

Epidemiological Evidence as a Basis for Causation: Implications for Suspected Pesticide-Induced Cancer

INTRODUCTION

“In protecting health, absolute proof comes too late. To wait is to invite disaster or to prolong suffering unnecessarily.”¹ This ominous sentiment echoes the concern of many consumers who perceive the environment as increasingly dangerous. Fueling that fear is mounting epidemiological² evidence suggesting a strong correlation between pesticide³ exposure and human cancer.⁴ In response, a developing body of law, toxic torts,⁵ has emerged. However, judicial commitment to traditional notions of causation and insistence on statistically significant indicators of causal inference have created a virtual bar to recovery.

The Environmental Protection Agency (EPA)⁶ registers agricultural

¹ William H. Stewart, quoted in U.S. ENVIRONMENTAL PROTECTION AGENCY, OFFICE OF NOISE ABATEMENT AND CONTROL, *NOISE: A HEALTH PROBLEM* 23 (1978).

² Elizabeth A. Stundtner, Comment, *Proving Causation in Toxic Tort Cases: T-Cell Studies As Epidemiological and Particularistic Evidence*, 20 B. C. ENVTL. AFF. L. REV. 335, 345 (1993). Epidemiology is the study of the dispersion of disease occurrence within and among human populations and the determination of the possible causes through the use of statistics.

³ As defined by the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. § 136 (u) (1997), a pesticide is “(1) any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest, (2) any substance or mixture of substances intended for use as a plant regulator, defoliant, or desiccant”

⁴ National Campaign for Pesticide Policy Reform, *Pesticides and Health* (visited Feb. 6, 1997) <<http://www.igc.apc.org:80/ncppr/Health.html>>.

⁵ Barbara Frederick, Note and Comment, *Daubert v. Merrell Dow Pharmaceuticals, Inc.: Method or Madness?*, 27 CONN. L. REV. 237, 240 (1994). Toxic torts refer to “litigation involving harm that allegedly results from exposure to purportedly hazardous substances.”

⁶ Federal agency charged under 7 U.S.C. § 136a(c)(5)(D) (1997) with determining whether the pesticide “when used in accordance with widespread and commonly recognized practice . . . will not generally cause unreasonable adverse effects on the environment.”

pesticides for use based on animal studies.⁷ Prominent researchers in the field of carcinogenesis question the reliability of animal studies as predictors of human carcinogenicity.⁸ Pesticide-exposed plaintiffs seeking damages based on injury due to exposure stand little chance of satisfying foundational judicial requirements absent a showing of scientifically significant epidemiological research linking plaintiff's injury to the alleged toxic pesticide.

Regulatory determination of acceptable cancer risk and heightened judicial scrutiny of scientific evidence operate as formidable barriers between exposed plaintiffs and the chemical industry. Yet, underlying both the regulatory assumptions of acceptable risk and judicial notions of causation are policy decisions from which the public is excluded.⁹ As a result, the public is continually exposed to potentially toxic pesticides with doubtful legal recourse if disease manifests.

The current judicial requirement of scientifically significant degrees of certainty as a matter of law places an unprecedented and unreasonable burden on the pesticide-exposed plaintiff. This comment explores the difficulty plaintiffs alleging injury or death from chronic, low-level exposure to pesticides face in sufficiently proving legal causation. This comment focuses specifically on the use of epidemiological evidence as the preferred scientific evidence. Further, this comment demonstrates how courts, by requiring epidemiological studies to satisfy a high degree of certainty as to causation, require plaintiffs to present more than the traditional preponderance of the evidence¹⁰ to survive judicial controls such as summary judgment, nonsuit and judgment notwithstanding the verdict. Discussion of causation will concentrate

⁷ Merrell Dow Pharmaceuticals, Inc. v. Havner, 907 S.W.2d 535, 554 (Tex. Ct. App. 1995).

⁸ Susan R. Poulter, *Science and Toxic Torts: Is There a Rational Solution to the Problem of Causation?*, 7 HIGH TECH. L. J. 189, 222 (1992). Carcinogenesis denotes the production or origin of cancer. See *STEDMAN'S MEDICAL DICTIONARY* 276 (26th ed. 1995). Carcinogenicity would then refer to the extent to which an agent is carcinogenic, or cancer producing.

⁹ Carl F. Cranor, *Scientific Conventions, Ethics and Legal Institutions*, (visited Jan. 14, 1997) <<http://www.fplc.edu/risk/voll/spring/cranor.htm>>. See W. PAGE KEETON ET AL., *PROSSER AND KEETON ON THE LAW OF TORTS* § 41, at 264 (5th ed. 1984) (discussing proximate cause that the legal limitation on the scope of liability is associated with policy considerations of what justice demands).

¹⁰ Harold Ginsburg, *Use and Misuse of Epidemiologic Data in the Courtroom: Defining the Limits of Inferential and Particularistic Evidence in Mass Tort Litigation*, 12 AM. J. L. & MED. 423, 431 (1986). Preponderance of the evidence or "more likely than not" is a superiority of weight test, requiring that 50.1% of the evidence weigh in favor of the plaintiff in order for him to prevail.

on the scientific confidence level¹¹ as it influences proof of general causation. This comment will not address Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) pre-emption of state tort actions against manufacturers of EPA-registered pesticides based on claims of inadequate labeling or packaging or alleged failure to warn.¹²

I. THE PROBLEM

A. Pervasive Use of Pesticides

Despite decades of heated controversy regarding the uncertain environmental effects of chemical pesticides,¹³ chemical pesticide use proliferates in the United States. The National Resource Defense Council announced that pesticide use reached an unprecedented level in 1995 of more than 1.2 billion pounds of toxic chemicals.¹⁴ Agriculture represents the single largest application of pesticides in the United States, comprising 77% of the 1 billion pounds of pesticides used in the 1980s.¹⁵

Dramatic changes in the pattern of pesticide use have occurred over

¹¹ Troyen A. 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, 23-25 (1989). Confidence-level uncertainty describes the situation where epidemiological evidence is ambiguous, ranging from strong causal associations to none at all.

¹² Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 U.S.C. § 136 (1997) is a comprehensive regulatory statute regulating the labeling, sale, and use of pesticides both in intrastate and interstate commerce. Specifically, section 136v(b) explicitly instructs that states can regulate the sale or use of federally registered pesticides, but precludes "any requirements for labeling or packaging in addition to or different from those required pursuant to this Act." For a comprehensive collection of federal and state cases addressing the question whether federal law pre-empts state common-law products liability claims asserted against manufacturers, distributors, or retailers of pesticides, see Beverly L. Jacklin, Annotation, *Federal Pre-emption of State Common-Law Products Liability Claims Pertaining To Pesticides*, 101 A.L.R. FED. 887 (1997).

¹³ FRANK GRAHAM, JR., SINCE SILENT SPRING 3-20 (1970) (chronicling biologist Rachel Carson's warning of the unrestricted proliferation of chemical pesticides in the environment in her book *Silent Spring*, published in 1962, and the ensuing controversy that continues unabated today).

¹⁴ Natural Resources Defense Council, *Pesticide Use at All-Time High* (visited Jan. 20, 1997) <<http://www.nrdc.org/find/topestup.html>>.

