9.

245. *Renaud*, 749 F. Supp. at 1552; *see* Letter from Dr. Hannah Pavlik, *supra* note 244, at 16.

246. The *Renaud* plaintiffs’ experts could have conducted experiments on the effects of chlorination on the chemicals in question. The only available information on that issue appeared to be the defendants’ own tests, however, which were consistent with their position. *See* Letter from Dr. Hannah Pavlik, *supra* note 244, at 9.

247. Data that is based on unsound assumptions, unverifiable assumptions, or erroneous input results in a manifestation of the “garbage in, garbage out” phenomenon. *See* Kezsborn & Goldman, *supra* note 228, at 116.

over which releases occurred.²⁴⁸ It found the single data point to be a fatal flaw in the plaintiffs' exposure case.²⁴⁹

V. DIVERGENCE OF OPINION

A. Deferential Review and the Accumulation of Errors

The foregoing Part has examined separately the problems associated with proof of exposure, capability of the substance to cause harm, and distinguishing among causes and concluded that the evidence deemed acceptable in many toxic tort cases is often grossly inadequate to prove the propositions on which it is offered. It is also important to examine how those issues are brought together in real cases, keeping in mind that the ultimate causation issue is whether exposure to a toxic substance caused the plaintiff's disease. This part discusses several recent cases that are particularly troubling when viewed as a whole, because the plaintiff's cases can, at best, be characterized as consisting of possibilities and speculation strung together in ways that fall far short of the legal requirements of proof.

The Third Circuit's decision in *In re Paoli Railroad Yard PCB Litigation*²⁵⁰ represents one of the most troubling decisions on the admissibility and sufficiency of challenged scientific evidence. *Paoli* involved an action by 38 neighbors and employees of an electric railcar maintenance facility contaminated by PCBs.²⁵¹ The action, which was brought against owners and operators of the site, and suppliers of PCBs and transformers, made claims for various injuries and for medical monitoring costs necessary to protect against latent disease.²⁵²

Defendants' motions to exclude plaintiffs' evidence of exposure to PCBs and other causation evidence, and for summary judgment were granted by the trial court.²⁵³ The Third Circuit, however, reversed, finding that the trial court had improperly excluded sufficient evidence to survive summary judgment.²⁵⁴ The case represents a virtually complete catalog of the unprobative and insufficient kinds of proof identified in this article.

Two factual issues on which scientific evidence was crucial were: (1) whether plaintiffs received any exposure above background levels of

248. *Renaud*, 749 F. Supp. at 1552-53.

249. *Id.*

250. 916 F.2d 829 (3d Cir. 1990), *rev'g* 706 F. Supp. 358 (E.D. Pa. 1988), *cert. denied* 111 S. Ct. 1584 (1991).

251. *Id.* at 832.

252. *Id.* at 849.

253. *Id.* at 835.

254. *Id.* at 862.

PCBs that could be attributed to the Paoli railyard; and (2) whether PCBs are capable of causing the ailments of which plaintiffs complained or of which they believed they were at risk.²⁵⁵ The primary problem with plaintiffs' evidence on exposure involves unvalidated methodology through which plaintiffs attempted to show that their exposure to PCBs exceeded background levels.

Plaintiffs offered several forms of evidence in addition to the blood/adipose tissue calculations discussed in the preceding Part,²⁵⁶ in support of their contentions of higher than background levels of PCB exposure. First, they offered the testimony of Dr. Herbert Allen, an environmental chemist who used a formula of his own devising to calculate airborne exposure levels from PCB levels measured in neighborhood soils.²⁵⁷ Nothing in either the district court's or the appellate court's opinions, however, suggests that Dr. Allen's formula had been tested, that is, that its validity had been demonstrated by comparing the airborne concentrations predicted by the formula and actual, measured air concentrations.²⁵⁸ In fact, the district court opinion states that the "actual measurements that were taken showed an amount much lower than [Allen] calculated."²⁵⁹

Plaintiffs also offered the testimony of Dr. Deborah Barsotti, a toxicologist employed by the Agency for Toxic Substances and Disease Registry, who claimed to have correlated gas chromatography tracings of PCBs in the plaintiff's blood with tracings from soil samples from the Paoli railyard.²⁶⁰ Dr. Barsotti, however, was apparently unable to support her general statements with reference to any specific plaintiffs' blood samples or soil samples.²⁶¹ Later, she apparently conceded that the equipment she had used was not capable of yielding the results she claimed.²⁶²

Plaintiffs' evidence on general causation and on distinguishing background causes was hardly more probative. On the question of whether PCBs are capable of causing the kinds of illnesses complained of, the plaintiffs were faced with various studies that had failed to find a correlation between PCB exposure and significant human disease. One such study was the ATSDR's study, *Toxicological Profile for Selected*

255. *See id.* at 860-62.

256. *See supra* notes 230-38 and accompanying text.

257. *Paoli*, 916 F.2d at 838-39.

258. *Id.* at 839, 842; *In re Paoli R.R. Yard PCB Litig.*, 706 F. Supp. 358, 370 (E.D. Pa. 1988), *rev'd*, 916 F.2d 829 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991).

259. *Paoli*, 706 F. Supp. at 370.

260. *Paoli*, 916 F.2d at 839.

261. *Id.* at 842.

262. *Id.*

PCBs.²⁶³ As summarized in the Foreword, the ATSDR study found that only skin lesions and liver effects that were not associated with "clinically detectable disease" had been observed in PCB-exposed workers. The study also concluded that adverse effects had not been observed in persons with non-occupational exposures.²⁶⁴

The Third Circuit, however, found various plaintiffs' witnesses' testimony sufficient to create a jury question.²⁶⁵ Some of this testimony can only be described as conclusory.²⁶⁶ Several of plaintiffs' experts relied on animal studies and on studies involving incidents of accidental ingestion of a mixture of PCBs and PCDFs,²⁶⁷ the "Yusho" and "Yu Cheng" incidents that occurred respectively in Japan in 1968, and Taiwan in 1979.²⁶⁸ Lastly, the plaintiffs offered the testimony of Dr. William J. Nicholson, a professor of community medicine who had performed a "meta-analysis" of existing (negative) epidemiologic studies²⁶⁹ and concluded that his analysis showed that PCBs can cause liver, biliary tract and gall bladder disorders.²⁷⁰

The evidence on general and individual causation was clearly insufficient to permit the inference that would satisfy the more likely than not standard of proof. Animal studies, as discussed earlier, are at best subject to large uncertainties when extrapolated to humans, particularly for effects of chronic, low-level exposures.²⁷¹

The use of the Yusho and Yu Cheng studies were not challenged as invalid,²⁷² but their use for the purposes of proving that PCBs cause significant adverse effects in humans involves invalid reasoning.²⁷³ The

263. *Paoli*, 706 F. Supp at 365 (citing Toxicological Profile for Selected PCBs (draft Nov. 1987)).

264. *Id.*

265. *Paoli*, 916 F.2d at 862. Dr. Barsotti testified that exposure to PCBs at Paoli was a substantial factor in causing plaintiffs' elevated triglycerides, cholesterol, and liver enzyme levels. *Id.* at 839. According to the court, she based her conclusions on her inspection of the Paoli railyard and her review of various reports and studies, and of soil samples from the railyard. *Id.*

266. Dr. Barsotti's affidavits on causation for each plaintiff were identical for the first fourteen pages, with only two additional paragraphs listing the alleged injuries and concluding they were caused by PCBs. *Id.* at 842-43. Thus, she never explained her reasoning beyond the fact that plaintiffs were exposed to the railyard PCBs, studies have indicated possible injuries from PCBs, and plaintiffs have injuries.

267. PCDFs are polychlorinated dibenzofurans, chemically related to PCBs. *See id.* at 839.

268. *Id.* at 840.

269. *Id.* at 841. A meta-analysis combines the results of epidemiologic studies to increase the total sample size and reanalyzes the data. *Id.*

270. *Id.*

271. *See supra* notes 140-68 and accompanying text.

272. *See In re Paoli R.R. Yard PCB Litig.*, 706 F. Supp. 358, 366 (E.D. Pa. 1988), *rev'd*, 916 F.2d 829 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991).

273. *Id.* at 368.

studies identified harmful effects from two incidents involving the ingestion of oil mixtures containing PCBs and PCDFs. Assuming that the conclusions regarding the Yusho and Yu Cheng incidents were accurate, the results can at most be said to prove the following proposition: The harmful effects observed in the Yusho and Yu Cheng incidents were caused by either: (1) PCBs; (2) PCDFs; or (3) PCBs and PCDFs in combination.²⁷⁴ The studies do not allow the conclusion that PCBs alone can cause the effects observed in the study. Additionally, because PCDFs are regarded as more toxic than PCBs,²⁷⁵ the proposition that plaintiffs argued from the study is not supported by the study.²⁷⁶

The meta-analysis of epidemiologic studies presents a somewhat different problem. Meta-analyses are not outside the scope of recognized scientific methodology.²⁷⁷ The defendants did raise questions, however, about the way in which Dr. Nicholson analyzed the existing data, contending that he omitted data that were inconsistent with his conclusions.²⁷⁸ Thus, the trial court could have examined the bases on which Dr. Nicholson included and excluded data to determine whether

274. This analysis assumes that there is a basis for concluding that the effects were not caused by other unnamed constituents.

