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PEERING INTO THE MICROSCOPE: THE RISE OF JUDICIAL GATEKEEPING AFTER *DAUBERT* AND ITS EFFECT ON FEDERAL TOXIC TORT LITIGATION

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I. INTRODUCTION

John Jackson is a corporate attorney who moved into a new house in the Silicon Valley area. The house is in a large subdivision that is quiet and relatively secluded. Shortly after John moved in, a paper mill set up a factory

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on an adjacent area of land about a mile away from the edge of the subdivision. The factory produced a moderate amount of smog, which gave off a noxious odor. Several of the residents protested the factory being built so close to their neighborhood, but their pleas were ignored. About 14 months after the plant was established, John began to experience recurring dizziness and chest pain. Fearing that John could be suffering from angina, John's doctor ordered John to undergo some cardiac examinations. However, the tests did not return any negative results. John returned home, still uncertain as to what ailed him. Two weeks later, he found out that a woman who lives down his street was recently diagnosed with lung cancer. The woman was a schoolteacher at a school that was rumored to have talc in its air conditioning system. Curious, John returned to his doctor for a reexamination. John's doctor discovered that John had developed lung cancer. Bewildered and outraged, John believed that the factory was the cause of his condition, since two people in the same environment had developed a relatively rare condition in a short time. However, John's wife was also a habitual smoker, who had smoked around John for their entire 12 year marriage. Additionally, John's father was diagnosed with and treated for prostate cancer 3 years ago.

There are several questions that John must answer in deciding whether or not to proceed with a toxic tort case against the factory. First, can John show with reasonable certainty that the factory smoke was capable of causing lung cancer? Even if John can show that the smoke is capable of causing lung cancer, can John prove that the amount of factory smoke to which he was exposed could cause his lung cancer? Moreover, if John can prove these points, can he show that the factory smoke by itself *did* cause his condition *and* disprove the possibility that his wife's smoking or his family history were significant factors in the development of his cancer? Above all, can John provide scientific proof to all of the above questions using expert witnesses who employ scientific research methods that are sufficiently reliable[1] to persuade a trial judge to admit the evidence to the jury? These are several important questions that John must face in proceeding with a toxic tort claim.

John's burden to prove that the toxin in question caused his injury relies on the ability of his expert witness to show through reliable scientific techniques such as animal and human laboratory tests, available scientific literature, analysis of the plaintiff, and a differential diagnosis, that the toxin in question was more likely than not capable of causing the John's injury and did in fact

[1] Under the leading Supreme Court case of *Daubert v. Merrell Dow Pharmaceuticals, Inc*., 509 U.S. 579 (1993) (incorporating the *Frye* "general acceptance" rule), a number of factors bear on the inquiry into the scientific validity of expert testimony:

(1) Whether the expert's technique or theory can be or has been tested;

(2) Whether the technique or theory has been subject to peer review and publication;

(3) The known or potential rate of error of the technique or theory when applied;

(4) the existence and maintenance of standards and controls; and

(5) whether the technique or theory has been generally accepted in the scientific community.

cause the injury. From the adoption of the "general acceptance" test in *Frye v. United States* to the development of Federal Rule of Evidence 702(2) to the current leading Supreme Court cases, *Daubert v. Merrell Dow Pharmaceuticals, Inc.*[2] and *Kumho Tire Company, Ltd. v. Carmichael*,[3] the law governing the admissibility of expert witness testimony in federal court, especially in complex toxic tort litigation, has undergone a drastic transformation. Since the Supreme Court's landmark decision in *Daubert*, there has been a greater focus in toxic tort cases on the underlying scientific principles and tests used by experts, as opposed to a simple acquiescence to the scientific community's acceptance of such standards. This shift has forced judges to become well-versed in the basic procedures and scientific norms of complex fields of science, which in turn has led to courts becoming more active in determining the admissibility of expert testimony. This intertwining of law and science has created several interesting issues that trial judges must face in determining whether expert testimony gives sufficient assurances of trustworthiness to be admissible under Federal Rule of Evidence 702. Today, federal courts must be equipped to digest top-notch scientific theories and data, including human and animal testing, the weight given to each in determining toxicity, the extrapolation of results between similar substances and species, the establishment of minimal dose response relationships, the temporal relationships between exposure and onset of disease, and the differential diagnosis and its meaning and role in causation within the legal and medical fields.

II. DEVELOPMENT OF RULES CONCERNING THE ADMISSIBILITY OF SCIENTIFIC EVIDENCE

A. The Frye Test: General Acceptance

The first case to create a widely-accepted rule for admitting scientific expert testimony was *Frye v. United States* in 1923.[4] Following an appeal by Frye from the Supreme Court of the District of Columbia, the Court of Appeals affirmed the lower court's exclusion of Frye's expert witness, who had based his testimony upon an experiment that recognized a higher systolic blood pressure in individuals who lied or concealed facts.[5] The lower court had stated that the expert's scientific methods were not "generally accepted" by his scientific peers.[6] This opinion would remain the unchallenged rule for

[2] 509 U.S. 579 (1993).

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

[4] *Id.* at 1014.

[5] *Id.* at 1013-14.

[6] James Frye appealed his conviction of second degree murder to the Court of Appeals for the District of Columbia on the single claim that the trial court had improperly refused his scientific experiment and expert witness's testimony thereon. Frye claimed that his experiment showed that conscious deception or falsehood or concealment of facts resulted

admission of scientific evidence for almost fifty years, until the creation of the Federal Rules of Evidence.