¹⁵ Pesticide Policy and Environmental Justice, GLOBAL PESTICIDE CAMPAIGNER (Pesticide Action Network North America, San Francisco, Cal.), Vol. 4, No. 2, June 1994.

the past twenty-five years.¹⁶ Since 1972, there has been increased use of the less persistent but more acutely toxic organophosphate¹⁷ and N-methyl carbamate¹⁸ insecticides, after the environmentally persistent chlorinated hydrocarbons,¹⁹ such as DDT,²⁰ were banned or restricted.²¹

B. Animal Toxicity Studies as Basis of EPA Pesticide Registration

The EPA relies solely on animal toxicity studies to determine the effects of chemicals²² based on the unproven assumption that animal studies are valid indicators of the effects of low doses on humans.²³

¹⁶ Marion Moses et al., *Environmental Equity and Pesticide Exposure*, 9 TOXICOLOGY AND INDUSTRIAL HEALTH No. 5, 913, 916 (1993).

¹⁷ HOWARD WEINBERG, CAL. DEP'T. OF FOOD AND AGRIC., GLOSSARY OF INTEGRATED PEST MANAGEMENT 50 (1983). Organophosphates are synthetic organic insecticides containing phosphorus, derived from phosphoric acid esters. See also RANDOM HOUSE WEBSTERS COLLEGE DICTIONARY 953 (1st ed. 1995) (Developed as nerve gases, now used as insecticides and fire retardants, organophosphates often cause intense neurotoxic activity); see also STUART M. SPEISER ET AL., THE AMERICAN LAW OF TORTS § 18.432, 1224 (1983) (Organophosphates present serious health hazards because of their high toxicity and ease of absorption by the human body).

¹⁸ WEINBERG, *supra* note 17, at 14. Carbamates are a class of synthetic organic pesticides derived from carbamic acid esters. Carbamates act by deactivating cholinesterase, an enzyme that breaks down acetylcholine to permit normal nerve and muscle function. *Id.* at 16.

¹⁹ WEINBERG, *supra* note 17, at 16. Chlorinated hydrocarbons denote a general category of compounds containing hydrogen, carbon, and chlorine. Characterized by long residual life and broad spectrum, they present a broad range of mammalian toxicity and chemical structure. Some examples of chlorinated hydrocarbons are endrin, DDT, and toxaphene. See also SPEISER ET AL., *supra* note 17, at 1224-25. Chlorinated organic chemicals are some of the most widely used synthetic pesticides known for the highest degree of persistence. The most familiar chlorinated hydrocarbon compound was DDT.

²⁰ WEBSTERS NEW COLLEGIATE DICTIONARY 295 (10th ed. 1993). Dichloro-diphenyl-trichloro-ethane, a colorless, odorless, water-soluble crystalline insecticide that tends to accumulate in ecosystems and has toxic effects on many vertebrates. DDT was formally used as an insecticide. RANDOM HOUSE WEBSTERS COLLEGE DICTIONARY 347 (1st ed. 1995).

²¹ Moses et al., *supra* note 16.

²² Merrell Dow Pharmaceuticals, Inc. v. Havner, 907 S.W.2d 535, 554 (Tex. Ct. App. 1995), *rev'd in part on other grounds*, 40 Tex. Sup. Ct. J. 846 (1997).

²³ Paolo F. Ricci & Louis Anthony Cox, Jr., *Acceptability of Chronic Health Risks*, BNA TOXICS LAW REPORTER, Feb 11, 1987, Vol. 1, No. 35, at 993. See also Gerald W. Boston, *A Mass-Exposure Model of Toxic Causation: the Content of Scientific Proof and The Regulatory Experience*, 18 COLUM. J. ENVTL. L. 181, 223 (1993). "It is the consensus of the scientific and regulatory communities that risk assessments based on animal assay bioassays represent worst case scenarios rather than best estimates of the potential cancer incidence."

Thus, as a general rule, regulators assume that substances that are carcinogenic in animals are also carcinogenic in humans.²⁴ Determining risk of chemical exposure requires an evaluation of both toxicity and length of exposure.²⁵ Dose-response relationships²⁶ quantify the level of exposure sufficient to cause harm and the expected harm for that level of exposure.

Use of animal toxicity studies as a basis for federal regulatory risk assessment has provoked substantial controversy among scientists.²⁷ The major objections relate to the number of extrapolations from animal species to humans required and the uncertainty these extrapolations "introduce into the predictive value of animal testing in proving causation of human disease."²⁸ Though at least one court admitted animal study evidence,²⁹ other courts have found it either inadmissible³⁰ or insufficient.³¹

²⁴ Boston, *supra* note 23, at 223. *But see* Poulter, *supra* note 8, at 220. Cancer is known for long latency periods. Animal testing for cancer, which has long latency periods and for which even low incidence rates are of concern, is conducted under conditions that are very different from the usual human exposure scenario. "Animal studies of carcinogenicity typically utilize doses at or near the maximum level tolerated by the animal. That practice is necessitated by the need to detect effects in relatively small groups of test subjects, in a relatively short period of time Additionally, the route may differ from the likely human exposure route."

²⁵ Boston, *supra* note 23, at 215. Exposure means the opportunity to absorb a chemical substance. *Id.* at 216. Exposure is affected by such variables as the source, proximity, and concentration of the chemical. *Id.* at 217. Toxicity is the state of being poisonous. *STEDMAN'S MEDICAL DICTIONARY* 1826 (26th ed. 1995).

²⁶ Boston, *supra* note 23, at 216.

²⁷ Edward J. Schwartzbauer and Sidney Shindell, Article: *Cancer and the Adjudicative Process: The Interface of Environmental Protection and Toxic Tort Law*, 14 *AM. J. L. & MED.* 1, 9 (1988). *See also* Boston, *supra* note 23, at 228-29. Some scientists argue that epidemiology is the proper tool to identify causes of human cancer and that animal toxicity studies should be used only to determine physiological effects of known carcinogens. Other scientists contend that animal studies are extremely valuable in evaluating risks to humans and may be the most probative of toxicological studies.

²⁸ Poulter, *supra* note 8, at 220. *See also* Schwartzbauer, *supra* note 27, at 9. The major objections to the use of animal studies are: (1) the use of the maximum tolerated dose and (2) the use of high-dose to low-dose extrapolations based upon linear assumptions.

²⁹ *In re Paoli R. R. Yard PCB Litig.*, 916 F.2d 829, 846, 862 (3d Cir. 1990).

³⁰ *See, e.g., In re "Agent Orange" Prod. Liab. Litig.*, 611 F. Supp. 1223, 1240-41 (E.D.N.Y. 1985), *aff'd*, 818 F.2d 187 (2d Cir. 1987).

³¹ *See, e.g., Brock v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307, 314-15 (5th Cir. 1989), *modified*, 884 F.2d 166 (5th Cir. 1989).

C. Adverse Health Effects of Pesticide Exposure

Health-care providers consider adverse health effects of exposure to cholinesterase³² inhibiting pesticides such as organophosphates and carbamates to be a major problem for farm workers in the United States.³³ This pesticide-exposed population is at risk for both acute and chronic health effects.³⁴ Although health effects of chronic or low-level exposures are uncertain,³⁵ long-term pesticide exposure has been implicated in several types of cancer, such as leukemia³⁶ and non-Hodgkins lymphoma.³⁷

Each year more than one-half million people die of cancer and more than 1 million cases are diagnosed.³⁸ Scientists have yet to discover how cancer occurs and why some chemicals are carcinogenic while others are not.³⁹ Pinpointing precise causes of cancer is very difficult because cancer comprises a broad class of diseases, each class of cancer involving different molecular processes and target organs.⁴⁰ Further complicating cancer-causation analysis is individual susceptibility, strongly influenced by such factors as genetics, age, ethnicity, gender, immune function, pre-existing disease and level of nutrition.⁴¹

Pesticides are strongly suspected in development of cancer.⁴² At

³² WEINBERG, *supra* note 18 (defining cholinesterase).