275. See *In re Paoli R.R. Yard Litig.*, 916 F.2d 829, 839, 843 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991). PCDFs are polychlorinated dibenzofurans. *Id.* at 839.

276. The Third Circuit noted that Dr. Herbert Allen testified that activities at the railyard such as welding and cutting contaminated equipment could have converted PCBs into dioxins and PCDFs. *Id.* at 839. Although the court characterized this testimony as "particularly significant." *Id.* It appears to offer only the most tenuous evidence of an unquantifiable possibility, since there is no indication that plaintiffs tested for or offered physical evidence of dioxin or PCDF contamination or exposure.

277. See *id.* at 857 (citing C. David Naylor, *Two Cheers for Meta-analysis: Problems and Opportunities in Aggregating Results of Clinical Trials*, 138 CAN. MED. ASS'N J. 891, 894 (1988)).

278. *Id.* at 845. The Third Circuit regarded the issue of how the meta-analysis was conducted as one of credibility, and therefore for the jury, although it qualified that conclusion with the statement that the meta-analysis would be excludable if no reasonable person could believe the study. *Id.* at 858. The district court appears to have excluded the meta-analysis primarily on relevance grounds, although it first discussed the standards for admitting novel scientific evidence in connection with the meta-analysis. *In re Paoli R.R. Yard Litig.*, 706 F. Supp. 358, 372-73 (E.D. Pa. 1988), *rev'd*, 916 F.2d 829 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991). It deemed the study irrelevant because the diseases the study attributed to PCB exposure were not those claimed by plaintiffs. *Id.* at 373. The Third Circuit rejected that rationale, however, because it also held that plaintiffs were entitled to proceed under a medical monitoring claim; it deemed the meta-analysis relevant to a determination of the risks of future disease to which the plaintiffs were exposed.

The issue of when evidence based on a technique that may have been improperly applied may be excluded, as opposed to submitted to the jury, is a current controversy in evidence law. If, however, it was apparent that the meta-analysis was a result-oriented manipulation of data from other studies, the trial court would have been justified in excluding it, even under the Third Circuit's standard. See *infra* notes 357-66 and accompanying text (discussing "data dredging" in connection with meta-analysis and reanalysis of epidemiological studies).

there were logical criteria, systematically applied, in combining and evaluating the data from previous studies.

Paoli also involved questions related to expert testimony on individual causation.²⁷⁹ Several witnesses appear to have asserted that based on test results indicating the presence of PCBs in the railyard and surrounding area, the presence of PCBs in plaintiffs' blood, plaintiffs' medical records, and the literature on effects of PCBs, they could state "to a reasonable medical certainty"²⁸⁰ that plaintiffs' various ailments were caused by exposure to PCBs.²⁸¹

Reference to the evidence on which these conclusions were purportedly based reveals that those conclusions amounted to nothing more than speculation. Animal studies and studies of incidents involving several chemicals provide only uncertain evidence that the substance will cause human disease at all. Animal studies simply do not produce results that permit reliable conclusions about the likelihood of human disease at particular exposure levels. The Yusho and Yu Cheng studies involved ingestion of much larger quantities of PCBs than the *Paoli* plaintiffs were exposed to, and that exposure involved another, probably more toxic chemical. In fact, *Paoli*, like other recent cases,²⁸² involves a scenario in which plaintiffs complaining of a variety of common ailments²⁸³ attempt to attribute those ailments to exposure to a toxic chemical for which human effects have not been demonstrated or are different from those

279. *Paoli*, 916 F.2d at 862. In some cases, the witnesses seemed to combine the question of whether PCBs can cause disease with the question of whether the assumed exposure caused a particular plaintiff's disease. See, e.g., *id.* at 839 (testimony of Dr. Deborah Barsotti); *id.* at 840 (testimony of Dr. Harry Shubin).

280. *Id.* at 851.

281. In some cases, the diagnoses themselves (not only their causes) were at issue. For example, Dr. Arthur Zahalsky opined that the plaintiffs suffered from immune system injuries. *Id.* at 840. At his deposition, however, Zahalsky admitted that testing (of his own design) required to validate his opinion had not been carried out. *Id.* at 843. The speculative nature of Zahalsky's contentions regarding whether PCBs can cause immune system damage is illustrated by his admission that he had not tested any of the plaintiffs. *Id.* at 843. The court also quotes Zahalsky as stating that "if his tests should support such a conclusion, 'then I will have done something with the clinical immunologists that has not yet been done.'" *Id.* (quoting Zahalsky).

Diagnoses relating to increased fear of illness and emotional distress seem particularly lacking in support. Dr. Deborah Barsotti apparently offered her opinion of this issue without having met or examined any of the plaintiffs, having spoken to only one plaintiff on the telephone. *Id.*

282. See, e.g., *Renaud v. Martin Marietta Corp.*, 749 F. Supp. 1545 (D. Colo. 1990) (childhood cancer, including leukemia; kidney cancer; seizure disorders), *aff'd*, 972 F.2d 304 (10th Cir. 1992); *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223 (E.D.N.Y. 1985) (plaintiffs alleged infertility, miscarriage, birth defects, cancer, emotional disturbance, and other commonplace ailments), *aff'd*, 818 F.2d 187 (2d Cir. 1987), *cert. denied*, 487 U.S. 1234 (1988).

283. *Paoli*, 916 F.2d at 839 (elevated blood pressure, triglycerides, and cholesterol, elevated liver enzymes, and emotional distress).

complained of by the plaintiffs. Even if one assumes that some level of exposure above background has occurred, a proposition that appears doubtful in *Paoli* and other cases,²⁸⁴ the question remains as to whether the individual plaintiffs' conditions were caused by the exposure or by the more commonplace causes of such diseases in the general population, whether known or unknown, a question that cannot be answered without evidence demonstrating that a substance can cause the plaintiff's disease and indicating increased disease incidence at the levels to which plaintiffs were exposed.²⁸⁵ Animal testing and studies involving high level exposure to several toxic substances simply cannot provide that information.

The logical extension of the plaintiffs' position is that virtually anyone with one or more of a whole host of commonplace ailments who may have come into contact with toxic substances should be able to recover from the entity responsible for the toxic substance. Such a proposition clearly goes too far; yet it is difficult to draw any principled distinctions about who should or should not recover if the reasoning of the *Paoli* plaintiffs and their experts is accepted.²⁸⁶

Concerns about the evidentiary basis of causation in toxic torts are not limited to cases involving large numbers of plaintiffs and an array of alleged injuries. Cases involving one or a few plaintiffs may raise similar concerns. Further, a court may tend to view such cases in isolation, even though extension of the case's underlying logic may lead to results similar to those in cases such as *Paoli*, namely, that there is no principled way to

284. See *supra* notes 260-89 and accompanying text.

285. On remand, the district court held a series of evidentiary hearings in accordance with the Third Circuit's directive. The rulings on the summary judgment motion and other evidentiary rulings can be found at *In re Paoli R.R. Yard PCB Litig.*, No. 86-2229, 1992 U.S. Dist. LEXIS 16287 & 18427-37 (E.D. Pa. Oct. 21, 1992) (numerous rulings); *In re Paoli R.R. Yard Litig.*, No. 86-2229, 1992 U.S. Dist. LEXIS 17602 (E.D. Pa. Nov. 13, 1992) (defendant granted summary judgment with respect to plaintiffs' property damage claims). The plaintiffs presented a somewhat different group of witnesses than it had prior to the first summary judgment and appeal. Judge Kelly analyzes the testimony of each of those witnesses in separate opinions. See *Paoli*, 1992 U.S. Dist. LEXIS 18427-37.

286. Similar concerns undoubtedly underlay Judge Weinstein's opinion in the Agent Orange "opt-out" cases, discussed *infra* text accompanying notes 319-21. The plaintiffs sought recovery for many commonplace ailments including infertility, birth defects, miscarriages, liver disorders, skin rashes, and gastrointestinal disorders. It seems obvious that many instances of those conditions would have occurred among Vietnam veterans and their families without any causal relation to their service in Vietnam. As Judge Weinstein observed: "There are roughly 7500 new cases of Hodgkin's Disease per year in the United States. The fact that seventeen of these persons happen to be Agent Orange plaintiffs proves nothing about the origin of their condition." *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. at 1253 (citation omitted). Judge Weinstein goes on to state: "[Plaintiffs' experts Doctors Singer and Epstein] fail to show how the myriad illnesses at issue are more likely to have been caused by Agent Orange than by something else." *Id.*

distinguish persons whose disease was caused by a toxic substance exposure from those whose diseases were not so caused.

The New Jersey Supreme Court's decision in *Rubanick v. Witco Chemical Co.*,²⁸⁷ another case involving injuries claimed to have resulted from PCB exposure, is an example of that scenario. Plaintiffs, the relatives of two Witco employees who had died of colon cancer, claimed that their decedents' cancers were caused by PCB contamination at the site.²⁸⁸ Their expert on causation was Dr. Balis, a Ph.D. biochemist with extensive research experience on colon cancer.²⁸⁹ Dr. Balis cited studies indicating that PCBs cause cancer in animals, reports on the effects of PCBs on animals and humans, a high rate of cancer at Witco "during the relevant period," and the personal history of one of the deceased, indicating the absence of other risk factors.²⁹⁰ The difficulties of drawing inferences from animal studies and studies of the effects of PCBs in humans paralleled the difficulties in *Paoli*.²⁹¹ Further, the absence of other risk factors is of little probative value where the causes of most instances of a disease are unknown.²⁹²

The New Jersey court focused disapprovingly on the trial court's finding that Dr. Balis' theory of causation was not generally accepted in the scientific community.²⁹³ Citing the need for a more liberal standard for determining the reliability of scientific theories of causation in toxic torts cases,²⁹⁴ the court held that "a scientific theory of causation that has not yet reached general acceptance may be found to be sufficiently reliable if it is based on sound, adequately-founded scientific

287. 593 A.2d 733 (N.J. 1991).