B. Daubert v. Merrell Dow Pharmaceuticals, Inc.

In 1993, the United States Supreme Court specifically addressed the controversial issue of the admissibility of scientific expert testimony and the *Frye* "general acceptance" test in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*[7] In what would be considered a landmark opinion for easing the admission of scientific evidence, Justice Blackmun rejected the rigid "general acceptance" test in *Frye* as the main test for admissibility of expert testimony, holding instead that the Federal Rules of Evidence inherently required judges to act as gatekeepers.[8] The Court stated that a judge must determine if the expert testimony is "scientifically valid" and will assist the trier of fact to understand the evidence or to determine a material fact.[9] The opinion then set out a list of factors that a judge may consider in its determination of the scientific validity of testimony:

(1) Whether the expert's technique or theory can be or has been tested;[10]

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in a person having a higher systolic blood pressure. On appeal, Frye stated what he believed to be the proper rule regarding scientific evidence in his brief:

> The rule is that the opinions of experts or skilled witnesses are admissible in evidence in those cases in which the matter of inquiry is such that inexperienced persons are unlikely to prove capable of forming a correct judgment upon it, for the reason that the subject matter so far partakes of a science, art, or trade as to require a previous habit or experience or common knowledge, but requires special experience or special knowledge, then the opinions of witnesses skilled in that particular science, art, or trade to which the question relates are admissible in evidence.

Id. at 1014. The Court of Appeals rejected this argument on the grounds that the scientific experiment that Frye had attempted to offer had not gained "general acceptance" in the scientific community such that the courts could admit the experiment and expert testimony to the jury. *Id.*

[7] *Daubert*, 509 U.S. 579 (1993).

[8] Justice Blackmun explained his rejection of *Frye*: "Nothing in the text of this Rule [702] establishes 'general acceptance' as an absolute prerequisite to admissibility. Nor does respondent present any clear indication that Rule 702 or the Rules as a whole were intended to incorporate a 'general acceptance' standard. The drafting history makes no mention of *Frye*, and a rigid 'general acceptance' requirement would be at odds with the 'liberal thrust' of the Federal Rules and their 'general approach of relaxing the traditional barriers to 'opinion' testimony.'" *Id.* at 588.

[9] Pursuant to the requirements of FED. R. EVID. 104(a): "Preliminary questions concerning the qualification of a person to be a witness, the existence of a privilege, or the admissibility of evidence shall be determined by the court, subject to the provisions of subdivision (b) [pertaining to conditional admissions]." This rule provided Justice Blackmun the necessary authority to grant judges the ability to act as gatekeepers.

[10] In other words, whether the expert's theory can be challenged in an objective sense, or whether it is instead a subjective, conclusory approach that cannot reasonably be assessed for reliability.

(2) Whether the technique or theory has been subject to peer review and publication;

(3) The known or potential rate of error of the technique or theory when applied;

(4) The existence and maintenance of standards and controls; and

(5) Whether the technique or theory has been generally accepted in the scientific community.[11]

Whether or not the evidence or testimony will assist the trier of fact to understand the evidence or to determine a material fact "goes primarily to relevance."[12] Consequently, "[e]xpert testimony which does not relate to any issue in the case is not relevant and, ergo, non-helpful."[13] The Court further stated that "Rule 702's 'helpfulness' standard requires a valid scientific connection to the pertinent inquiry as a precondition to admissibility."[14] Thus, to be admissible, the trial judge must find an expert's testimony to be both scientifically valid, based on an evaluation of the five non-exclusive factors, and helpful to the jury on the issue for which it is presented.

C. Kumho Tire Company, Ltd. v. Carmichael

Six years later, the Supreme Court again addressed the issue of the gatekeeping role of trial judges in *Kumho Tire Company, Ltd. v. Carmichael*.[15] In that case, plaintiff Patrick Carmichael sued the manufacturer of a faulty tire that exploded and caused his car to overturn.[16] The 11th Circuit rejected the District Court's contention that the *Daubert* factors for determining scientific validity applied to expert testimony, stating that *Daubert* applied only to testimony where an expert "relies on the application of scientific principles" and not to testimony where an expert relies "on skill- or experience-based observation."[17] The Supreme Court noted that the *Daubert* factors of reliability helped to evaluate experience-based expert testimony as well: "It is the Rule's word 'knowledge,' not the words (like 'scientific') that modify that word, that establishes a standard of evidentiary reliability."[18] The Court also noted that "in certain cases, it will be appropriate for the trial judge to ask, for example, how often an engineering expert's experience-based methodology

[11] The Court states that "many factors will bear on the inquiry, and we do not presume to set out a definitive checklist or test . . . . The inquiry envisioned by Rule 702 is, we emphasize, a flexible one." *Daubert*, 509 U.S. at 591-95.

[12] *Id.* at 591.

[13] *Id*.

[14] *Id*. at 591-92.

[15] Kumho Tire Company, Ltd. v. Carmichael, 526 U.S. 137 (1999).

[16] *Id.* at 137.

[17] *Id*. at 151.

[18] *Id*. at 147.

has produced erroneous results, or whether such a method is generally accepted in the relevant engineering community."[19] The Court then discussed how much latitude should be given to trial courts in determining the reliability of expert testimony under *Daubert* and the standard of review that appellate courts should apply to district court decisions on admissibility.[20] The Court noted that district courts must be able to decide ***how*** to test for reliability of an expert's testimony as well as whether or not the expert's testimony is ultimately reliable.[21] It would be nearly impossible, and highly impractical, for a judge to hear an expert's experience-based testimony and make an accurate determination of reliability without being able to investigate the reliability of the expert's underlying method by examining methods of other experts in the field.

D. Federal Rule of Evidence 702

The Federal Rules of Evidence, authored in 1973 and amended in 2000 in response to *Daubert* and *Kumho Tire*, provide guidance for the admissibility of evidence in federal courts. Rule 702 specifically addresses testimony given by expert witnesses, stating:

> 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, if:
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> (1) The testimony is based upon sufficient facts or data
> (2) The testimony is the product of reliable principles and methods, and
> (3) The witness has applied the principles and methods reliably to the facts of the case.[22]

Rule 702 creates two important premises: first, that the expert must apply a methodology to his or her analysis that consists of a reliable method within the particular field of science; and second, that the methodology (and the facts upon which it relies) properly "fit" the conclusion to which the expert testifies.

The 2000 Amendment to Rule 702 codified the major premises of *Daubert* and *Kumho Tire* that emphasize the gatekeeper role of the trial court. As the advisory committee notes to Rule 702 summarize:

> [the] amendment affirms the trial court's role as gatekeeper and provides some general standards that the trial court must use to assess the reliability and helpfulness of proffered expert testimony. Consistent with *Kuhmo Tire*, the Rule as amended provides that all types of expert testimony present questions of admissibility for the trial court in deciding

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[19] *Id*. at 151.