³³ Stephen Ciesielski et al., *Pesticide Exposures, Cholinesterase Depression, and Symptoms Among North Carolina Migrant Farm workers*, 84 AM. J. PUB. HEALTH, 446 (1994).

³⁴ Moses et al., *supra* note 16, at 926. Acute effects occur within minutes or hours of exposure and can range from minor skin rash and eye and upper respiratory irritations to fatal poisoning. Chronic illnesses appear after several years and are associated with repeated exposures to the pesticide.

³⁵ George S. Rust, *Health Status of Migrant Farm workers: A Literature Review and Commentary*, 80 AM. J. PUB. HEALTH 1213, 1215 (1990).

³⁶ Linda M. Brown et al., *Pesticide Exposures and Other Agricultural Risk Factors for Leukemia Among Men in Iowa and Minnesota*, 50 CANCER RESEARCH 6585 (1990).

³⁷ Sheila H. Zahm & Aaron Blair, *Pesticides and Non-Hodgkin's Lymphoma*, 52 CANCER RESEARCH SUPP. 5485s (1992).

³⁸ Frederica P. Perera, *Molecular Epidemiology: Insights Into Cancer Susceptibility, Risk Assessment, and Prevention*, 88 J. NATL. CANCER INST. 496, 497 (1996).

³⁹ Pesticide Management Education Program, Cornell University EXTOKNET Pesticide Information Notebook, *Carcinogenicity*, (last modified Dec. 1, 1995) <<http://www.iet.msu.edu/local/carcinog.htm>>.

⁴⁰ Carl B. Meyer, *The Environmental Fate of Toxic Wastes, the Certainty of Harm, Toxic Torts, and Toxic Regulation*, 19 ENVTL. L. 321, 366 (1988).

⁴¹ Perera, *supra* note 38, at 496.

⁴² James E. Huff & Joseph K. Haseman, *Exposure to certain pesticides may pose real carcinogenic risk*, CHEMICAL & ENGINEERING NEWS (Am. Chem. Soc'y, Wash., D.C.), Jan. 7, 1991, at 33.

least 107 different active ingredients in pesticides have been found to cause cancer in animals or humans.⁴³ Eighty-three of those ingredients are still in use today; seventy-one are used on food crops.⁴⁴ It is no longer debatable that children are at greater physiological risk from pesticides because their major organs are still growing, their respiratory rate is higher, they have more exposed surface area and greater caloric and fluid intake.⁴⁵

D. Emergence of Toxic Tort Litigation and Heightened Scrutiny of Scientific Evidence

Toxic tort litigation has forced judges to address foundational issues of relevancy and sufficiency in evaluating scientific methodology and divergence of scientific theory as to causation of chemical-related injury. The uncertainty surrounding proof of causation in toxic tort litigation directly impacts a plaintiff's chance of surviving summary judgment and a court's perception of scientific certainty.⁴⁶

The heightened standard set forth by the court in *In re Agent Orange Product Liability Litigation*⁴⁷ had a profound effect on the admissibility of expert witness testimony in toxic tort cases.⁴⁸ Amid the controversy over Agent Orange, there arose a similar issue of causation related to the drug Bendectin, prescribed for pregnant women suffering from morning sickness.⁴⁹ More than 2,000 suits were filed against the manufacturer, Merrell Dow Pharmaceuticals, Inc., starting in 1977, alleging that Bendectin caused a wide variety of serious birth defects.⁵⁰

⁴³ National Campaign for Pesticide Policy Reform, Washington, D.C., *Pesticides and Health*, (visited Feb. 2, 1997) <<http://www.igc.apc.org:80/ncppr/Health.html>>.

⁴⁴ *Id.*

⁴⁵ *Id.* See Moses et al., *supra* note 16, at 921.

⁴⁶ Poulter, *supra* note 8, at 211-12.

⁴⁷ *In re Agent Orange Product Liab. Litig.*, 611 F. Supp. 1223, 1261-63 (E.D.N.Y. 1985), *aff'd*, 818 F.2d 187 (2d Cir. 1987). Plaintiffs attempted to prove that exposure to Agent Orange, a defoliant used during the Vietnam War, had caused them adverse health effects. Judge Weinstein granted summary judgment against opt-out plaintiffs on the basis that they had been unable to prove that exposure to low levels of dioxin caused their health problems. The court found the epidemiological evidence insufficient and rejected the proffered animal toxicity studies. *Id.* at 1228, 1241, 1250, 1259.

⁴⁸ Michael D. Green, *Legal Theory: Expert Witnesses and Sufficiency of Evidence in Toxic Substances Litigation: The Legacy of Agent Orange and Bendectin Litigation*, 86 NW. U. L. REV. 643 n.3 (1992) citing PETER H. SCHUCK, *AGENT ORANGE ON TRIAL: MASS TOXIC DISASTERS IN THE COURTS* 234 (1987).

⁴⁹ *Id.* at 661.

⁵⁰ *Id.* at 661 n.82. Birth defects ranged from limb reductions to heart defects and neurological problems.

The courts adjudicating the Bendectin issue not only adopted the *Agent Orange* court's preference for epidemiological evidence as to causation,⁵¹ but created additional evidentiary barriers. Through an extensive review of epidemiological findings regarding Bendectin's teratogenicity,⁵² the courts established a foundational scientific requirement that severely restricts the admissibility of expert witness testimony on causation.⁵³ A number of courts have followed the lead, leaving chemically exposed plaintiffs with no evidence.⁵⁴

II. THE EVIDENCE

Inferring Causation

An undisputed and fundamental scientific principle is that statistics cannot prove causation⁵⁵ because they provide inferential rather than direct evidence. This unavoidable reality poses one of the major obstacles, and often defeats the claims of plaintiffs seeking recovery in toxic tort litigation.⁵⁶ As a precondition for recovery of damages, a plaintiff must prove the substance caused the plaintiff's disease or injury.⁵⁷ Specifically, the exposed plaintiff must prove: (1) the toxic substance is capable of causing the harm complained of; (2) the plaintiff was exposed to the toxic substance in a quantity sufficient to cause disease; and (3) the toxic substance exposure caused the particular plaintiff's injury or disease.⁵⁸

This causal link is particularly onerous in cancer cases due to the potentially long latency period between exposure and disease manifestation, presence of independent risk factors and the fact that cancer occurs in the general population.⁵⁹ Epidemiological studies are one of the most widely used approaches for studying carcinogenicity⁶⁰ and for es-

⁵¹ *In re Agent Orange Product Liab. Litig.*, 611 F. Supp. 1223, 1231 (E.D.N.Y. 1985), *aff'd*, 818 F.2d 187 (2d Cir. 1987).

⁵² STEDMAN'S MEDICAL DICTIONARY 1771 (26th ed. 1995). Teratogenicity refers to the property or capability of producing fetal malformation.

⁵³ Green, *supra* note 48, at 643 n.6.

⁵⁴ *Id.*

⁵⁵ Frederick, *supra* note 5, at 243.

⁵⁶ Jean M. Eggen, Symposium: *Toxic Torts, Causation, and Scientific Evidence After Daubert*, 55 U. PITT. L. REV. 889, 892-93 (1994).

⁵⁷ Poulter, *supra* note 8, at 198.

⁵⁸ *Id.*

⁵⁹ *Id.* at 199-200.

⁶⁰ Edward Christie, *Toxic Tort Disputes: Proof of Causation and the Courts*, 9 ENVTL. & PLAN. J. 302, 303 (1993). Other approaches used are cell assay analysis and small animal studies.

establishing a general causal inference. Medical opinion evidence offers evidence on individual causation through diagnosis, medical history, and the presence or absence of other risk factors.⁶¹

A. Epidemiology as Preferred Probabilistic Evidence

Epidemiological risk analysis is not only recognized as the most probative scientific evidence to establish a cognizable relationship between a substance and the injury claimed,⁶² but has been required as a minimal showing of causal inference in some courts where the cause of the disease has not been definitively proven by other medical opinion evidence.⁶³ Courts vary in the magnitude and statistical significance of epidemiological evidence deemed acceptable.