288. *Id.* at 735.

289. *Id.*

290. *Id.* at 735-36.

291. *See supra* notes 260-89 and accompanying text.

292. There also seems to have been considerable doubt about the extent of Rubanick's exposure to PCBs. The New Jersey Supreme Court quotes Dr. Balis' summary of the evidence of exposure as follows:

that there was some thirty-five thousand parts per million PCBs in the soil around there, that he would come home covered with this stuff and the material was oozing out of his clothes, according to I guess it was his wife's testimony, it was something, and I think that report that he lifted these heavy drums and slopping around in this muddy PCB mix, and you also showed me some document about the State of New Jersey, some agency complaining about contamination from that stuff.

Rubanick, 593 A.2d at 736 (quoting testimony of Dr. Balis). One of the defendant's witnesses stated, "[T]here is no evidence that I have seen to this date that would definitively suggest that the individual actually did have extensive exposure to PCBs." *Id.* (quoting testimony of Dr. Fahey).

293. The trial court also found that although Dr. Balis was qualified to offer an opinion on human carcinogenesis generally, he was not a physician and thus was not qualified to offer an opinion on the cause of a specific person's cancer. *Id.* at 737.

294. *Id.* at 740.

methodology involving data and information of the type reasonably relied on by experts in the scientific field."²⁹⁵ The court went on to state that the theory must be offered by an expert with "a demonstrated professional capability to assess the scientific significance of the underlying data and methodology, and to explain the bases for the opinion reached."²⁹⁶

Remanding the case for further proceedings on the admissibility of Dr. Balis' testimony, the court admonished the trial court not to scrutinize the expert's methodology itself to determine its soundness, however, but to refer to the opinions of comparable experts in the field.²⁹⁷ The problem with that recommendation is that it was unclear that the expert used any methodology at all. The trial court's opinion makes it clear that Dr. Balis testified in terms of possibilities, not probabilities.²⁹⁸ Moreover, the trial court had the benefit of the testimony of the defendant's witnesses, who opined that the scientific literature did not support the plaintiffs' expert's opinion that PCBs can cause cancer in humans.²⁹⁹ The court itself had read the articles cited by the plaintiff's expert and concluded that they "do not say what plaintiff's expert concludes."³⁰⁰

Rubanick, like *Paoli*, is a case in which an appellate court appears to approve of toxic tort causation testimony based on uncertain exposure levels, animal testing and other indicators of possible carcinogenicity, despite the absence of any evidence suggesting a connection between PCB exposure and the plaintiff's specific disease. The court cites the appropriate criteria, including reliability, but neither conducts nor allows the trial court to conduct a reliability analysis. Rather than accepting the trial court's findings, which were based on testimony of other experts, the appellate court interjects its own assessment. In reality, the New Jersey Supreme Court's rationale is based almost entirely on the qualifications of the expert, since it harks back to the witness's qualifications as a point of

295. *Id.* at 747-48.

296. *Id.* at 748. The New Jersey Supreme Court emphasized the need for the court to scrutinize the expert's "status" and to direct the jury's attention to "factors that bear relevantly on the expert's credibility." *Id.* at 750.

297. *Id.* at 747-48.

298. When plaintiff's counsel questioned Dr. Balis on the issue of whether the scientific community accepts PCBs as human carcinogens, Balis replied that the people he contacted would not say "probable," but rather that it was a "high possibility." *Rubanick v. Witco Chem. Corp.*, 542 A.2d 975, 983 (N.J. Super. Ct. Law Div. 1988), *rev'd*, 576 A.2d 4, 14 (N.J. Super. Ct. App. Div. 1990) (discussing Dr. Balis' comment), *modified*, 593 A.2d 733 (N.J. 1991).

299. *Id.* at 983.

300. *Id.*

reference for determining the reliability of the data on which the expert relies as well as his methodology.³⁰¹

The problems of deferential review are not restricted to environmental exposure cases; they also occur in products liability cases where the costs of erroneous findings of liability in terms of withdrawal of useful products and disincentives to new product development are perhaps more apparent. *Ferebee v. Chevron Chemical Co.*,³⁰² perhaps the paradigm decision involving deferential review, involved injuries allegedly caused by a pesticide.³⁰³ Plaintiff's causation case was essentially based on the testimony of treating or examining physicians who claimed to have seen a few similar cases. It therefore illustrates the pitfalls of medical testimony based on the coexistence of exposure and disease.

The Bendectin cases are based on a more complex assemblage of evidence and testimony, consisting of chemical structure-activity analysis, *in vitro* testing, animal studies and purported reanalyses of existing epidemiologic studies.³⁰⁴ A review of one of the early cases decided in favor of plaintiffs, *Oxendine v. Merrell Dow Pharmaceuticals, Inc.*³⁰⁵ reveals much of the same evidence that plaintiffs have argued in other cases alleging birth defects caused by Bendectin. The chemical structure-activity analysis consisted of the observation that one of Bendectin's ingredients is an antihistamine and that some antihistamines are teratogenic.³⁰⁶ The *in vitro* and *in vivo* animal test results cited by plaintiffs' witness Dr. Done are subject to the same concerns for high rates of false positives that were discussed previously. The remaining evidence

301. *Rubanick*, 576 A.2d at 7-8, 14. The New Jersey Supreme Court's opinion in *Landrigan v. Celotex Corp.*, 605 A.2d 1079 (N.J. 1992), appears to have tightened the standard for admission of expert testimony. In regard to the issue of whether epidemiologic studies could provide the basis for an expert's opinion on causation, the court stated that such studies "must have been 'soundly and reliably generated' and be 'of a type reasonably relied on by comparable experts in the particular field.'" *Id.* at 1087 (quoting *Rubanick*, 593 A.2d 733). The court went on to state: The court must also examine the manner in which experts reason from the studies and other information to a conclusion [T]hat conclusion must derive from a sound methodology that is supported by some consensus of experts in the field. *Id.* Nonetheless, the court remanded the case for further proceedings on the issue of whether the plaintiff could satisfy the more-probable-than-not standard of proof despite relative risk data that showed less than a doubling of background risk. *Id.* at 1088.

302. 736 F.2d 1529 (D.C. Cir.), *cert. denied*, 469 U.S. 1062 (1984).

303. *Id.* at 1531-32.

304. See generally *Sanders*, *supra* note 17.

305. 506 A.2d 1100 (D.C. 1986).

306. *Id.* at 1104.

consisted primarily of Dr. Done's unpublished reanalysis of a previous epidemiologic study, which involved selective elimination of data.³⁰⁷

As will be discussed in more detail in Section VI.B.2 of this Article, reanalyses of epidemiologic studies are particularly susceptible to manipulation to achieve a preconceived result. The reanalyses offered by plaintiffs studies stand in contrast to a large body of epidemiologic evidence that has failed to confirm a statistically significant association between Bendectin and birth defects. Further, the fact that the studies offered by plaintiffs have been unpublished and therefore not subjected to peer review,³⁰⁸ lends further support to other courts' decisions to exclude them.³⁰⁹

B. Active Review Exemplified

In contrast to the deferential, uncritical review accorded expert testimony in *Paoli*, *Rubarick* and *Oxendine*, there are a growing number of decisions that utilize active review to make discerning judgments about scientific evidence. Judge Weinstein has been widely criticized for his exclusion of plaintiffs' evidence in the Agent Orange "opt out" cases,³¹⁰ but basically, he got it right. Plaintiffs claimed a wide variety of commonplace ailments, cancers and birth defects as injuries due to Agent Orange or more specifically, the contaminant dioxin.³¹¹ Their evidence consisted of animal studies, and workplace exposure studies that apparently did not indicate an association of dioxin or Agent Orange exposure with the diseases complained of.³¹² There was simply no evidence from which a fact-finder could conclude that any of the plaintiffs suffered from conditions attributable to Agent Orange rather than the causes of such disease in the general population, a fact recognized by the court.³¹³ That conclusion is valid even without taking into account the many studies of

307. See *id.* at 1107-08; see also *DeLuca v. Merrell Dow Pharmaceuticals, Inc.*, 911 F.2d 941, 946-49, 954-57 (3d Cir. 1990) (discussing the failure of Done's reanalysis of other studies to meet traditional statistical significance criteria).

308. See, e.g., *Daubert v. Merrell Dow Pharmaceuticals*, 951 F.2d 1128 (9th Cir. 1991), *cert. granted*, 113 S. Ct. 320 (1992); *Lynch v. Merrell-Nat'l Lab.*, 830 F.2d 1190, 1194-96 (1st Cir. 1987) (discussing reanalyses by Dr. Done and Dr. Shanna Swan).