[20] *Id.* at 152-53.

[21] *Id*. at 152.

[22] FED. R. EVID. 702.

> whether the evidence is reliable and helpful. Consequently, the admissibility of all expert testimony is governed by the principles of Rule 104(a). Under that Rule, the proponent has the burden of establishing that the pertinent admissibility requirements are met by a preponderance of the evidence.[23]

III. CAUSATION

A. Causation in Toxic Tort Litigation: A Brief Introduction

A toxic tort, in its most general sense, is a physical or psychological harm to an individual due to exposure to a chemical factor. Common examples include harm caused by asbestos, lead poisoning, and air pollution. Two essential elements that a plaintiff must prove in a toxic tort case are *general causation* and *specific causation*. To prove general causation, a plaintiff must show that the alleged toxin is capable of causing the plaintiff's particular disease.[24] Specific causation requires a showing that the alleged toxin did in fact cause the plaintiff's disease.

In order to prove general causation, the plaintiff's expert witness must conduct laboratory testing. Often, laboratory rats are exposed to chemical X and structurally-similar chemicals and results are extrapolated to determine if exposure to chemical X in a certain amount results in an increased risk of illness in humans. Such testing is common where there is no existing scientific literature or test results showing that chemical X is capable of causing result Y. After determining the minimal dose-response relationship (the minimal exposure level necessary to trigger the plaintiff's illness), the expert must examine the plaintiff's particular case by comparing the plaintiff's level of exposure to this threshold level. This allows the expert to determine whether or not the plaintiff's exposure could have caused his illness.

In examining specific causation, an expert will conduct a differential diagnosis. Differential diagnosis, in a medical sense, is "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."[25] In a legal sense, differential diagnosis, or "differential etiology," is a standard scientific technique that identifies the cause of a medical problem by eliminating potential causes until the most probable one is

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[23] FED. R. EVID. 702 advisory committee's note on 2000 Amendments.

[24] Disease is defined as:

> 1) An interruption, cessation, or disorder of body function, system, or organ. Syn: illness, morbus, sickness.
>
> 2) A morbid entity characterized usually by at least two of these criteria: "recognized etiologic agent(s), identifiable group of signs and symptoms, or consistent anatomic alterations."

STEDMAN'S MEDICAL DICTIONARY 509 (27th ed. 2000).

[25] *Id.* at 492.

isolated.[26] This procedure, when properly performed, has been accepted by all jurisdictions as reliable methodology for the basis of an expert's testimony.[27]

A medical expert testifying that a chemical exposure caused the plaintiff's injury must be able to prove the ability of the chemical to cause the injury in the same manner that would be required of a toxicologist. Amedical expert must consider laboratory studies and other relevant scientific data in rendering his opinion on causation. The standard that experts must follow when giving a "legal" differential diagnosis is illustrated in *Kannankeril v. Terminex Int'l, Inc.*:

> The elements of a differential diagnosis may consist of the performance of physical examinations, the taking of medical histories, and the review of clinical tests, including laboratory tests. A doctor does not have to employ all of these techniques in order for the doctor's diagnosis to be reliable. . . A differential diagnosis may be reliable with less than all the types of information set out above.[28]

B. General Causation

Although virtually all courts in toxic tort litigation require an expert to perform a differential diagnosis to arrive at his or her opinion on specific causation, the expert must also be able to prove that the chemical in question is capable of causing the plaintiff's injury. The federal courts have identified several key issues in determining what constitutes an acceptable methodology by which an expert must abide in rendering an opinion on causation.

1. "Ruling In" Before "Ruling Out"

The majority of courts hold that an expert must "rule in" an agent as a potential cause of the plaintiff's injury, then "rule out" other possible causes until only the most likely cause remains. This point is illustrated in *Cavallo v. Star Enterprises*:

> The process of differential diagnosis is undoubtedly important to the question of "specific causation." If other possible causes of an injury cannot be ruled out, or at least the possibility of their contribution to

[26] Baker v. Dalkon Shield Claimants Trust, 156 F.3d 248, 252-253 (1st Cir. 1998). Many courts have interchanged the terms "differential diagnosis" and "differential etiology" synonymously: Westberry v. Gislaved Gummi AB, 178 F.3d 257, 262-263 (4th Cir. 1999) ("Differential diagnosis, or differential etiology, is a standard scientific technique of identifying the cause of a medical problem by eliminating the likely causes until the most probable one is isolated"); Glaser v. Thompson Med. Co., 32 F.3d 969, 978 (6th Cir. 1994) (differential diagnosis defined as "standard diagnostic tool used by medical professionals to diagnose the most likely cause or causes of illness, injury and disease"); McCullock v. H.B. Fuller Co., 61 F.3d 1038, 1044 (2d Cir. 1995) (differential etiology defined as analysis "which requires listing possible causes, then eliminating all causes but one.").

[27] *See supra* note 26.

[28] Kannankeril v. Terminex Int'l, Inc., 128 F.3d 802, 807 (3d Cir. 1997).

> causation minimized, then the "more likely than not" threshold for proving causation may not be met. But, it is also important to recognize that a fundamental assumption underlying this method is that the final, suspected "cause" remaining after this process of elimination must actually be capable of causing the injury. That is, the expert must "rule in" the suspected cause as well as "rule out" other possible causes. And, of course, expert opinion on this issue of "general causation" must be derived from scientifically valid methodology.[29]

The majority opinion is a reasonable one: requiring an expert to "rule in" the agent as capable of causing the plaintiff's injury, i.e. showing that there is a strong statistical correlation between the amount of the toxin to which the plaintiff was exposed and the adverse effect that such an amount has on human beings, ensures that the expert bases his or her opinion on solid scientific principles and that unfounded opinions and guesswork science are kept out of the courtroom.