As an observational science, epidemiology represents the most direct method of evaluating the potential impact on human health from chemicals.⁶⁴ Through observations of exposed and nonexposed populations, epidemiologists quantify the association between exposure to a particular agent and the incidence of disease or injury in a given population.⁶⁵ Epidemiologists consider an agent a cause of disease or injury if when present it increases and when absent decreases the relative frequency of disease or injury.⁶⁶ It cannot, however, predict which individuals will develop disease following exposure to a known chemical.⁶⁷

1. Establishing Association Through Relative Risk

Epidemiological studies enable the investigator over time to calculate the comparative rates of disease within the exposed and nonexposed groups and to compare those two rates.⁶⁸ "Relative Risk"⁶⁹ is

⁶¹ Poulter, *supra* note 8, at 231.

⁶² Frederick, *supra* note 5, at 249. See also *Brock v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307, 311 (5th Cir. 1989), *modified*, 884 F.2d 166 (5th Cir. 1989).

⁶³ *In re Agent Orange Product Liab. Litig.*, 611 F. Supp. 1223, 1231, 1261-62 (E.D.N.Y. 1985), *aff'd*, 818 F.2d 187 (2d Cir. 1987).

⁶⁴ Christie, *supra* note 60, at 308. Animal studies, though considered less valuable because of major differences in biology, cell receptivity, routes of administration and exposure process between species, remain the best way of predicting effects on humans when reliable epidemiological data is not available.

⁶⁵ Frederick, *supra* note 5, at 241.

⁶⁶ *Id.* at 243.

⁶⁷ Christie, *supra* note 60, at 308.

⁶⁸ Boston, *supra* note 23, at 234.

⁶⁹ *Id.* at 235. *Relative Risk (RR)* = $R'1'/R'2'$, where $R'1'$ = risk of disease in the exposed population and $R'2'$ = the risk of disease in a nonexposed population. Rela-

considered the most reliable statistical indicator for establishing sufficient association between exposure and incidence of disease to infer causation. If the relative risk equals 1.00, the risk in the exposed group is the same as the risk in the nonexposed group, and there is no association between the factor and the suspected disease.⁷⁰ If the relative risk is greater than 1.00, the risk in the exposed group is greater than in the nonexposed group, and a positive association between the exposure and the suspected disease can be inferred.⁷¹ Epidemiological probability of causation can then be determined by the "Attributable Risk," the difference between risk in the exposed and nonexposed group.⁷² The following example illustrates this relationship. A study of asbestos-exposed workers revealed that workers were dying from lung cancer at a rate of 64 per 100,000 per year, as compared with the general population of males of the same age and during the same period who died at a rate of 31 per 100,000 per year.⁷³ The relative risk for this study would be expressed as $64/31=2.06$.⁷⁴ Attributable Risk would be relative risk minus 1 divided by relative risk or mathematically expressed as $AR=(2.06-1.00)/2.06$, or 51%.⁷⁵ The probability that a given case of lung cancer in the exposed group was attributable to asbestos exposure would be 51%.⁷⁶

A relative risk greater than 1.00 only reveals a positive association between exposure and the disease.⁷⁷ It does not constitute scientific knowledge.⁷⁸ As a foundational matter, many courts require a relative risk of over 2.00 to meet the preponderance of the evidence standard.⁷⁹ The association does not necessarily establish a causal relationship be-

tive Risk is a number that describes the increased or decreased incidence of the disease in question in the population exposed to the factor as compared with the control population not exposed to the factor.

⁷⁰ *Id.*

⁷¹ *Id.*

⁷² *Id.* at 236. Attributable Risk is expressed as $AR(RR-1)/PRR$, where RR = Relative Risk of the study group.

⁷³ *Id.* at 235.

⁷⁴ *Id.*

⁷⁵ *Id.* at 236.

⁷⁶ *Id.*

⁷⁷ *Id.* at 235.

⁷⁸ Amicus Curiae Brief of the American Medical Association et al. in support of Respondent at 34, *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991) (No. 92-102).

⁷⁹ *In re Joint Eastern and Southern District Asbestos Litigation*, 758 F. Supp. 199, 202 (S.D.N.Y. 1991).

cause other confounding factors may be present.⁸⁰ Epidemiologists have developed criteria to assess causal inference in exposure-relationships.⁸¹ The most critical of these are (1) strength of the association; (2) likelihood that the association is not spurious; (3) biological plausibility of the association; and (4) consistency from study to study.⁸²

The relative risk must be further refined to eliminate numerical instability.⁸³ Numerical instability is a function of the variability of sample population size between studies.⁸⁴ For example, if a new treatment were found to have a success rate of 75% while an older treatment has a success rate of 50%, that information would appear significant.⁸⁵ However, if the 75% rate represented only three successes in four patients and the 50% success rate represented two successes in four patients, the results would be numerically unstable.⁸⁶ This results because the effect of the next patient would drastically alter the success rate of each group.⁸⁷ If the next patient in each group fails with the new treatment and succeeds with the old, then the results in each group would be identical at 3/5=60%.⁸⁸ If, however, the results were based on a study of 400 patients, then the effect of subsequent patients on the success rate would be minimal.⁸⁹ Where numerical instability is not so easily detected, epidemiologists use other statistical methods to achieve numerical stability.⁹⁰ The two most common methods are the statistical method or null hypothesis and the confidence interval.⁹¹

⁸⁰ Boston, *supra* note 23, at 237.

⁸¹ *Id.* at 237-41. Most prominent are the standards proposed by Sir Austin Bradford Hill in 1965. They are: (1) strength of the association; (2) consistency; (3) specificity; (4) temporality; (5) biological gradient; (6) biological plausibility; (7) coherence; (8) experiment; and (9) analogy.

⁸² Christie, *supra* note 60, at 311.

⁸³ Amicus Curiae Brief of Professor Alvan R. Feinstein in Support of Respondent at 21, *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991) (No. 92-102).

⁸⁴ *Id.*

⁸⁵ *Id.*

⁸⁶ *Id.*

⁸⁷ *Id.*

⁸⁸ *Id.*

⁸⁹ *Id.*

⁹⁰ *Id.*

⁹¹ *Id.* at 21, 23.

2. Significance Testing; the Null Hypothesis

Significance testing is a statistical tool that attempts to examine chance as a potential explanation for a set of observations.⁹² The process begins with an assumption, called the null hypothesis, which asserts that the two treatments are the same so that any difference in observation must be due to chance.⁹³ The hypothesis is evaluated using a statistical tool known as the *p* value or alpha.⁹⁴ If the *p* value is small, then the null hypothesis (that the result was due to chance) would be rejected and the results would be deemed statistically significant. To distinguish between small probabilities, an arbitrary *p* value, usually .05, is selected to classify whether an observation is significant or not significant.⁹⁵ If $p < .05$, the observed association is statistically significant and the null hypothesis is rejected; if $p > .05$, the null hypothesis is not rejected.⁹⁶ When the *p* value exceeds .05, it tells the investigator only that the null hypothesis is not rejected to the 95% degree of certainty.⁹⁷

Significance testing is often used in developing inferences based on hypothesis testing.⁹⁸ Reliance on statistical testing in evaluating the association between exposure and disease has been criticized as misleading.⁹⁹ Instead of contributing to the proof of the hypothesis, whether the toxic substance caused the harm, significance testing focuses less on the information presented by the observations and more on the role chance may have played in bringing about the observations.¹⁰⁰

⁹² Amicus Curiae Brief of Professor Kenneth Rothman et al. in Support of Petitioners at 4, *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991) (No. 92-102).