309. At least one published reanalysis of epidemiologic data has found no association between Bendectin and birth defects. See *infra* notes 373-76 and accompanying text.

310. See, e.g., *Brennan*, *supra* note 25, at 9 n.40, 53-56; *Green*, *supra* note 65.

311. See *Green*, *supra* note 65, at 659.

312. See *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223, 1236 (E.D.N.Y. 1985) (liver disorders in animal and industrial studies differed from those reported by plaintiffs), *aff'd*, 818 F.2d 187 (2d Cir. 1987), *cert. denied*, 487 U.S. 1234 (1988).

313. *Id.* at 1239.

Vietnam veterans put before the court that failed to show any increased incidence of serious disease.³¹⁴

The Bendectin litigation has also produced opinions that discerningly review scientific evidence; two such cases are *Brock v. Merrell Dow Pharmaceuticals, Inc.*³¹⁵ and *Lynch v. Merrell-National Laboratories*.³¹⁶ Bendectin has been the subject of over 2000 suits for birth defects allegedly caused by in utero exposure to the anti-nausea drug. Plaintiffs have sought recovery for a variety of malformations, but a number of the cases have involved limb reduction defects.³¹⁷ In *Brock*, the court based its reversal of a jury verdict for plaintiffs on the absence of any statistically significant epidemiologic evidence of an association between Bendectin and birth defects.³¹⁸ Both the *Brock* and the *Lynch* courts concluded that the plaintiffs' *in vitro* testing and animal studies evidence was insufficient, the *Lynch* court noting particularly the inability of *in vivo* and *in vitro* animal studies to prove causation in humans "in the absence of confirmatory epidemiologic data," which it contrasted with a number of studies that failed to find an association between Bendectin and birth defects.³¹⁹

In what has become one of the more controversial aspects of the Bendectin litigation, both courts rejected reanalyses of existing epidemiological studies that purported to show an association between Bendectin exposure and birth defects. The *Lynch* court noted the plaintiffs' failure to file any description of the expected testimony of Dr. Shanna Swan, whose reanalysis of epidemiologic data was offered by plaintiffs. The court went on to examine the basis of Swan's opinion from testimony in other litigation, observing that Swan's control group consisted of children with genetic birth defects, a group that had a lower than background risk for certain types of birth defects, raising the

314. More recent information concerning the hazards of dioxin does not significantly change the analysis. New data on chemical workers exposed to dioxin for more than a year, with more than twenty years' latency, has indicated a 46% increase in all cancers (although not any individual cancer). David J. Hanson, *supra* note 158, at 7, 10. According to Marilyn Fingerhut, the author of the study, the serum levels of dioxin correlated well with duration of exposure. *Id.* at 10. The Fingerhut study is consistent, however, with the Ranch Hand study of Vietnam veterans, which has not detected an increase in cancer at the lower exposure levels experienced by veterans, *id.* at 9, although it has recently revealed significant increases in body fat and diabetes that correlated with dioxin concentration, *id.* at 9. This information does not appear to provide a basis for distinguishing background causes from dioxin for most of the ailments claimed to result from dioxin in the Agent Orange litigation.

315. 874 F.2d 307 (5th Cir.), *modified*, 884 F.2d 166 (5th Cir. 1989), *cert. denied*, 494 U.S. 1046 (1990).

316. 830 F.2d 1190 (1st Cir. 1987).

317. *See Sanders, supra* note 17, at 398-99.

318. *See Brock*, 874 F.2d at 314-15.

319. *Lynch*, 830 F.2d at 1194.

question whether genetic defects might make that control group less susceptible to non-genetic defects such as limb reduction. A lower susceptibility in the control group would skew the relative risk observed for the Bendectin-exposed group.³²⁰

In contrast, the *Brock* court's rationale focused on the fact that the elevated risk found in the reanalysis conducted by Dr. Jay Glasser lacked statistical significance.³²¹ As will be discussed in more detail in the following Section, reanalyses of epidemiological data are susceptible to advertent and inadvertent introduction of bias. Although the statistical significance point is arguable, the reanalyses were unpublished and therefore lacked the safeguards against biased or result-oriented data selection that peer-reviewed publication would have provided.

VI. ACTIVE REVIEW: THE ANTIDOTE FOR JUNK SCIENCE

As the foregoing Sections have demonstrated, active review of scientific evidence and expert testimony can go far to eliminate the arbitrary and unfair results that can result from the acceptance of junk science in toxic torts cases. Courts nonetheless cite a number of reasons for deferential review of scientific evidence, including the lack of any special expertise and, perhaps more significantly, the belief that traditional tort law, with its typical reliance on established science, is inadequate to redress toxic injuries of the industrial age. Those reasons, however, do not stand up to careful examination.

A. Courts' Ability to Review Scientific Evidence

As noted previously, one of the concerns regarding scrutiny of scientific evidence is the belief that courts lack the ability to understand scientific evidence and therefore should not deprive the jury of the opportunity to consider possibly relevant and probative evidence. It should be evident from the foregoing discussion, however, that courts are quite capable of determining whether there is a reasoned basis, grounded in fact, for expert opinion, as well as a level of reliability consistent with the applicable standard of proof.

The Third Circuit and the New Jersey Supreme Court, who authored the *Paoli* and *Rubanick* decisions respectively, have demonstrated their understanding of complex scientific evidence. In *DeLuca v.*

320. *Id.* The court also addressed a reanalysis of epidemiologic studies by Dr. Alan Done. Neither the Swan nor the Done study had been published. The court also questioned the bases for exclusion of certain data in each. *Id.* at 1194-96.

321. The Glasser study yielded a relative risk of 1.49, with a confidence interval of 0.17 to 3.0. *Brock*, 874 F.2d at 312. Because the confidence interval included the value 1.0, which represents no increased risk, the result did not satisfy statistical significance criteria. *See infra* notes 367-82 and accompanying text (discussing statistical significance).

Merrell Dow Pharmaceuticals, Inc.,³²² the Third Circuit discussed the epidemiologic evidence on Bendectin and birth defects. At issue was the admissibility of a meta-analysis of existing epidemiologic studies. The meta-analysis in question³²³ did not meet the level of statistical significance³²⁴ typically required for epidemiologic studies.³²⁵ The court's view of the meta-analysis was overly generous,³²⁶ but the opinion demonstrates the court's understanding of the concepts of statistical significance and the effects of bias in epidemiologic studies.³²⁷ Similarly, when confronted with a causation issue on which epidemiologic evidence was offered, the New Jersey Supreme Court also evidenced a sophisticated understanding of such evidence. In *Landrigan v. Celotex Corp.*,³²⁸ the court discussed the proffered epidemiologic evidence and the causal inferences to be drawn from it, as well as the concept of attributable risk.³²⁹

322. 911 F.2d 941 (3rd Cir. 1990).

323. One issue concerning admissibility is publication of studies; one meta-analysis of Bendectin epidemiologic studies has been published, unlike the study offered in *DeLuca* by Dr. Alan Done. See Thomas R. Einarson et al., *A Method for Meta-Analysis of Epidemiological Studies*, 22 DRUG INTELLIGENCE & CLINICAL PHARMACY 813 (1988); Sanders, *supra* note 17, at 341 n.182.

324. See *DeLuca*, 911 F.2d at 946-48.

325. *Id.* at 955-56.

326. On remand, the district court once again dismissed the plaintiffs' case on summary judgment. See *DeLuca v. Merrell Dow Pharmaceuticals, Inc.*, 791 F. Supp. 1042 (D.N.J. 1992). The court excluded Dr. Alan Done's reanalysis of epidemiologic studies, finding that Done's calculations and presentation of his results contained numerous errors and his methodology could not be discerned or replicated by the other experts of either plaintiffs or defendants. *Id.* at 1047-48. Plaintiffs' other expert was Dr. Shanna Swan, who has also appeared in other Bendectin cases, including *Daubert v. Merrell Dow Pharmaceuticals, Inc.* In *DeLuca* on remand, she apparently commented on the Done reanalysis based on Done's representations of how it was performed. *Id.* at 1047.

327. The Third Circuit reversed the trial court's summary judgment for defendants and directed the trial court to evaluate the reliability of the proffered evidence "with an eye to all the risks of error posed" by it. *DeLuca*, 911 F.2d at 955. The court further stated, "The root issue . . . is what risk of what type of error the judicial system is willing to tolerate." *Id.* The court suggested that additional expert testimony on statistical significance would be helpful, but also stated a preference for admitting evidence with probative value and "dealing with the risk of error through the adversary process." *Id.* at 956. The ultimate issue, however, is whether that evidence would be sufficient to support a jury finding that Bendectin "more likely than not caused the [plaintiff's] birth defects." *Id.* at 958. The court characterized that requirement as requiring a relative risk greater than two in the exposed population. *Id.*

328. 605 A.2d 1079 (N.J. 1992).

329. *Id.* at 1085-88. The *Landrigan* court, however, refused to hold that a relative risk of 2.0 or greater is required to prove that individual causation was more probable than not. *Id.* at 1087. The court's assumption appears to have been that by ruling out other causes, plaintiff's expert could opine that causation of plaintiff's disease was more probable than not, a proposition that depends on how well developed the evidence is on other risk factors and the relationships among them. *Id.*

No doubt there are times when expert witness testimony and scientific evidence are obscure. The details of statistical significance calculations could undoubtedly lose all but the most mathematically inclined and dedicated lay observer. But judges need not examine expert testimony and scientific evidence at that level of detail. Courts can and should, however, require the proponent of such evidence to demonstrate to the court that the evidence is valid and reliable, that is, that it makes sense and is sufficiently likely to produce an accurate result.