However, courts differ as to the extent of proof that an expert must provide when attempting to "rule in" a cause. For example, the Second Circuit in *McCullock v. H.B. Fuller Co.* affirmed the admission of a treating doctor's testimony despite the fact that he "could not point to a single piece of medical literature that says glue fumes cause throat polyps."[30] The court explained that the expert's reliance upon his "care and treatment of McCullock; her medical history (as she related it to him and as derived from a review of her medical and surgical reports); pathological studies; review of [Defendant] Fuller's [Material Safety Data Sheet], his training and experience, use of a scientific analysis known as differential etiology (which requires listing possible causes, then eliminating all causes but one); and reference to various scientific and medical treatises" was reasonable.[31]

Nevertheless, in the field of toxicology, there are recognized standards that toxicologists must follow in performing their analysis. These standards help courts answer questions regarding causation. Courts can hold even non-toxicologists to these standards[32]in order to assure that relied upon facts and data are appropriate for the field.[33] Thus, if a medical expert testifies in a toxic tort case as to the carcinogenicity (capability of causing cancer) of a particular substance, the expert must be able to back up that claim with epidemiological

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[29] Cavallo v. Star Enter., 892 F. Supp. 756, 771 (E.D. Va. 1995), *aff'd* on this ground, *rev'd* on other grounds 100 F.3d 1150 (4th Cir. 1996).

[30] *McCullock*, 61 F.3d at 1043.

[31] *Id*. at 1044.

[32] Mancuso v. Consol. Edison Co. of N.Y., Inc., 967 F. Supp. 1437, 1445 (S.D.N.Y 1997) ("Courts have held that even if an expert seeking to testify is not a toxicologist, he must employ principles and methods of toxicology if he is to give an opinion on an issue relating to that specialty.").

[33] *Id*. ("Additionally, under Rule 703, the facts and data relied upon by the expert must be of the type 'reasonably relied upon by experts in that particular field.'").

data, laboratory tests, and other relevant information employed by toxicologists and epidemiologists.

2. Epidemiology, Animal Testing, and Risk Assessment

a. Lack of Determinable Exposure Level

It is an accepted maxim in toxicology that a toxicologist must ascertain the necessary level of exposure to a toxin that would cause an adverse reaction and then quantify the plaintiff's level of exposure to see if it reaches that threshold level. This strategy has been emphasized by several regulatory agencies and referenced publications. The Federal Judicial Center's Reference Manual on Scientific Evidence explains that "the 'dose makes the poison' and that all chemical agents, including water, are harmful if consumed in large quantities."[34] The World Health Organization's method for determining the possible effects of a toxin on an individual is as follows:

> 1) [A]n evaluation is made of the chemicals to which the individual might have been exposed and of the concentrations of these chemicals in air breathed by the individual[;]
>
> 2) [An evaluation is made], based on published scientific literature, of the exposures necessary to produce the adverse effects associated with the chemicals to which individuals may be exposed[; and]
>
> 3) These two evaluations are then combined in the final step of the risk assessment to provide an estimate of the likelihood that any of the harmful properties of any or all of the chemicals might have been expressed in the exposed individual.[35]

In real world situations, it is often incredibly difficult to estimate certain factors with any degree of accuracy, including the precise level of toxin to which the plaintiff was exposed. Imagine for a moment that our old friend John Jackson had been spending less time at home as the 14-month span between his initial presumed exposure to the smoke and his diagnosis passed. It would be tough to establish a set amount of time that he was in his house, outside doing work, or even on the property. Moreover, determining the relative amount of factory smoke to which he was exposed would be difficult as well. The concentration of the smoke inside the house would be different from the concentration outside. Thus, it would be difficult for an expert to testify that Jackson was exposed to a certain level of the alleged toxin.

Courts recognize just how difficult it may be for a plaintiff to quantify the amount of toxin that he or she was exposed to, or even the amount of time that he or she may have been exposed. This dilemma was emphasized by the

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[34] Bernard D. Goldstein & Mary Sue Henifen, *Reference Guide on Toxicology*, *in* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 185, 187 (Federal Judicial Center 1994).

[35] Cavallo v. Star Enter., 892 F. Supp. 756, 764 (E.D. Va. 1995).

FourthCircuit in *Westberry v. Gislaved Gummi AB*.[36] A worker at a window-manufacturing plant was hospitalized with a severe sinus infection after inhaling talc powder at the plant.[37] He brought suit against GGAB, claiming that it failed to warn him of the dangers of the talc.[38] GGAB argued that the plaintiff's expert was unable to reliably "rule in" talc as a cause because he could not accurately quantify the level of exposure necessary to cause the plaintiff's injury.[39] The court noted that the "plaintiff must demonstrate 'the levels of exposure that are necessary to human beings generally as well as the plaintiff's actual level of exposure.'"[40] However, the court emphasized a practical consideration:

> Only rarely are humans exposed to chemicals in a manner that permits a quantitative determination of adverse outcomes . . . Human exposure occurs most frequently in occupational settings where workers are exposed to industrial chemicals like lead or asbestos; however, even under these circumstances, it is usually difficult, if not impossible, to quantify the amount of exposure.[41]

The court recognized that although the expert "had no scientific literature on which to rely to 'rule in' talc as a possible basis for Westberry's sinus condition, it was undisputed that inhalation of high levels of talc irritates mucous membranes."[42] Westberry was inundated with talc while employed as a gasket cutter.[43] The talc was so condensed that the black gaskets appeared white from the talc.[44] The talc was blown into the air through the cutting machines and settled on the floor in such quantity as to reveal footprints in it on the floor.[45] Based upon this, the court decided that the exposure was substantial enough that, coupled with data on a Material Safety Data Sheet (MSDS)[46] on talc provided by GGAB, it was reasonable for the expert to conclude that the exposure was capable of causing Westberry's sinus

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[36] Westberry v. Gislaved Gummi AB, 178 F.3d 257 (4th Cir. 1999).

[37] *Id.* at 260.

[38] *Id.*

[39] *Id.* at 263.

[40] *Id*. at 263 (quoting Mitchell v. Gencorp Inc., 165 F.3d 778, 781 (10th Cir. 1999)).

[41] *Id*. at 264 (quoting Bernard D. Goldstein & Mary Sue Henifen, *Reference Guide on Toxicology*, *in* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 185, 187 (Federal Judicial Center 1994)).

[42] *Id*.

[43] *Id.* at 264.