⁹³ Feinstein, *supra* note 83, at 21.

⁹⁴ Boston, *supra* note 23, at 252-53. The *p* value is defined as the probability, assuming the null hypothesis is true, that the observed data will depart from the null to the extent that they do, or to a greater extent, based on chance. Thus, the *p* value is the probability that an association at least as strong as that disclosed by the data might occur even if the null hypothesis were true; that is, by random chance. The *p* value ranges from 0 to 1.

⁹⁵ *Id.*

⁹⁶ *Id.*

⁹⁷ *Id.*

⁹⁸ Rothman, *supra* note 92, at 4.

⁹⁹ *Id.* at 5.

¹⁰⁰ *Id.* at 6.

3. Confidence Intervals

An increasingly favored approach to evaluating the error in scientific measurement is the use of "confidence intervals."¹⁰¹ A confidence interval is a range of possible values for risk between two studied groups.¹⁰² The confidence interval provides a mathematical expression representing the magnitude of a possible error.¹⁰³ Calculation of the interval requires choosing a level for alpha and the interval is expressed as $1 - \alpha$.¹⁰⁴ If alpha is .05, then the confidence level is 95% or $(1 - .05)$.¹⁰⁵ A confidence level of 95% means there is only a 5% chance that the actual distinction between the two studied groups falls outside the range of numeric possibilities representing the expected value (i.e., that the observation is due to something other than chance).¹⁰⁶ If the confidence interval includes the relative risk, then there is no statistically significant association between the factor and the disease.¹⁰⁷ The confidence level provides greater sensitivity to small variations in observations and reduces the likelihood that an investigator will conclude an observation insignificant when it is in fact significant.¹⁰⁸

4. Methodological Weaknesses of Epidemiology

The reliability of epidemiological studies may be diminished by a variety of inherent problems, such as difficulty in identifying comparable control groups,¹⁰⁹ lack of uniform scientific standards, difficulty in

¹⁰¹ *Id.*

¹⁰² Feinstein, *supra* note 83, at 23.

¹⁰³ Brock v. Merrell Dow Pharmaceuticals, Inc., 874 F.2d 307, 312 (5th Cir. 1989), *modified*, 884 F.2d 166 (5th Cir. 1989).

¹⁰⁴ Feinstein, *supra* note 83, at 23. Note that the confidence level is the inverse of the *p* value so that a null hypothesis of .05 is a statistical alternative to a 95% confidence level. The mathematical reasoning and data are identical in either approach.

¹⁰⁵ *Id.*

¹⁰⁶ *Id.* The use of a 95% confidence interval is precisely analogous to a *p* value of .05, which represents statistical significance. *Id.* at 24.

¹⁰⁷ Brock v. Merrell Dow Pharmaceuticals, Inc., 874 F.2d 307, 312 (5th Cir. 1989), *modified*, 884 F.2d 166 (5th Cir. 1989).

¹⁰⁸ Feinstein, *supra* note 83, at 24.

¹⁰⁹ Eric W. Weichmann, *Standard of Proof for Increased Risk of Disease or Injury*, 61 DEF. COUNS. J. No. 1, 59, 62 (1994). *But see* Deluca v. Merrell Dow Pharmaceuticals, Inc., 911 F.2d 941, 954 (1990). Expert testimony based on epidemiological data is generally appropriate for judicial notice because epidemiology is a well established branch of science and medicine and epidemiological evidence has been accepted in many cases. Where epidemiological analysis deviates from that which has been consistently admitted, the court must conduct a hearing to establish reliability consistent with Federal Rule of Evidence 702.

assessing exposure, recall bias, and confounding factors.¹¹⁰ Combined effects of multiple pesticide exposure on populations of varied susceptibility would pose significant confounding factors for cancer-exposure epidemiological studies.¹¹¹

B. Medical Opinion Evidence

Plaintiffs frequently offer medical testimony either alone or in combination with epidemiological evidence.¹¹² This testimony is most compelling where the treating physician either provides expert testimony of diagnostic tests designed to establish a cause or distinguish among possible causes, or testifies to the existence of other factors for the disease.¹¹³ Unwilling to accept scientific limitations in identifying causation, the court in *Ferebee v. Chevron Chemical Co.* held that a cause-effect relationship did not need to be established by epidemiological studies before a doctor could testify that such a relationship existed.¹¹⁴

Other courts view medical expert testimony as enhancing the reliability of some level of epidemiological evidence. In *In re Joint Eastern and Southern District Asbestos Litigation*, the District Court for the Southern District of New York held that plaintiff could meet the burden of preponderance of the evidence either through epidemiological studies conclusively establishing a relative risk ratio of 2.00, or through epidemiological evidence falling short of 2.00 in combination with clinical or experimental evidence.¹¹⁵

¹¹⁰ Boston, *supra* note 23, at 241-46.

¹¹¹ See generally, Pesticide Management Education Program, Cornell University, Ithaca, N.Y., EXTTOXNET Pesticide Information Notebook, *Epidemiology* (1993).

¹¹² Poulter, *supra* note 8, at 231.

¹¹³ *Id.* at 232.

¹¹⁴ *Ferebee v. Chevron Chem. Co.*, 736 F.2d 1529, 1535-36 (D.C. Cir. 1984). The court upheld a jury verdict for plaintiff where plaintiff's case was based on expert testimony of two treating pulmonary specialists who concluded that paraquat poisoning caused plaintiff's pulmonary fibrosis. Note that the District of Columbia Circuit Court clarified its reasoning in *Ferebee* when it considered a Bendectin case in *Richardson ex rel Richardson v. Richardson-Merrell, Inc.*, 857 F.2d 823, 826, 832 (D.C. Cir. 1988). There the court affirmed the lower court's grant of judgment notwithstanding the verdict to defendant, finding the reasoning of plaintiff's expert opinion inadequate. The court distinguished this from the *Ferebee* holding by stating that it was willing to look behind the conclusions of experts where there is a lot of epidemiological evidence available, as opposed to cases such as *Ferebee*, where there was no epidemiological evidence available to link low-level exposure to toxic chemicals with human disease.

¹¹⁵ 827 F. Supp. 1014, 1027, 1030 (S.D.N.Y. 1993), *rev'd on other grounds* 52 F.3d

III. JUDICIAL EVIDENCE: FOUNDATIONAL CONSIDERATIONS

A. *Reliability and Relevancy*: Daubert v. Merrell Dow

The Supreme Court in *Daubert v. Merrell Dow*¹¹⁶ granted certiorari to resolve the disputed vitality of the traditional "general acceptance" standard for admissibility of expert scientific evidence established by the District of Columbia Circuit Court of Appeals in *Frye v. United States*.¹¹⁷ Writing for a unanimous Court, Justice Blackmun stated that the rigid "general acceptance" requirement of *Frye* had been superceded by the more receptive language of the Federal Rules of Evidence.¹¹⁸

More importantly, however, the Court articulated a new standard governing the admissibility of scientific evidence. Federal Rules of Evidence [hereinafter FRE] 702¹¹⁹ permits scientific evidence that will assist the trier of fact. Under *Daubert*, the trial judge is to pose a two-pronged inquiry when scientific evidence is proffered: (1) does this evidence constitute scientific knowledge? and (2) will this evidence assist the trier of fact?¹²⁰ These questions should be decided by the judge as a preliminary matter pursuant to FRE 104(a).¹²¹

1124 (2d Cir. 1995). Appellant sued on behalf of her deceased husband, claiming that the colon cancer that resulted in his death was caused by exposure to appellee's asbestos spray. A jury returned a verdict for plaintiff. The district court granted appellee's motion for judgment as a matter of law and set aside the jury verdict on the grounds that the epidemiological and clinical evidence of causation were insufficient to meet the preponderance of the evidence standard.