B. Overcompensating for the Deficiencies and Inequities of the Tort System

Another reason courts cite for lenient review of expert testimony is perceived inequities and deficiencies of the tort system. The Sections below examine several aspects of the perception and show that there, too, the cited reasons do not justify the remedy.

1. THE BELIEF THAT MOST CANCERS AND BIRTH DEFECTS ARE CAUSED BY TOXIC PRODUCTS AND ENVIRONMENTAL POLLUTANTS.

Rubanick and *Paoli* illustrate the perception that many, if not most, cancers and birth defects are caused by toxic substances introduced into the environment in products or as waste injuries that they believe will go uncompensated if traditional evidentiary standards are applied. The New Jersey Supreme Court's opinion in *Rubanick* states that concern explicitly:

There are undeniable indications that persons do in fact suffer grave and lethal injury as a result of the wrongful or tortious exposure to toxic substances. Those indications do not spring simply from conjecture; they conform to our common experience and informed intuition. Judge Petrella noted in his opinion below that "[i]t has been widely considered that PCBs are a carcinogenic substance." Our common sense, with some empirical support, tells us of the deleterious effects of PCBs.³³⁰

The Third Circuit expressed similar beliefs in *Paoli*.³³¹ Those perceptions appear to be based on widely quoted statements that most

330. *Rubanick v. Witco Chem. Corp.*, 593 A.2d 733, 747 (N.J. 1991) (citations omitted).

331. In addressing whether Pennsylvania would recognize a medical monitoring claim, the court noted the need to "accommodate a society with an increasing awareness of the danger and potential injury caused by the widespread use of toxic substances." *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829, 850 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991). The court went on to note:

The necessity of addressing problems of toxic exposure becomes particularly important with the continued widespread use of chemicals in American industrial and agricultural development. One commentator has pointed out that there are approximately 50,000 hazardous waste sites nationwide. In

cancers are caused by environmental factors.³³² A more careful reading of the sources of such sweeping statements, however, reveals that the

all, over 65,000 chemicals are in commercial use today which have not been tested for their effects on human health or the environment. According to varying estimates, workplace exposure to hazardous substances alone accounts for from five percent to as much as thirty-eight percent of all cancers.

Id. at 850 n.22 (quoting Leslie Gara, Note, *Medical Surveillance Damages: Using Common Sense and the Common Law to Mitigate the Dangers Posed by Environmental Hazards*, 12 HARV. ENVTL. L. REV. 265 (1988)).

332. *See id.* In 1978, David Doniger wrote the following:

From comparisons of different rates of different cancers throughout the world, the World Health Organization and other prominent institutions and individual experts have concluded that 60 to 90 percent of all human cancers are caused by exposure to chemical substances (and, to a lesser extent, radiation) present in our air, workplaces, food, water, and the rest of our environment.

Doniger, *supra* note 131, at 509.

Doniger was not alone in his concern about chemicals and carcinogenesis. *See id.* and references cited therein. Professor Bruce Ames, the developer of the "Ames" mutagenicity test, expressed similar concerns in a 1979 publication recommending mutagenicity assays as methods for identifying mutagens and carcinogens:

A variety of data supports the hypothesis that environmental factors are a major cause of cancer. Epidemiologic studies show different rates of incidence for certain types of cancer in different parts of the world. For example, in Japan there is an extremely low rate of breast and colon cancer and a high rate of stomach cancer, whereas in the United States the reverse is true. When Japanese immigrate to the United States, within a generation or two they show the high colon and breast cancer rates and low stomach cancer rates characteristic of other Americans. Known environmental mutagens that can cause human cancer include cigarette smoke tar, ultraviolet light, x-rays, and asbestos, and the list of human chemical carcinogens is steadily lengthening.

Ames, *supra* note 29, at 587 (citations omitted). Those concerns were prompted in part by the rapid increase in production and exposure of the workforce and the general public to synthetic chemicals. These concerns were summarized by Ames:

Clearly, many more chemicals will be identified as human mutagens and carcinogens. Currently over 50,000 synthetic chemicals are produced and used in significant quantities and close to 1000 new chemicals are introduced each year. Only a small fraction of these were tested for carcinogenicity or mutagenicity before their use. In the past this problem was largely ignored, and even very high-production chemicals with extensive human exposure were produced for decades before adequate carcinogenicity or mutagenicity tests were performed. Such chemicals now known to be both carcinogenic and mutagenic include vinyl chloride (produced at a rate of about 6 billion pounds per year in the United States in 1977) and 1,2-dichloroethane (ethylene dichloride, about 10 billion pounds per year) and a host of high-production pesticides.

The increase in production and use of chemicals has been particularly great since the mid-1950's This flowering of the chemical age may be followed by genetic birth defects and a significant increase in human cancer during the 1980 decade (because of the 20- to 30-year lag) if many of these

environmental factors encompassed by such statements include commonplace causative factors such as background radiation and probably biological processes such as aging, that are largely beyond human control, as well as cigarette smoking, alcohol consumption and dietary factors such as a high fat diet that are the result of lifestyle, not industrial pollutants.³³³

The fraction of cancers and other diseases that could be prevented by reducing or eliminating exposure to man-made toxic chemicals is still in dispute. Studies that have attempted to estimate the fraction of cancers caused by environmental pollution have placed the figure at about six percent, up to as much as fifteen percent.³³⁴ Other exposures and industrial products are thought to add an additional four to five percent, perhaps as much as ten percent.³³⁵

The debate about the role of synthetic chemicals in cancer causation has occurred against a backdrop of increasing cancer rates.³³⁶ The meaning of the data is unclear, however, because most if not all of the increase can be attributed to increases in smoking-related cancers and

chemicals with wide-spread human exposure are indeed powerful mutagens and carcinogens.

Ames, *supra* note 29, at 587-88.

333. Richard Doll and Richard Peto have noted that the phrase "environmental factors" has been "misinterpreted by many people to mean only 'man-made chemicals,' which was certainly not the intent of the WHO committee." Richard Doll & Richard Peto, *The Causes of Cancer: Quantitative Estimates of Avoidable Risk of Cancer in the United States Today*, 66 J. NAT'L CANCER INST. 1192, 1197 (1981). The Doll and Peto article was commissioned as a report to the Office of Technology Assessment of the U.S. Congress. *Id.* at 1193. For a discussion of various avoidable risks, including those of smoking, alcohol use, diet, and other causes, see *id.* at 1220-56.

334. *Id.* at 1256. The six percent figure is the sum of the percentages attributed to occupation, pollution and industrial products. The 15% figure is the sum of the high end of the ranges estimated for each of those sources, which is likely an overestimate because it is the sum of worst case estimates and because the contribution of risk factors is not necessarily additive. See *supra* notes 209-22. This analysis omits medical sources, which include diagnostic X-rays.

335. Doll & Peto, *supra* note 333, at 1256. These figures contrast markedly with a much-cited report filed with the Occupational Safety and Health Administration, which asserted that up to about 40% of all cancers in the U.S. might be occupationally related. NATIONAL CANCER INSTITUTE ET AL., ESTIMATES OF THE FRACTION OF CANCER IN THE UNITED STATES RELATED TO OCCUPATIONAL FACTORS 1 (1978). Doll and Peto point out errors in the methodology of the OSHA report, however, which they believe resulted in overestimation of the proportion of cancers attributable to occupational exposures. Doll & Peto, *supra* note 333, at 1240-41. Causes are not mutually exclusive, however, as the example of asbestos and smoking indicates. See *supra* note 222 and accompanying text. Thus, fractions of total cancer death attributable to various causes could exceed 100%. Doll & Peto, *supra* note 333, at 1219-20. Consequently, attribution of a large fraction of cancers to occupational factors would not necessarily be inconsistent with attributing a similarly large proportion to other factors, such as smoking and alcohol consumption. See ROTHMAN, *supra* note 44, at 14.

336. See, e.g., Earl S. Pollack & John W. Horm, *Trends in Cancer Incidence and Mortality in the United States, 1969-76*, 64 J. NAT'L CANCER INST. 1091 (1980); Smith, *supra* note 33, at 998.

aging of the population.³³⁷ Even if the more pessimistic experts are correct in their conclusion that age adjusted rates are increasing for some cancers,³³⁸ the data do not support the proposition that most cancers are caused by toxic pollution or toxic products (other than cigarettes). Thus, there is no factual basis for a presumption that environmental pollutants cause most cancers.