[44] *Id.*

[45] *Id.*

[46] A Material Safety Data Sheet (MSDS) is a listing of information about a hazardous substance that the manufacturer of such substance is required to compile and make available under regulations established by the Occupational Safety and Health Administration (OSHA). *See* 29 C.F.R. § 1910.1200(g) (2006).

condition.[47]

In contrast, the Eleventh Circuit, specifically rejecting the *Westberry* decision, held in *Rink v. Cheminova, Inc.*[48] that a differential diagnosis alone does not support a finding of causation where no expert testimony from a treating physician or toxicologist is presented, or any toxicological evidence produced.

The Southern District of New York likewise shunned *Westberry* when it held in *Mancuso v. Consolidated Edison Co. of New York, Inc.*[49] that an expert must do more than merely cite corporate regulatory documents that indicate the toxicity of a particular substance.[50] In *Mancuso*, the plaintiff and his family had allegedly suffered skin disorders, dizziness, and learning and behavioral impairment as a result of exposure to polychlorinated biphenyls (PCB) from an electric substation adjacent to the plaintiff's marina.[51] The district court, in rejecting the plaintiff's expert witness Dr. Schwartz's reliance on the defendant's corporate documents confirming the toxicity of PCB, added: "Nor do we accept plaintiffs' argument that ConEd's documents admit that 'minute exposure can be extremely hazardous,' and that therefore Dr. Schwartz did not need to know more than that plaintiffs were exposed to minute levels of PCBs before making his diagnosis."[52] The court made this declaration despite its admission that the documents "do recite deleterious health effects that can result from acute or chronic toxicity, including dermal exposure to PCBs."[53] In fact, the court recognized that PCB exposure has been known to cause skin irritation, acne, and form dermatitis,[54] which were among the plaintiffs' primary complaints.

Despite these concessions, the court rejected the expert's reliance on the defendants' documents because they did not speak to adverse effects from prolonged exposure to low levels of PCB, nor did the expert quantify the level of the plaintiff's exposure to PCB.[55] The court recognized that "it is improper for an expert to presume that the plaintiff 'must have somehow been exposed to a high enough dose to exceed the threshold [necessary to cause the illness], thereby justifying his initial diagnosis.' This is circular reasoning."[56] The court emphasized that the expert had assumed that the plaintiff and his family were exposed to a level of PCB sufficient to cause their specific injuries, in

[47] *Id.* at 264-66.

[48] 400 F.3d 1236 (11th Cir. 2005).

[49] Mancuso v. Consol. Edison Co. of N.Y., Inc., 967 F. Supp. 1437 (S.D.N.Y. 1997)

[50] *Id.* at 1457.

[51] *Id.* at 1439-41.

[52] *Id*. at 1447.

[53] *Id*. at 1448.

[54] *Id*. at 1448 n.12.

[55] *Id.* at 1449.

[56] *Id*. at 1450 (citing O'Conner v. Commonwealth Edison Co., 807 F. Supp. 1376, 1396 (C.D.Ill. 1994)); Cavallo v. Star Enter., 892 F.Supp. 756, 764 n.12, (E.D.Va. 1995)).

essence claiming that the expert derived his opinion from the plaintiff's conditions and not from scientific evidence of exposure.

Ironically, this case is similar to the situation in *Westberry*, where testimony of Westberry's expert was admitted. In *Westberry*, the expert had relied on defendant corporation's document affirming the toxicity of the airborne talc, had failed to precisely quantified the level of the plaintiff's exposure, and could not point to any scientific proof (other than the corporate sheet) that linked sinusitis to talc. Nevertheless, the results of these cases can be distinguished by their facts and the contents of the defendants' MSDS statements regarding the threshold concentrations of toxicity. In *Westberry*, it was unknown what exact concentration of talc was sufficient to cause sinusitis, while in *Mancuso*, the defendant's Health and Safety Plan claimed that a reading of 50 ppm in the water would be dangerous and would require immediate cleanup.[57] However, the expert in *Mancuso* had not attempted to determine or even estimate the amount of the plaintiffs' exposure to the allegedly toxic elements, whereas in *Westberry*, the evidence strongly indicated that the plaintiff had been exposed to a very high content of airborne talc.[58]

b. Weight of the Evidence

In modern-day toxic tort litigation, expert witnesses rely a great deal on statistical information in scientific literature and the results from laboratory tests to prove a suspected toxin's capability of causing the plaintiff's disease. Laboratory tests commonly employed by these experts include inter vivo animal tests (exposure of an agent to an animal test subject, commonly infant and adult mice), in vitro tests (tests involving the reaction of cells to exposure to an agent), and epidemiological tests (studies involving reaction of different human test groups to exposure to an agent). However, there are several problematic issues in evaluating such test results that make it difficult to determine the reliability of a particular result. An example is the situation where a structurally similar chemical to the chemical at issue is being tested, a different type of cancer develops in the test subject than in the patient, and a different species is the test subject.

There are several sets of guidelines authored by various government agencies and organizations such as the Environmental Protection Agency (EPA), the World Health Organization (WHO), and the International Agency for Research on Cancer, that are widely accepted sources among toxicologists and epidemiologists in determining how much weight should be given to epidemiological and animal studies. Also, leading experts in the field of epidemiology have published studies and guides that are accepted and

[57] Mancuso v. Consol. Edison Co. of N.Y., Inc., 967 F. Supp. 1437, 1447-48 (S.D.N.Y. 1997).

[58] *Id.* at 1448.

followed by many epidemiologists. [59] Many courts consult these guidelines in addressing these difficult issues.