¹¹⁶ 509 U.S. 579, (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991). Plaintiffs filed suit against Merrell Dow Pharmaceuticals, Inc., the manufacturer of Bendectin, a prescription anti-nausea drug, alleging that its ingestion caused birth defects. The federal district court granted Merrell Dow's motion for summary judgment, finding that plaintiff's expert testimony relying on reanalyses of previously published epidemiological studies failed to meet *Frye's* "general acceptance" standard.

¹¹⁷ 293 F. 1013 (D.C. Cir. 1923). *Frye* was a criminal case that involved the admissibility of blood-pressure deception measurements as evidence of defendant's guilt. The *Frye* court stated that the basis of expert testimony "must be sufficiently established to have gained general acceptance in the particular field in which it belongs." *Id.* at 1014.

¹¹⁸ *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 589 (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991).

¹¹⁹ FED. R. EVID. 702 provides: "If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise."

¹²⁰ *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 592 (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991).

¹²¹ *Id.* FED. R. EVID. 104(a) provides in pertinent part relative to questions of admis-

The first prong addresses reliability and would exclude evidence that is not "scientific knowledge."¹²² The Court set forth four nonexclusive criteria to guide the lower federal courts in identifying "scientific knowledge."¹²³ Judges are also permitted to develop their own standards.¹²⁴ The Court stressed, however, that good science is based not on the conclusions drawn, but upon the methodology used to reach those conclusions.¹²⁵

The second prong of *Daubert* is the determination of relevancy of the testimony to the disputed issue.¹²⁶ To meet this requirement of FRE 702, the testimony must "assist the trier of fact to understand the evidence or to determine a fact in issue."¹²⁷ The question to be asked is whether the reasoning or methodology relied upon can be usefully applied to help resolve the facts in dispute.¹²⁸ *Daubert* also permits exclusion of evidence due to lack of probative value,¹²⁹ failure to satisfy the requirement that expert testimony rely on facts and data reasonably relied upon by experts in the particular field,¹³⁰ and exercise of other available judicial controls such as directed verdict and summary judgment.¹³¹

sibility: "Preliminary questions concerning the qualification of a person to be a witness, the existence of a privilege, or the admissibility shall be determined by the court, subject to the provisions of subdivision (b)."

¹²² *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 592, 589-590 (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991). "Scientific" requires reasoning that is grounded on accepted scientific methods of hypothesis formulation and testing validity by experimentation. "Knowledge" requires more than subjective belief or speculation.

¹²³ *Id.* at 593-94. The judge should examine the principles and methodology and consider: (1) whether the principles and methodology have been tested; (2) whether they have been subjected to peer review and publication; (3) whether the known or potential rate of error is acceptable and (4) whether the underlying principles have gained "general acceptance" in the scientific community.

¹²⁴ *Id.* at 594.

¹²⁵ *Id.* at 580.

¹²⁶ *Id.* at 591.

¹²⁷ *Id.*

¹²⁸ *Id.*

¹²⁹ FED. R. EVID. 403 provides: "Although relevant, evidence may be excluded if its probative value is substantially outweighed by the danger of unfair prejudice, confusion of the issues, or misleading the jury, or by considerations of undue delay, waste of time, or needless presentation of cumulative evidence."

¹³⁰ FED. R. EVID. 703 provides in relevant part: "The facts or data in the particular case upon which an expert bases an opinion or inference may be those perceived by or made known to the expert at or before the hearing."

¹³¹ *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 596 (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991).

Epidemiology is considered a well established scientific methodology, thus any studies based on its method would satisfy the first prong of a *Daubert* analysis.¹³² It has been suggested, however, that under *Daubert's* relevancy prong, epidemiological evidence "is only probative if the correlation between the exposure and the disease supports an inference that exposure was more likely than not the cause of injury."¹³³ Under the traditional preponderance standard, plaintiff can only prevail if the relative risk ratio is shown to be greater than 2.00. Admitting testimony based only on studies showing relative risk greater than 2.00 prevents consideration of valuable studies providing evidence of a strong but slightly lower level of risk.¹³⁴

Epidemiological studies are most vulnerable to attack of testability due to problems with control groups, insufficient allowance for confounding factors, insufficient sample size, and extrapolation of animal or cellular studies.¹³⁵ The *Daubert* Court stated, however, that the subject of scientific testimony does not have to be "known" to a certainty.¹³⁶ It only required that the process used to derive the inference must be based on scientific method.¹³⁷

B. Sufficiency; Brock v. Merrell Dow

Sufficiency of evidence addresses whether the collective weight of plaintiff's evidence is adequate to present a jury question.¹³⁸ In evaluating the sufficiency of evidence to present a question to the jury, it is generally accepted that the court cannot weigh the evidence, judge the credibility of witnesses, or substitute its judgment of the facts for that of the jury.¹³⁹ The Court in *Daubert* considered exclusionary methods

¹³² DeLuca v. Merrell Dow Pharmaceuticals, Inc. 911 F.2d 941, 954 (3d Cir. 1990). See also *In re Agent Orange Product Liab. Litig.*, 611 F. Supp. 1223, 1239 (E.D.N.Y. 1985), *aff'd*, 818 F. 2d 187 (2d Cir. 1987).

¹³³ Jeffrey D. Cutler, Comment: *Implications of Strict Scrutiny of Scientific Evidence: Does Daubert Deal a Death Blow to Toxic Tort Plaintiffs?*, 10 J. ENVTL. L. & LITIG. 189, 200 (1995). This would require a Relative Risk of at least 2.00 resulting in an Attributable Risk of 51% or more. *Id.* at 200 n.57.

¹³⁴ *Id.* at 200 n.57.

¹³⁵ Roland A. Giroux, Note, *Daubert v. Merrell Dow: Is This Just What the EMF Doctor Ordered?*, 12 PACE ENVTL. L. REV. 393, 440 (1994).

¹³⁶ *Daubert v. Merrell Dow Pharmaceuticals Inc.*, 509 U.S. 579, 590 (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991).

¹³⁷ *Id.*

¹³⁸ *In re Joint Eastern & Southern Dist. Asbestos Litig.*, *Arlene Maiorana v. U.S. Mineral Prod. Co.* 52 F.3d 1124, 1132 (2nd Cir. 1995).

¹³⁹ *Brock v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307, 308 (5th Cir. 1989).

such as summary judgment and judgment as a matter of law "appropriate safeguards" where plaintiff's evidence is insufficient to present to a jury.¹⁴⁰

In *Brock v. Merrell Dow Pharmaceuticals, Inc.*, the United States Court of Appeals for the Fifth Circuit reversed a jury verdict for plaintiff, finding defendant entitled to judgment notwithstanding the verdict.¹⁴¹ The court held plaintiff's epidemiological evidence insufficient regarding causation to allow a trier of fact to make a reasonable inference.¹⁴² Though the court stated that epidemiological evidence is not a necessary element of proof in a toxic tort case, where presented, it must yield statistically significant conclusions. Therefore, because the relative risk ratio derived from plaintiff's epidemiological evidence adjusted by confidence intervals included the relative risk ratio of 1.00, the evidence was insufficient as a matter of law to establish the foundational causal inference.¹⁴³

The United States Court of Appeals for the Second Circuit in *In re Joint Eastern & Southern District Asbestos Litigation* reasoned that sufficiency of epidemiological evidence should be made based on the sum total of plaintiff's evidence.¹⁴⁴ The issue considered by the court was whether *Daubert* extends the district judge's role to consideration of scientific evidence already admitted.¹⁴⁵ Subsequent to a jury award for plaintiff, the district judge granted judgment as a matter of law to defendants, finding plaintiff's epidemiological evidence insufficient to support a causal connection between decedent's asbestos exposure and ensuing colon cancer.¹⁴⁶ The court reviewed the evidence of relative risk of each epidemiological study in light of five sufficiency criteria.¹⁴⁷ Those criteria were strength and consistency of association, dose-response relationship, experimental evidence, plausibility, and co-

¹⁴⁰ *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 596 (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991).