2. THE BELIEF THAT SCIENCE'S ABILITY TO IDENTIFY CAUSES IS TOO LIMITED.

A second factor, which is related to the belief that toxic substance exposures are causing large amounts of disease, is courts' frustration over the limitations inherent in science's ability to identify causes. Unwilling to accept those limitations, the *Ferebee* court stated:

A cause-effect relationship need not be clearly established by animal or epidemiologic studies before a doctor can testify that, in his opinion, such a relationship exists. As long as the basic methodology employed to reach such a conclusion is sound, such as use of tissue samples, standard tests, and patient examination, products liability law does not preclude recovery until a "statistically significant" number of people have been injured or until science has had the time and resources to complete sophisticated laboratory studies of the chemical. In a courtroom, the test for allowing a plaintiff to recover in a tort suit of this type is not scientific certainty but legal sufficiency; if reasonable jurors *could* conclude from the expert testimony that paraquat more likely than not caused Ferebee's injury, the fact that another jury might reach the opposite conclusion or that science would require more evidence before conclusively considering the causation question resolved is irrelevant.³³⁹

Not surprisingly, *Ferebee* is widely quoted, particularly by courts that are disposed to admit purported scientific evidence without scrutiny of the underlying reasoning.³⁴⁰ Indeed, the premise of *Ferebee*, namely that the law does not in general require statistical evidence of causation, is hardly subject to dispute. *Ferebee* also appeals to fairness by appearing to

337. Cancer death rates for males from lung cancer have increased dramatically since 1930, while death rates from stomach cancer have steadily declined. See Eliot Marshall, *supra* note 33, at 901. Trends for other common cancers in males are less pronounced. There has been considerable debate about the inferences drawn from the data. A number of statisticians and epidemiologists argue that once the data are adjusted for age and the effects of smoking, the overall incidence of cancer is decreasing. See Smith, *supra* note 33, at 998. Other factors that make interpretation difficult are the effects of increased accuracy of diagnosis and disagreement over the significance of increasing cancer rates among the aged. See Marshall, *supra* note 33, at 901-02.

338. See Marshall, *supra* note 33, at 901.

339. *Ferebee v. Chevron Chem. Co.*, 736 F.2d 1529, 1535-36 (D.C. Cir.), cert. denied, 469 U.S. 1062 (1984).

340. See, e.g., *Rubanick v. Witco Chem. Corp.*, 593 A.2d 733 (N.J. 1991).

correct the imbalance that disfavors toxic torts plaintiffs, created by the unavailability, high costs, and insensitivity of epidemiologic studies required to link toxic substance exposures to latent injuries.³⁴¹

The inability of epidemiologic studies to detect small increases in risks has been a major concern in the debate over toxic tort causation evidence.³⁴² The power of an epidemiologic study to identify a small increase in risk is a function of the size of the study groups and the background rate of disease, with larger study groups corresponding to greater statistical power.³⁴³ Meta-analysis, in which the data from a number of smaller studies are combined and reanalyzed, can enhance the likelihood of detecting an effect, if one exists.³⁴⁴ Meta-analysis can also provide the opportunity to refine the selection of data included in the analysis to address potential bias in sample selection, as can reanalysis of a single study.³⁴⁵

Systematic error, of which bias is one form, can be introduced into epidemiologic studies in a number of ways, including the failure to control for causal factors other than the factor under study and the failure to accurately delineate exposed and unexposed populations.³⁴⁶ One of the potential sources of bias in the Bendectin studies is recall bias, the possibility that mothers of children born with defects will be more likely to recall drug use during pregnancy than mothers of normal infants. Such recall bias will tend to result, in some kinds of studies, in an overestimation of the effect of the drug.³⁴⁷ Another concern with inaccurate recall is that the "unexposed" group will, in fact, have some individuals who were exposed and who exhibit effects caused by the exposure.³⁴⁸ If there is an effect, part of that effect will be attributed to the

341. Epidemiologic studies require considerable time and money to conduct, often beyond the means of the toxic tort plaintiff. Further, epidemiologic studies are a crude method for detection of small increases in disease that have long latency periods and significant background risks. See Brennan, *supra* note 25, at 54; Doll & Peto, *supra* note 333, at 1219; see also Ames, *supra* note 29, at 587 (advocating the use of short-term assays to identify mutagens and carcinogens). Further, epidemiologic studies are often designed to detect a relative risk of two or more. See M.J. Adams Jr. et al., *The Use of Attributable Fraction in the Design and Interpretation of Epidemiologic Studies*, 42 J. CLINICAL EPIDEMIOLOGY 659, 659 (1989).

342. Green and Brennan have argued that such insensitivity requires that plaintiffs be allowed to resort to other kinds of toxicological evidence to prove their cases. See Brennan, *supra* note 25, at 56; Green, *supra* note 65, at 680-81.

343. See ROTHMAN, *supra* note 44, at 79-80. Power is "the probability of detecting (as 'statistically significant') a postulated level of effect." *Id.* at 79.

344. See Naylor, *supra* note 277, at 892.

345. Both meta-analyses and reanalyses of existing studies have been at issue in the Bendectin litigation. See *supra* notes 65-70 and accompanying text.

346. See ROTHMAN, *supra* note 44, at 82-94.

347. *Id.* at 85. This possibility applies to case control studies. *Id.*

348. See *id.* at 85-87.

unexposed group, tending to diminish the magnitude of the observed effect.³⁴⁹

To counter the negative epidemiologic evidence that predominates in the published literature concerning Bendectin, several plaintiffs have variously offered meta-analyses or reanalyses by one or both of two expert witnesses, Dr. Alan Done, a professor of pediatrics and pharmacology, and Dr. Shanna Helen Swan, an epidemiologist and chief of the a unit of the California Department of Health Services.³⁵⁰ Meta-analyses are subject to questions about the propriety of combining data from studies in which the original criteria for selection of subjects and controls differed.³⁵¹ Both meta-analyses and reanalyses involve selection of data for inclusion and exclusion, which create the opportunity for "data dredging" that may turn up statistically significant correlations that are actually due to chance.³⁵² The methodology by which data were selected for inclusion and exclusion in meta-analyses and reanalyses should therefore be carefully scrutinized.

A number of objections can be made to the reanalyses and meta-analyses offered by various Bendectin plaintiffs. In the case of Dr. Done's reanalysis at issue in *Lynch*, the basis of the data selection seems less than clear,³⁵³ although the *Oxendine* opinion indicates that in the reanalysis offered by Done in that case, some pairs of exposed and unexposed children were eliminated because Done considered the risk of recall bias to be especially high among Canadian subjects who could have purchased Bendectin without a prescription.³⁵⁴ Dr. Shanna Swan's methodology is explained more completely in *Lynch*; it involved the reanalysis of data previously analyzed by four members of the Center for Disease Control.³⁵⁵ All of the subjects in the original group had involved abnormal children. Swan reanalyzed the data, using only children with genetic abnormalities as the control group so that the control group's abnormalities could not have resulted from Bendectin.³⁵⁶ Her reanalysis

349. *See id.*

350. *See Lynch v. Merrell-Nat'l Lab.*, 830 F.2d 1190, 1194-95 (1st Cir. 1987). In *Brock v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307 (5th Cir.), *modified*, 884 F.2d 166 (5th Cir. 1989), *cert. denied*, 494 U.S. 1046 (1990), plaintiffs offered a reanalysis by Dr. Jay Glasser. *Id.* at 312.; *see supra* note 321 and accompanying text.

351. *See Naylor, supra* note 277, at 893. Although Naylor is discussing the aggregation of data from clinical trials rather than retrospective exposure cases, the argument still applies.

352. *See id.*, at 894.

353. *Lynch*, 830 F.2d at 1196.

354. *Oxendine v. Merrell Dow Pharmaceuticals, Inc.*, 506 A.2d 1100, 1107-08 (D.C. 1986).

355. *See Lynch*, 830 F.2d at 1195; *see also* Eliot Marshall, *Supreme Court to Weigh Science*, 259 SCIENCE 588, 590 (1993).

356. *Lynch*, 830 F.2d at 1195.

concluded that Bendectin is associated with an increased risk of birth defects. Swan's reanalysis raises questions because the control group for her reanalysis was acknowledged to have only a 0.57 relative rate (i.e., a 40% lower rate) for certain categories of birth defects. As the First Circuit noted, "Swan made no allowance for the possibility that the very fact of having such a severe genetic deficiency as Down's Syndrome might operate to make other rare deficiencies such as limb reduction less likely," thus skewing the apparent differences between the exposed and control groups.³⁵⁷ The possibility that both Done's and Swan's reanalyses were based on result oriented "data dredging" or other inadvertent introduction of bias cannot be ignored; further, none of the reanalyses or meta-analyses has been published in peer-reviewed scientific journals, although ample time has elapsed for review and publication.³⁵⁸ The failure of either to publish their results leaves courts without any reassurance that concerns about bias are unwarranted.

In any event, the insensitivity of epidemiologic studies in the case of Bendectin is probably an overrated concern. Although the studies cannot be said to eliminate all possibility that Bendectin is teratogenic, they at least indicate that if Bendectin is a teratogen, it is a weak one.³⁵⁹ Moreover, the insensitivity of epidemiologic studies does not improve the probative value of other evidence. Animal studies, mutagenicity testing and structure-activity relationships do not become more persuasive because of the absence of other kinds of proof.

3. THE BELIEF THAT SCIENTISTS REQUIRE TOO MUCH CERTAINTY.

A third argument courts cite for abandoning scientific criteria for proof of causation is the perception that scientists require too great a degree of certainty before they will accept a factual proposition as established. *Rubanick v. Witco Chemical Corp.*³⁶⁰ makes numerous references to the high level of proof required by scientists³⁶¹ and concludes that "the scientific method . . . fails to address or accommodate the needs and goals of the tort system."³⁶² That scientists may require a higher level of certainty than the legal system may in some instances be true. In part, the mismatch between expert testimony and legal requirements is the result of the failure of lawyers and courts to articulate legal requirements

357. *Id.*

358. A meta-analysis offered by Dr. Done in another case also failed to satisfy statistical significance criteria. See *DeLuca v. Merrell Dow Pharmaceuticals, Inc.*, 911 F.2d 941, 954-57 (3d Cir. 1990); *Lynch*, 830 F.2d at 1195-96.