The EPA has adopted several guidelines for assessing the health risks posed by toxins, including its Guidelines for Carcinogen Risk Assessment.[60] These guidelines describe a process by which carcinogenicity, or capacity to cause cancer in humans, is calculated. It first recognizes that:

> Evidence of possible carcinogenicity in humans comes primarily from two sources: long-term animal tests and epidemiologic[al] investigations. Results from these studies are supplemented with available information from short-term tests, pharmacokinetic studies, comparative metabolism studies, structure-activity relationships, and other relevant toxicologic[al] studies. The question of how likely an agent is to be a human carcinogen should be answered in the frame-work [sic] of a weight-of-evidence judgment. Judgments about the weight of evidence involve considerations of the quality and adequacy of the data and the kinds and consistency of responses induced by a suspect carcinogen.
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> There are three major steps to characterizing the weight of evidence for carcinogenicity in humans:
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> 1)Characterization of the evidence from human studies and from animal studies individually;
>
> 2)Combination of the characterizations of these two types of data into an indication of the overall weight of the evidence for human carcinogenicity; and
>
> 3)Evaluation of all supporting information to determine if the overall weight of evidence should be modified.[61]

The guidelines also outline which tests may be used in human and animal studies to properly assess the weight of the evidence for carcinogenicity.[62]

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[59] Epidemiology is "the field of public health and medicine that studies the incidence, distribution, and etiology of disease in human populations." Michael D. Green, et al., *Reference Guide on Epidemiology*, in FEDERAL JUDICIAL CENTER, REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 335 (2d ed. 2000).

[60] Guidelines for Carcinogen Risk Assessment, 51 Fed. Reg. 33992 (Sept. 24, 1986). Additional Guidelines set out concurrently by the EPA include:

Guidelines for Estimating Exposures

Guidelines for Mutagenicity Risk Assessment

Guidelines for the Health Assessment of Suspect Developmental Toxicants

Guidelines for the Health Risk Assessment of Chemical Mixtures

The drafts were peer-reviewed by expert scientists in the field of carcinogenosis from universities, environmental groups, industry, labor, and other governmental agencies.

[61] *Id*. at 33996.

[62] Evidence of carcinogenicity from human studies comes from three main sources:

1. Case reports of individual cancer patients who were exposed to the agent(s);

Next, a "weight of the evidence" classification is listed for both human and animal studies. There are five groups of carcinogenic assessment levels for both humans and animals: sufficient evidence, limited evidence, inadequate evidence, no data, and no evidence.[63] Finally, an ultimate categorization of the agent is made based on a combination of the test results and groups of the animal and human studies.[64] If tests reveal "sufficient evidence" of the agent's carcinogenicity through human testing, it is classified as a human carcinogen regardless of any animal studies.[65] Where a human study yields limited results and an animal test proves "sufficient evidence" of carcinogenicity, the agent is a probable human carcinogen.[66]

While the EPA attempted to create a methodology that toxicologists and

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2. Descriptive epidemiologic studies in which the incidence of cancer in human populations was found to vary in space or time with exposure to the agent(s); and

3. Analytical epidemiologic (case-control and cohort) studies in which individual exposure to the agent(s) was found to be associated with an increased risk of cancer.

Three criteria must be met before a causal association can be inferred between exposure and cancer in humans:

1. There is no identified bias that could explain the association;

2. The possibility of confounding has been considered and ruled out as explaining the association; and

3. The association is unlikely to be due to chance.

In general, although a single study may be indicative of a cause-effect relationship, confidence in inferring a causal association is increased when several independent studies are concordant in showing the association, when the association is strong, when there is a dose-response relationship, or when a reduction in exposure is followed by a reduction in the incidence of cancer. *Id.* at 33999.

[63] To briefly demonstrate evidence of each grouping, the test results from human studies that correlate with the carcinogenicity groupings are:

1. Sufficient evidence – there is a causal relationship between the agent and human cancer;

2. Limited evidence – a causal interpretation is credible, but alternative explanations, such as chance, bias, or confounding, could not adequately be excluded;

3. Inadequate evidence – either (a) there were few pertinent data, or (b) the available studies, while showing evidence of association, did not exclude chance, bias, or confounding, and thus causal interpretation is not credible;

4. No data – data not available; and

5. No evidence – no association was found between exposure and an increased risk of cancer in well-designed and well-conducted independent analytical epidemiologic studies.

Id.

[64] The agents are categorized into 5 groups: human carcinogen, probable human carcinogen, possible human carcinogen, not classifiable as to human carcinogenicity, and evidence of non-carcinogenicity for humans. See Table 1 to see how specific combinations of human and animal test groups define each agent category. *Id.* at 34000.

[65] *Id.* at 33997.

[66] *Id.*

other experts could look to for guidance, the problem that they purported to solve is extremely complex. The guidelines that the EPA implemented were created "to promote quality and consistency of carcinogen risk assessments within the EPA and to inform those outside the EPA about its approach to carcinogen risk assessment."[67] However, the guidelines do not fully explain all of the intricacies of the testing process, including what procedure is necessary to reliably extrapolate data from a particular animal species to humans or what types of chemical compounds are structurally or otherwise similar for the purpose of determining carcinogenicity.

c. Extrapolation of Animal Studies to Humans

If an expert plans to rely heavily on animal studies to establish causation, it is important that the expert be able to reliably extrapolate a substance's effects on humans from the minimum dosage levels necessary to cause an adverse response in animal test results. If a laboratory test on a rat shows a chemical to be carcinogenic to the rat at a high exposure level, the test will not prove carcinogenicity in humans if the expert cannot explain how rats and animals have a similar physiological makeup and rate of chemical absorption, or if the expert cannot provide an accurate minimal dose-response relationship in humans based on the animal results. The Third Circuit in *In re Paoli R.R. Yard PCB Litigation* explains:

> Admissibility depends in part on "the proffered connection between the scientific research or test result to be presented and particular disputed factual issues in the case" . . . . For example, animal studies may be methodologically acceptable to show that chemical X increases the risk of cancer in animals, but they may not be methodologically acceptable to show that chemical X increases the risk of cancer in humans. *Daubert* explains that, "[f]it is not always obvious, and scientific validity for one purpose is not necessarily scientific validity for other, unrelated purposes
>
> . . . Rule 702's 'helpfulness' standard requires a valid scientific connection to the pertinent inquiry as a precondition to admissibility" . . . For example, in order for animal studies to be admissible to prove causation in humans, there must be good grounds to extrapolate from animals to humans, just as the methodology of the studies must constitute good grounds to reach conclusions about the animals themselves. Thus, the requirement of reliability, or "good grounds," extends to each step in an expert's analysis all the way through the step that connects the work of the expert to the particular case.[68]

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[67] *Id*. at 33993 (the Guidelines also state: "[t]hese Guidelines emphasize the broad but essential aspects of risk assessment that are needed by experts in the various disciplines required (e.g., toxicology, pathology, pharmacology, and statistics) for carcinogen risk assessment.").