¹⁴¹ *Brock v. Merrell Dow Pharmaceuticals, Inc.*, 874 F.2d 307 (5th Cir. 1989).

¹⁴² *Id.* at 315.

¹⁴³ *Id.* at 312, 315.

¹⁴⁴ *In re Joint Eastern & Southern Dist. Asbestos Litig., Arlene Maiorana v. U.S. Mineral Prod. Co.*, 52 F.3d 1124, 1133 (2d Cir. 1995).

¹⁴⁵ *Id.* at 1131. Plaintiff filed suit on behalf of her deceased husband, a 40-year-old sheet metal worker. Plaintiff presented both epidemiological and clinical evidence to prove that exposure to asbestos caused the colon cancer that resulted in her husband's death. The case was tried before a jury, which found in favor of plaintiff and awarded \$4,510,000. Defendants then moved for and the court awarded judgment as a matter of law pursuant to Federal Rules of Civil Procedure 50(b). *Id.* at 1126-27.

¹⁴⁶ *Id.* at 1127.

¹⁴⁷ *Id.* at 1128. See Hill's causal inference criteria, *supra* note 81.

herence.¹⁴⁸ The district court, finding plaintiff's epidemiological evidence failed to satisfy any of the sufficiency criteria, concluded the evidence was insufficient to support the general proposition that asbestos exposure causes colon cancer.¹⁴⁹

On appeal, respondent, United States Mineral Products, argued that *Daubert*, in addition to changing the standards governing admissibility of scientific evidence, applied similar changes to sufficiency decisions.¹⁵⁰ According to respondent, "admissibility and sufficiency determinations are functionally equivalent."¹⁵¹ The Court of Appeals for the Second Circuit, however, found no textual support for respondent's proposition and concluded *Daubert* left the traditional sufficiency standard intact.¹⁵² The appellate court reversed, finding the district court's analysis was "rife with independent assessments of witnesses' conclusions and comparative credibilities" to the extent of substituting its judgment for that of the jury by assessing the weight of conflicting evidence and passing on the credibility of witnesses.¹⁵³

Though *Daubert* would appear to have little effect on foundational issues, the implications for claims of pesticide-induced cancer are clear. As a minimal requirement, an exposed plaintiff proffering epidemiological evidence would have to demonstrate its scientific validity as well as its statistical significance. Where epidemiological evidence is not widely available, *Daubert* would not preclude admissibility of other probative evidence such as animal toxicology studies¹⁵⁴ and ex-

¹⁴⁸ *Id.* See also Boston, *supra* note 23, at 238-40. "Strength of association" is reflected by the Relative Risk Ratio. The greater the Relative Risk Ratio, the stronger the association and the less likely that the association is explained by chance. "Consistency" refers to the presence of repeated consistent observations among studies. "Dose-response relationship" refers to the relationship of severity or frequency of disease due to increased level or duration of exposure. "Experimental evidence" refers to clinical evidence that would support a causal relationship between exposure and the disease. "Plausibility" refers to the compatibility between the association and the biological knowledge then known as derived from other studies. "Coherence" determines whether the associational data seriously conflict with the natural history and biology of the disease.

¹⁴⁹ *In re* Joint Eastern & Southern Dist. Asbestos Litig., Arlene Maiorana v. U.S. Mineral Prod. Co., 52 F.3d 1124, 1130 (2d Cir. 1995). The court reached this conclusion despite its concession that the presence of colon cancer in a 40-year-old man was uncommon. *Id.*

¹⁵⁰ *Id.* at 1132.

¹⁵¹ *Id.*

¹⁵² *Id.*

¹⁵³ *Id.* at 1133.

¹⁵⁴ *Daubert v. Merrell Dow Pharmaceuticals Inc.*, 509 U.S. 579, 592 (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991).

pert medical opinion.¹⁵⁵

IV. BALANCING THE BURDEN; SOME PROPOSALS

Insofar as judges scrutinize scientific methodology, part of that active review should be scrutiny of the scientific "standard of proof."¹⁵⁶ The mathematics of epidemiological methodology, as applied to unavoidably small sample sizes and rare diseases, thrust serious policy choices on researchers and regulators when the results of these studies are used to estimate human cancer risk.¹⁵⁷ By establishing legal sufficiency of epidemiological evidence on a relative risk ratio of 2.00 at the standard 95% degree of confidence, courts are requiring a level of certainty considerably higher than the preponderance standard would seem to suggest.¹⁵⁸

A. Focus on Relative Risk

Some commentators question whether statistical significance is relevant to the preponderance of the evidence standard.¹⁵⁹ One commentator suggests that focusing on the relative risk found in a study is more appropriate.¹⁶⁰ Such a suggestion was made in *DeLuca v. Merrell Dow Pharmaceutical, Inc.*, where the court likened a relative risk ratio of 2.00 to a 50% chance that a particular disease was caused by the event under investigation.¹⁶¹

That approach, however, would arguably establish relevancy based on association alone, providing no evidence of causation.¹⁶² Even if association were sufficiently probative, a relative risk ratio greater than 1.00 does not establish association of disease unless there is reasonable certainty that distribution of disease is not due to chance.¹⁶³ Thus, evaluation of relative risk without application of statistical testing or confidence intervals retains inherent problems of numerical instability and increases the likelihood that causal conclusions will be drawn where observations are in fact due to chance.

¹⁵⁵ *Ferebee v. Chevron Chem. Co.*, 736 F.2d 1529, 1535-36 (D.C. Cir. 1984).

¹⁵⁶ *Cranor*, *supra* note 9, at 8.

¹⁵⁷ *Id.* at 4.

¹⁵⁸ *Poulter*, *supra* note 8, at 261.

¹⁵⁹ *Id.* at 262.

¹⁶⁰ *Id.*

¹⁶¹ *DeLuca v. Merrell Dow Pharmaceuticals, Inc.* 911 F.2d 941, 958-59 (3d Cir. 1990).

¹⁶² *Poulter*, *supra* note 8, at 262.

¹⁶³ *Id.*

Relative risk greater than 1.00, however, alerts scientists that there may be some positive relationship between an exposure and disease. Given enough epidemiological data, opponents of statistical testing argue that the findings attain significance in that the results will tend to cluster around the true relative risk even if no single study qualifies as statistically significant.¹⁶⁴

B. Apply Decreased and Varied Confidence Intervals to Relative Risk

Judicial reliance on the established 95% confidence interval, typically used by epidemiologists, may not only be misguided, but may actually maximize errors to the detriment of the plaintiff.¹⁶⁵ The more probable than not standard of proof would thus seem to tolerate epidemiological data on the issue of general causation at confidence intervals lower than the 95% level typically employed by epidemiologists.¹⁶⁶ The choice of the 95% confidence interval is arbitrary, reflecting a conservative scientific approach to minimization of chance.¹⁶⁷ A renowned epidemiologist proposes reporting results at various confidence levels to focus on the more important size and location of the confidence intervals.¹⁶⁸ An evaluation of the collective data in the context of confidence intervals and the most likely estimate for

¹⁶⁴ *Id.* at 263.