359. See *Sanders*, *supra* note 17, at 348.

360. 593 A.2d 733 (N.J. 1991).

361. See *id.* at 737, 739-41.

362. *Id.* at 741.

of proof to scientists. Unless the examining attorneys explore what a scientist-expert witness means by "proof," the risk that the expert understands such terms differently from their legal meaning will always exist.³⁶³

The appropriate level of certainty is particularly an issue when epidemiologic evidence that does not meet epidemiologists' criteria for certainty is offered. Epidemiologists typically are unwilling to conclude that increased disease incidence in an exposed population is associated with a toxic substance exposure unless a statistical analysis of the data shows that the probability of a false positive is 5% or less.³⁶⁴ That requirement represents a 95% confidence level,³⁶⁵ a level that is considerably higher than the more probable than not standard would seem to suggest.³⁶⁶ Moreover, the 5% cutoff for statistical significance is

363. In *Rubanick*, it was clear that the plaintiffs' expert was discussing possibilities and was unable to state that it was more probable than not that PCBs caused the decedents' colon cancers. *Rubanick v. Witco Chem. Corp.*, 576 A.2d 4, 14-15 (N.J. Super. Ct. App. Div. 1990), *modified*, 593 A.2d 733 (N.J. 1991); *see supra* note 305 and accompanying text. The mismatch is also due to mechanical application of the *Frye* rule. When the *Frye* general acceptance test is applied to an expert's opinion on whether a toxic substance can cause a particular disease, the test incorporates scientists', rather than the legal system's, standards of proof.

364. *See supra* note 103 and accompanying text.

365. The statistical analysis sometimes focuses on the calculation of a "*p*-value," which represents the probability that the relative risk produced by the study is due to random variability or chance. *See* ROTHMAN, *supra* note 44, at 115-19. Often, an upper limit for the *p*-value is selected as $p = 0.05$; if the *p*-value of the study falls at or below the cutoff, the results of the study are said to be "statistically significant." A *p*-value of 0.05 corresponds to a five percent chance that an increase in relative risk is actually a false positive, described as a type I error or alpha-error. *Id.* Alternatively, the statistical analysis may be used to generate confidence intervals, that is, ranges of relative risk that are associated with a specified level of confidence. A 95% confidence interval is the range in which the relative risk would be expected to fall 95% of the time if the study were repeated (hence, a 95% confidence level). *Id.* at 119-20. The confidence level is equal to one minus the probability of type I error; thus, a 95% confidence level corresponds to a statistical significance cutoff value of *p* equal to 0.05. *See id.* at 119. In *Brock v. Merrell Dow Pharmaceuticals Inc.*, 874 F.2d 307 (5th Cir.), *modified*, 884 F.2d 166 (5th Cir. 1989), *cert. denied*, 494 U.S. 1046 (1990), the court discussed epidemiologic data for which the statistical analysis was expressed in terms of confidence intervals. *See id.* at 312. The court recognized that where a confidence interval includes a relative risk of 1.0 (which represents no effect from the exposure), the study could not be said to demonstrate a statistically significant increased risk of limb defects associated with exposure. *Id.* at 312-13. Confidence intervals are usually calculated for a predetermined confidence level, usually 90% to 95% but occasionally lower. ROTHMAN, *supra* note 44, at 119.

366. This issue was explicitly raised in *DeLuca v. Merrell Dow Pharmaceuticals, Inc.*, 911 F.2d 941 (3d Cir. 1990), in which the plaintiffs sought to present Dr. Done's reanalysis of epidemiologic data as evidence of an increased relative risk associated with *in vitro* Bendectin exposure. Dr. Done's reanalysis did not satisfy statistical significance criteria. *Id.* at 955.

arbitrary, and has been used to meet epidemiologists' perceived needs for certainty.³⁶⁷

Some commentators have questioned whether statistical significance is relevant to the more probable than not standard of proof.³⁶⁸ Green suggests that focus on the relative risk found in a study is more appropriate.³⁶⁹ That approach seems untenable, however, because it fails to distinguish the issue of whether exposure to the toxic substance causes any effect at all, which is the function of statistical significance testing, from the issue of the likelihood that a particular plaintiff's case resulted from the exposure rather than background or other causes, a conclusion that is inferred from the magnitude of the relative risk.

Relative risk greater than 1.0 in an exposed population is sufficient evidence of an association of disease with exposure only if we can be reasonably certain that the unequal distribution of disease in exposed and unexposed populations is not due to chance. Ignoring the possibility that an increased incidence of disease is due to chance leads to the obviously absurd result that a disease cluster, no matter how small, could be argued as sufficient evidence of an association between an exposure and disease, a result that is indefensible. The evaluation of the role of chance in an epidemiologic study is thus an essential part of determining the probative value of the evidence.

The appropriate confidence level is a more difficult question, however. At a minimum, the more probable than not standard of proof would seem to tolerate epidemiologic data on the issue of general causation if there is less than a 50% probability that the result is due to chance, a confidence level far lower than the 95% level typically employed by epidemiologists. Additionally, Green and others have noted that typical statistical significance testing is concerned only with the risk of false positives, that is, the risk that an effect will be inferred when there is actually no effect.³⁷⁰ The legal system is also concerned, however, with the risk of false negatives, namely, in toxic torts the risk

367. ROTHMAN, *supra* note 44, at 118-19. The use of $p = 0.05$ lessens the possibility that an effect will be assumed when, in fact, there is no association between exposure and disease incidence. The use of low p -values, however, increases the probability that no association will be assumed when, in fact, there is an association. *Id.* The considerations that have led epidemiologists to require 95% confidence interval as a cut-off for statistical significance are not necessarily appropriate for tort law. Commentators have been unable to agree on appropriate alternatives, however.

368. See Green, *supra* note 65, at 682, 687; David H. Kaye, *Is Proof of Statistical Significance Relevant?*, 61 WASH. L. REV. 1333, 1334 (1986) (decrying the mechanical application of statistical significance criteria without explanation and suggesting confidence interval testing as more useful).

369. See Green, *supra* note 65, at 647.

370. See *id.* at 683.

that no effect will be detected when there actually is an effect.³⁷¹ Decreasing the risk of false positives tends to increase the risk of false negatives, though not in a straightforward way.³⁷² Thus, there is an argument that in some instances, epidemiological studies should be admitted with less stringent significance criteria than are typically applied. Before such a rule, which significantly lowers the standard of acceptability of epidemiologic evidence of increased risk, is adopted, however, it would be well to consider other sources of error. Epidemiologic studies are plagued to a greater or lesser degree with other, nonrandom sources of error. Exposure data can be highly uncertain. There is always the possibility that there are unknown confounding causes that are not randomly distributed between the exposed and control populations. Although statistical testing usually does not address nonrandom error, the possibility of other confounding factors may have a great deal to do with the high confidence levels that epidemiology has typically required to minimize the risk of error due to chance.

It may be instructive to consider Bendectin because it has been the subject of over thirty epidemiologic studies and at least one published meta-analysis of those studies.³⁷³ If statistical significance criteria are indeed too stringent, causing scientists to miss a real effect, one would expect to see relative risks from the various studies falling above 1.0 more often than below that number. In other words, the results should vary around the "true" relative risk even if no single study qualifies as statistically significant.³⁷⁴ In his comprehensive study of the Bendectin litigation, Sanders notes that of twenty-six studies from which he was able to extract a value indicative of relative risk, thirteen reported a value greater than one, twelve reported values less than one, and one study reported a value of exactly one.³⁷⁵ That result is roughly consistent with a published meta-analysis of seventeen prior studies that concluded that

371. David Kaye has analyzed the preponderance of the evidence rule as having the effect of minimizing erroneous verdicts. See David H. Kaye, *The Limits of the Preponderance of the Evidence Standard: Justifiably Naked Statistical Evidence and Multiple Causation*, 1982 AM. B. FOUND. RES. J. 487, 496-503. In the statistical analysis of epidemiologic studies, the assumption that there is no effect where there is, in fact, an effect (i.e., a false negative) is referred to as type II or beta-error. ROTHMAN, *supra* note 44, at 117-18.

372. See ROTHMAN, *supra* note 44, at 117-18.

373. See Sanders, *supra* note 17, at 341 n.182.

374. This is a commonsense application of the rationale behind the meta-analysis of existing studies, in which smaller studies are combined to obtain larger sample and control populations. Meta-analysis runs the risk of comparing populations that differ in nonrandom ways, however, and thus some caution is warranted in drawing conclusions in the casual manner suggested in the text. See also ROTHMAN, *supra* note 44, at 334-36 (discussing trend estimation based on differing exposure levels even where individual studies do not satisfy statistical significance criteria).