[68] *In re* Paoli R.R. Yard PCB Litig. 35 F.3d 717, 743 (3d Cir. 1994) (quoting United

The United States Supreme Court directly and concisely addressed this issue in *General Electric Company v. Joiner*.[69] Joiner, an electrician employed by the City of Thomasville, GA, alleged that he had developed small-cell lung cancer after several years of dermal contact with polychlorinated biphenyls (PCB's), a chemical found in electrical transformer coolant.[70] In reversing the Eleventh Circuit's reversal of the district court's exclusion of Joiner's expert testimony for failure to establish a causal link between PCB's and small-cell lung cancer, Chief Justice Rehnquist noted that the conditions in the animal studies that Joiner's expert relied on were extremely different from Joiner's exposure.[71] The infant mice in the studies were injected directly in the stomach with "massive doses" of PCB's, whereas Joiner was dermally exposed to a "far less[er]" concentration of PCB, namely fluid with a diluted PCB concentration between 0-500 parts per million.[72] Also, the type of cancer developed in the mice was different than that of Joiner—the infant mice developed alveologenic adenomas, whereas Joiner had developed small-cell carcinomas.[73] Finally, there was no evidence that PCB's led to any type of cancer in any other species, which is important because it shows that animals that are more similar physically to humans than mice, in particular primates, exhibited no cancerous effects from PCB exposure.[74]

Joiner failed to address the glaring differences between his exposure and that of the test mice, and instead argued "as if the only issue [was] whether animal studies can ever be a proper foundation for an expert's opinion."[75] However, one cannot ignore that while Joiner allegedly developed small-cell lung cancer from dermal exposure to a diluted concentration of PCB's, the mice were directly injected with massive doses of pure PCB's into their stomachs and developed a different type of cancer than that of Joiner. Indeed, in light of these differences, the Court noted that "the studies were so dissimilar to the facts presented in this litigation that it was not an abuse of discretion for the District Court to have rejected the expert's reliance on them."[76]

d. Evaluation of Chance and Bias: Effect On Relative Risk and Weight of the Evidence in Epidemiological and Animal Studies

Courts have adopted scientific guidelines for determining the rate of

States v. Downing, 753 F.2d 1224, 1237 (3d Cir. 1985) and Daubert v. Merrell Dow Pharms., 509 U.S. 579, 589 (U.S. 1993)).

[69] General Electric Company v. Joiner, 522 U.S. 136 (1997).

[70] *Id.* at 136.

[71] *Id.* at 137.

[72] *Id*. at 144.

[73] *Id*.

[74] *Id.* at 143.

[75] *Id*.

[76] *Id*.

increased risk of an illness that a toxin purportedly causes incorporating factors such as chance and bias. *Magistrini v. One Hour Martinizing Dry Cleaning* is an excellent example of a court analyzing and rejecting an expert's opinion because it was based on lab tests that did not account for pure chance and bias.[77] In *Magistrini*, the plaintiff was employed by defendant One Hour Martinizing Dry Cleaning for just over two years.[78] Magistrini was exposed to the chemical perchloroethlyne, or PCE, during the tenure of her employment.[79] Fourteen months after resigning from the dry cleaner, she was diagnosed with acute myelomonocytic leukemia (AMML), a subtype of acute myelogenous leukemia (AML).[80] She brought suit against several parties, including the dry cleaner and Dow Chemical Company.[81] Before trial, each side filed motions to exclude the opposing side's expert testimony.[82]

The court began its analysis of the plaintiff's expert, Dr. Ozonoff's opinion by identifying the two categories of epidemiological studies: experimental studies and observational studies.[83] The court narrowed its focus to the two types of observational studies: cohort and case control studies. As the court noted, "[c]ohort studies compare the incidence of disease among individuals exposed to an agent with an unexposed group, while case control studies look at the frequent of exposure in individuals who have the disease as compared to a group of individuals who do not have the disease."[84] From there, an epidemiologist must determine if there is an association between the agent and the disease such that the two would occur together more frequently than just by chance.[85] The strength of such association is measured by its *relative risk*.[86]

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[77] Magistrini v. One Hour Martinizing Dry Cleaning, 180 F. Supp. 2d 584 (D.N.J. 2002).

[78] *Id.* at 588.

[79] *Id.*

[80] *Id.*

[81] *Id.*

[82] "Specifically, the Defendants assert that Dr. Ozonoff's opinion is unreliable both as to the general cause of AML and to the cause of Plaintiff's AML because he: 1) improperly relies on inconclusive epidemiological data that does not show that PCE doubles the risk of developing cancer; 2) fails to take into account negative epidemiological studies; 3) relies on/extrapolates from studies involving cancer and blood diseases other than AML; 4) relies on/extrapolates from studies involving chemicals other than PCE; 5) relies on high dose animal studies that do not "fit" with the facts in this case; 6) fails to quantitatively assess the dose of PCE received by Plaintiff; 7) fails to account for background risks (including history of cancer in Plaintiff's family); 8) fails to rule out alternative causes; and 9) fails to properly consider the latency period of Plaintiff's illness." *Id*. at 597.

[83] "Experimental studies, in the form of randomized trials, clinical trials, or true experiments, generally involve two groups, one of which is exposed to the agent in question, while the other is not. In observational studies, individuals who have been exposed to the agent at issue are observed and compared to a group of individuals who have not been so exposed." *Id*. at 590.

[84] *Id*. at 591.