¹⁶⁵ D. H. Kaye, *Apples and Oranges: Confidence Coefficients and the Burden of Persuasion*, 73 CORNELL L. REV. 54, 58-59, 72 (1987). See also, Boston, *supra* note 23, at 253. Such errors are called false positives or type I errors, which occur when the null hypothesis is true but rejected.

¹⁶⁶ Poulter, *supra* note 8, at 262.

¹⁶⁷ *DeLuca v. Merrell Dow Pharmaceuticals, Inc.*, 911 F.2d 941, 948 (3d Cir. 1990).

¹⁶⁸ *Id.* Professor Rothman, Editor of the journal EPIDEMIOLOGY and Professor of Public Health (Epidemiology and Biostatistics) at the Boston University School of Medicine and Public Health, advocated reporting study results at 90%, 95%, and 99% confidence levels. *Id.* See also Rothman, *supra* note 92, at 3. Professor Rothman's theory was the basis for the expert testimony of Dr. Done proffered in many of the Bendectin cases. See *DeLuca v. Merrell Dow Pharmaceuticals, Inc.*, 911 F.2d 941, 949 (3d Cir. 1990). Dr. Done's testimony was deemed not only insufficient, but also inadmissible in *Lynch v. Merrell-National Laboratories*, 830 F.2d 1190, 1191, 1197 (1st Cir. 1987), and *Richardson ex rel Richardson v. Richardson-Merrell, Inc.*, 857 F.2d 823, 826 (D.C. Cir. 1988). In *DeLuca*, exclusion of Dr. Done's testimony as inadmissible was overturned. *DeLuca v. Merrell Dow Pharmaceuticals, Inc.*, 911 F.2d 941, 959 (3d Cir. 1990). Note, however, that Professor Rothman's approach is considered a minority one, as articulated in Oral Argument Transcript at 74, *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991).

the true parameter suggested by that data reduces the possibility that researchers will accept a false premise.¹⁶⁹

C. Preponderance of the Available Evidence

One commentator proposed that plaintiffs alleging a toxic exposure should be required to prove causation only by a preponderance of the available evidence.¹⁷⁰ He notes, consistent with the courts' treatment of this issue, where epidemiological evidence is substantial, reliable and consistent, there is no need to rely on other evidence of toxicity such as on animal studies.¹⁷¹ But where epidemiological evidence is lacking or inconclusive, it is unjustifiable to exclude other toxicological evidence.¹⁷² According to this commentator, imposing the current heightened evidentiary threshold when the required scientific evidence may never be forthcoming is contrary to judicial notions of fairness and social responsibility.¹⁷³

The preponderance of the available evidence approach has been criticized as permitting unlimited and arbitrary liability where only a possibility and not a probability exists.¹⁷⁴ However, statistical significance is only a part of a meaningful evaluation of reliability.¹⁷⁵ Courts have demonstrated their ability to examine complex scientific evidence within the analytical framework of *Daubert* and to utilize judicial controls available.¹⁷⁶ Plaintiffs are not required to prove causation to a scientific certainty¹⁷⁷ or that the alleged cause is the only cause.¹⁷⁸ All plaintiff is required to prove is that the toxic substance was a substantial factor.¹⁷⁹ Furthermore, jurors are not told at what level of significance a factor must be found.¹⁸⁰ They are merely asked to determine whether it was "significant."¹⁸¹

¹⁶⁹ DeLuca v. Merrell Dow Pharmaceuticals, Inc., 911 F.2d 941, 948 (3d Cir. 1990).

¹⁷⁰ Green, *supra* note 48, at 680.

¹⁷¹ *Id.*

¹⁷² *Id.*

¹⁷³ *Id.* at 681.

¹⁷⁴ Poulter, *supra* note 8, at 265-66.

¹⁷⁵ DeLuca v. Merrell Dow Pharmaceuticals, Inc., 911 F.2d 941, 955 (3d Cir. 1990).

¹⁷⁶ *Id.* at 949-52.

¹⁷⁷ *Daubert v. Merrell Dow Pharmaceuticals Inc.*, 509 U.S. 579, 590 (1993), *vacating and remanding* 951 F.2d 1128 (9th Cir. 1991).

¹⁷⁸ Gasko v. Johns-Manville and Celotex, 248 N.J. Super. 446, 457 (1991).

¹⁷⁹ *Id.*

¹⁸⁰ *Id.*

¹⁸¹ *Id.*

CONCLUSION

The EPA is entrusted with the weighty responsibility of promoting the health and safety of consumers. EPA policy decisions regarding risk of harm attributable to pesticides are based on considerations of cost and benefit. Cost represents the cost imposed on chemical manufacturers to minimize the risk associated with pesticides, cost of the EPA to regulate pesticides, cost of not devoting resources to other life-saving programs such as medical testing and the cost of death and disease to exposed consumers. Costs imposed on the EPA and chemical industry are self-determining issues of policy and economics. Consumers, however, are involuntarily and pervasively exposed to multiple toxic pesticides.

Long-term effects of chronic, low-level exposure to specific pesticides alone or in combination are uncertain. However, clinical evidence supported by epidemiological studies strongly implicates pesticides in the development of cancer. Strong implications are not enough, however, to impose liability on chemical manufacturers when disease or death due to pesticide exposure is alleged.

Toxic tort claims alleging disease or death caused by pesticide exposure require, as a foundational matter, that causation be established by proving a statistically significant association between the exposure and the injury. Uncertainty of cancer causation, absence of statistically significant association and high threshold limitation on the admissibility of epidemiological evidence combine to create a bar to recovery.

Science is the study of uncertainty. Scientists admittedly do not understand the complexities of cancer development or the long-term health effects of interacting and prolific toxic pesticides. To await scientific proof that pesticides are a significant factor in the cause of cancer in a dynamically changing toxic environment is both scientifically and legally unreasonable.

Courts determine liability based upon principles of law. Toxic tort cases, however, force a confluence of scientific and legal theory where the burdens of proof are significantly different. Scientifically significant association between exposure and injury has been translated into the required civil burden of preponderance of the evidence. There are persuasive arguments, however, that this threshold requirement is more stringent than the preponderance of the evidence requires.

Questions of which scientific indicator best supports causation must be resolved by the scientific and legal scholars. Though an association established by relative risk may not be adequate proof of causation, statistical significance to a high degree of certainty appears to be un-

justifiably burdensome. Clearly, there must be a middle-level scientific approach that would provide both acceptable scientific confidence and probative legal evidence of causation.

This middle-level approach should consider the availability of all evidence, to include epidemiological, animal toxicological and medical opinion evidence. The rigor of scientific analysis of the scientific evidence could then be modified depending upon the nature of the proffered evidence. Where there are numerous epidemiological studies treating the effects of a particular toxin, higher degrees of statistical confidence and restricted admissibility of other clinical or animal toxicological studies are warranted. However, where there is an inadequate number of epidemiological studies, a meaningful evaluation of the available evidence would permit a lower degree of statistical confidence and examination of clinical and animal toxicity studies.

The dilemma posed by scientific and legal causation raises complex theories. Theoretical posturing, however, does not quantify the cost of disease and death or assign responsibility when it occurs. Barriers to recovery where unjustified facilitate industrial profit at the expense of human lives. Real or perceived, people are suffering from the effects of pesticides. A principled examination of current toxic tort causation evidence is not only appropriate, it is ethically unavoidable.

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