375. Sanders, *supra* note 17, at 340-41.

Bendectin is not associated with human birth defects.³⁷⁶ If statistical significance criteria were lowered to a 50% confidence level, one is left to wonder whether both plaintiffs and defendants would be offering "statistically significant" evidence, respectively, that Bendectin causes and prevents birth defects. Thus, it is not clear without further evaluation that scientific confidence level criteria are too stringent where epidemiologic evidence is concerned.

A more basic concern with courts' perceptions that scientists require too much certainty is that such views seem to form the basis for rejection of scientific reasoning altogether. The problem with *Ferebee* and its progeny is that they fail to recognize that in most cases,³⁷⁷ there are no alternative proofs available that amount to anything more than speculation or estimation with a great deal of uncertainty.³⁷⁸ Courts' unwillingness to scrutinize testimony on disease causation leaves the door open to the self-validating experts who can be found to testify to virtually any proposition.³⁷⁹ Even the courts that have deemed such evidence admissible have recognized the hazards of their approach.³⁸⁰ Nonetheless, they are willing to risk that kind of error because scientific evidence is unavailable to satisfy traditional standards of proof.³⁸¹ The irony of that rationale is that it rests on courts' and commentators' acceptance and even distortion of scientific speculation that widespread dissemination of new chemicals might result in increases in cancer, birth defects and other disease. Having accepted scientific speculation, they then reject the cautionary statements of scientists who want greater certainty before they reach conclusions.

C. The Costs of Overcompensation

The position taken herein runs counter to the views of several recent commentators. Troyan Brennan has urged courts to admit and consider all the kinds of evidence that toxicologists bring to bear on the question of whether a substance causes disease, including animal studies, short term

376. See *id.* at 341 & n.182.

377. See *supra* note 57 and accompanying text.

378. See *supra* notes 64-67 and accompanying text (discussing structure-activity relationships, short-term testing, and animal studies).

379. See *In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223, 1242 (E.D.N.Y. 1985), *aff'd*, 818 F.2d 187 (2d Cir. 1987), *cert. denied*, 487 S. Ct. 1234 (1988).

380. See, e.g., *Rubanick v. Witco Chem. Corp.*, 593 A.2d 733, 744 (N.J. 1991) ("There are, assuredly, genuine concerns engendered by a test of reliability of complex scientific theories of causation that does not fully embrace the views of a dominant or of a significant segment of the scientific community.").

381. See, e.g., *id.* at 745 (other courts' demands for "near-scientific certainty are unrealistic" because the level of scientific proof is unavailable).

assays and structure-activity relationships.³⁸² Michael Green goes even further, urging courts to approve of all of the foregoing and even individual case reports as a sufficient evidentiary basis for plaintiffs' verdicts.³⁸³ Moreover, those commentators do not significantly disagree with this author about the uncertainty inherent in those kinds of evidence.³⁸⁴ They do, however, differ on the conclusions reached in the face of those uncertainties.

Brennan's primary suggestion is to propose that questions involving significant scientific uncertainty be resolved by referring those questions to court-appointed experts or science panels.³⁸⁵ There are obviously cases, however, that are not significant enough to warrant science panels, or perhaps even court-appointed experts. Moreover, Brennan does not really come to grips with how evidence with such uncertain probative value can satisfy the more probable than not standard of proof, whether reviewed by a science panel or a lay jury. He recognizes that the acceptance of evidence associated with a high degree of uncertainty is a policy question, but does not provide a rationale for such a radical change in policy.³⁸⁶

Green, on the other hand, recognizes that difficulty. His solution is equally troubling: He states that "plaintiffs should be required to prove causation by a preponderance of the *available evidence*."³⁸⁷ This proposal is at least directly addresses the problem with animal studies and other, even more uncertain kinds of proof. The problem that Green's and Brennan's proposals present, however, is that they create potentially unlimited and ultimately arbitrary liability for cancer, birth defects, and other diseases that lack definitive causal explanations. Rare will be the cancer victim who cannot find some arguably toxic exposure, whether it be the pesticide application on the neighbor's lawn, pumping her own gas at the gas station or other such cause. Rarer still will be the plaintiff who cannot find a treating physician or other expert who is willing to state that based on past experience and review of the literature, that a particular toxic substance exposure is consistent with the plaintiff's disease and that the plaintiff lacked other predisposing factors. Reliance on the available evidence when such evidence suggests only the

382. See Brennan, *supra* note 25, at 21-26.

383. See Green, *supra* note 65, at 646, 674-75.

384. See Brennan, *supra* note 25, at 21-26 (discussing the kinds of uncertainty associated with animal tests, short term assays, and epidemiologic evidence); Green, *supra* note 65, at 680-81 (discussing animal testing, *in vitro* testing, short-term assays, structure-activity analysis, and case studies).

385. See Brennan, *supra* note 25, at 62-71. He suggests that science panels and lists of potential experts be coordinated under a federal science board.

386. See Brennan, *supra* note 15, at 523-32.

387. Green, *supra* note 65, at 680 (emphasis added).

possibility, not the probability, of causation suggests that plaintiffs would do well to proceed to court when the evidence on whether a substance can cause disease is in an unformed stage. Such plaintiffs apparently will not have to contend with the messy questions of distinguishing background risk or other known risks that become issues when epidemiologic evidence is available. Indeed, they would have no basis for making such distinctions.

If there were a way to ease plaintiffs' evidentiary burdens without opening the door to arbitrary and potentially devastating liability for defendants, it would undoubtedly garner considerable support. The zone of uncertainty about the role of toxic chemicals in the causation of many diseases is simply too wide however, to suggest a reasonable way to split the difference.

It must be noted that courts' concerns are not all scientific. Other policy concerns, sometimes unspoken but often implied, seem to underlie courts' willingness to entertain unfounded and poorly reasoned evidence. Those concerns are the indignation and outrage felt by the public in general and plaintiffs in particular over exposure to contaminants or products involving substances suspected of causing harm or whose properties are simply unknown.³⁸⁸ In many of the environmental exposure cases, the exposures or the contamination that could have led to exposure occurred without the plaintiffs' knowledge or consent.³⁸⁹ In the case of potentially toxic products such as breast implants, the exposures have occurred with implicit or explicit assurances that the products were safe.

Traditional tort doctrines, however, do not provide for compensation for egregious conduct without causally related physical injury unless it rises to the level of intentional infliction of emotional distress.³⁹⁰ Commentators have suggested creation of causes of action based on creation of risk,³⁹¹ and a limited number of courts have adopted

388. Studies of risk perception have documented the phenomenon that public acceptance of risk is adversely influenced by the involuntariness of the risk. See Paul Slovic, *Perception of Risk*, 236 SCIENCE 280, 283 (1987).

389. See, e.g., *In re Paoli R.R. Yard PCB Litig.*, 916 F.2d 829, 835 (3d Cir. 1990), cert. denied, 111 S. Ct. 1584 (1991); *Sterling v. Velsicol Chem. Corp.*, 855 F.2d 1188 (6th Cir. 1988); *Renaud v. Martin Marietta Corp.*, 749 F. Supp. 1545 (D. Colo. 1990), *aff'd*, 972 F.2d 304 (10th Cir. 1992).

390. See generally 1 DORE, *supra* note 5, §§ 4.01-.05, 7.01-.08. Recovery based on negligent infliction of emotional distress has been traditionally limited to cases involving physical impact or injury. 1 *id.* § 7.02[2], at 7-3. The limitations of this doctrine have been mitigated somewhat by courts' relaxation and broadening the notion of physical impact to include exposure or subclinical changes. See 1 *id.* at 7-4 to 7-5.

391. See, e.g., Robinson, *Probabilistic Causation*, *supra* note 50, at 783.

such theories.³⁹² Those theories are implicitly and sometimes explicitly premised on assumptions that some significant level of risk can be proved,³⁹³ assumptions that in many cases would be erroneous.³⁹⁴

In any event, the tort system is probably not the best forum for addressing public concerns over uncertain risk. The inability of toxic tort claimants to prove causation has been one of the more important rationales for environmental regulation.³⁹⁵ Indeed regulation is an area in which risk is explicitly recognized as a basis for restricting the dissemination of a substance in products or in the environment. Regulation does not compensate those who are injured despite regulation or by unregulated risks, but it has an important role to play in minimizing risks.

However desirable it might be to have the tort system fill all the gaps where toxic injury occurs, the current state of knowledge simply does not permit the necessary causal connections to be made. Given that state of affairs, what is at stake is whether the "more probable than not" standard of proof will continue to apply to toxic torts. Whether that burden should be lessened or even shifted to defendants are policy issues of the greatest importance. They should be addressed directly and changes, if any, should be based on their fullest consideration of the implications. To effect a reallocation of burdens of proof under the pretext of admitting reliable evidence which is in fact not probative, is not the appropriate way to bring about a change in such a fundamental principle of tort law.

392. The claims have been variously cast as claims for emotional distress, increased risk of future injury, and medical monitoring costs. See generally 1 DORE, *supra* note 5, §§ 7.01-.08.

393. See 1 *id.* § 7.07, at 7-16.5, 7-27.6 (citing cases refusing to recognize claims based on unquantified risk of injury).

394. See *supra* notes 140-79 and accompanying text for a discussion of uncertainty in risk estimation from nonepidemiologic evidence.

395. The breast implant controversy, however it is ultimately resolved, represents a holdover from a period in which medical devices did not require approval by the Food and Drug Administration, a situation that does not apply to new devices.