[85] *Id.*

Relative risk is the increased risk of disease in individuals exposed to the agent compared to the risk of unexposed individuals.[87] Relative risk is measured by a number correlating to the increased percentage of risk:

> Relative risk is commonly calculated by dividing the risk of developing a disease observed in an exposed group by the risk observed in an unexposed, but otherwise similar group. If the risks of the unexposed and exposed are the same, then the relative risk estimate is 1.0 . . . Thus, a relative risk of 1.0 means that the agent has no effect on the incidence of disease. Similarly, if the relative risk estimate is 1.3, then risk appears to be 30% higher among the exposed compared to the non-exposed. When the relative risk reaches 2.0, the risk has doubled, indicating that the risk is twice as high among the exposed group as compared to the non-exposed group. Thus, "the threshold for concluding that an agent was more likely than not the cause of an individual's disease is a relative risk greater than 2.0."[88]

The court noted that this relative risk coefficient can be disrupted by chance, bias, and real effect.[89] Bias is common where the two comparison groups are different in more than just the variable being tested by the study.[90] Chance, the "random distribution of unidentified differences between the two groups being compared," is measured by statistical significance and confidence intervals.[91] Statistical significance is measured on a P-value scale, which is a function of the likelihood that the observed association would occur in the absence of a true association between the agent and the disease.[92] The smaller the P-value, the less likely that chance is a factor in the association.[93] Confidence intervals are commonly used to estimate the statistical stability of an association.[94] Specifically, the interval "provides information about the precision of the estimate of the association and how well other estimates of the association would be supported by the data."[95] This is an important assessment for an expert to include in a study, since virtually every illness can be contracted in some way without exposure to a toxic agent.

Keeping in mind the scrutiny cautioned by the Guidelines in analyzing the expert's method of weighing the evidence, the *Magistrini* court examined the basis of the plaintiff's expert's testimony that PCE causes leukemia. The

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[86] *Id.*

[87] *Id.*

[88] *Id*. (citing Michael D. Green, et al., *Reference Guide on Epidemiology*, in FEDERAL JUDICIAL CENTER, REFERENCE MANUAL ON SCIENTIFIC EVIDENCE 384 (2d ed. 2000)).

[89] *Id*. at 591-92.

[90] *Id*. at 592.

[91] *Id*. (citing Green, *supra* note 88, at 354).

[92] *Id.*

[93] *Id*.

[94] *Id.*

[95] *Id*.

expert performed three animal bioassays on rats, fourteen epidemiological studies,[96] and toxicological studies[97] on PCE. However, the expert almost completely neglected to account for bias and chance in his studies. In his studies of rodents for cancer, the court noted that the expert's test was inherently biased, in that it tested for a form of cancer that was not even analogous to human AMML and was unique to the species of rodent being tested.[98] The expert's faulty methodology did not stop there: he also only accounted for confidence intervals in two of fourteen studies.[99] Only one study had a relative risk factor greater than 1.0, and, in that study, the confidence interval was so high that the plaintiff's own statistical expert doubted the reliability of the study.[100]

Moreover, the court found that the most damning aspect of the expert's methodology was his inability to explain how he weighed the evidence reliably.[101] In determining the respective weight to be given to each study, the expert left out the methods used for calculating the internal and external validity of his studies and failed to provide evidence of how he had calculated the statistical significance and confidence interval of each respective study. [102] The expert also never accounted for the low confidence intervals in his studies or why these statistics did not affect his opinion, nor did he discredit other

[96] The liberal basis of the expert's human epidemiological testing was that: 1) the chemicals TCE and PCE "are sufficiently similar such that they can be treated together when determining their toxicological effects" and 2) "lymphohematopoietic cancers [cancers of the lymphatic and blood systems] can be treated together for etiological purposes." Based on these unexplained assumptions, the expert performed studies that involved chemicals other than PCE and cancers of the blood other than leukemia, which he often failed to specifically reference in the evidence provided. *Id*. at. 599 (citing Initial Report at 27-28).

[97] The Court noted that the expert's reliance upon PCE as a carcinogen was highly circumstantial: "Dr. Ozonoff acknowledges that 'the basic studies of the toxicological mechanisms of PCE supplement but are not the basis for the conclusion that PCE is a human carcinogen.' Dr. Ozonoff instead relies on toxicology data to support his reliance on the animal bioassays. Specifically, he asserts and explains that 'evidence suggests' that humans metabolize PCE in the same way that it is metabolized by some animals. Additionally, Dr. Ozonoff cites to a review of the carcinogenicity of PCE by the IARC, which concluded . . . that: 1) PCE is a probable carcinogen; 2) PCE induced leukemia in rats and 3) several epidemiological studies showed elevated risks from esophageal cancer, non-Hodgkin's lymphoma, and cervical cancer." *Id*. at 600 (citing Initial Report at 34).

[98] *Id*. at 604 n.24.

[99] *Id.* at 605

[100] *Id*. at 606.

[101] *Id.*

[102] *See id*. at 602, 606 (court refers to previously mentioned EPA Guidelines for Carcinogen Risk Assessment in determining weight of evidence for carcinogenicity in humans).

studies with higher confidence intervals that found no association.[103] For example, no governmental or international organization has found any positive association in PCE, nor even classified PCE as a possible cause of leukemia in humans.[104] The tests on PCE performed by the IARC returned limited evidence of carcinogenicity, and did not show a positive association between PCE and leukemia.[105] The expert testified that "weight of the evidence" is

> like a jigsaw puzzle . . . [b]ecause you've got these pieces, there are gaps between the pieces, there can be uncertainty as to whether this piece goes in the middle of the picture, or it's a piece that's really at the edge, or one that's a piece of blue sky that doesn't really add information, but it does go somewhere.[106]

Recognizing this method of weighing evidence as being inconsistent with *Daubert* and Rule 702, the court addressed the problem, stating that "[w]here, as here, elements of judgment pervade the methodology, it is essential that the expert set forth the method for weighing the evidence upon which his opinion is based. Absent that, this Court's role as gatekeeper to assess the reliability of the methodology applied in this case is nullified."[107] In essence, the expert explained his testimony by stating that his opinion should be given deference because he, as the better-qualified expert, chose which pieces of evidence were important in ultimately determining the carcinogenicity of PCE.[108] The expert never explained to the Court why he relied upon several studies with low confidence intervals or discredited studies with much higher confidence levels that showed no increased risk of cancer in PCE; this failure in explanation kept the court from performing its gatekeeping role.[109]

e. Effect of Time on Epidemiological Studies and Animal Tests: Temporal Relationships and Duration of Exposure

Time is also an important factor in evaluating results for general causation in two different ways. First, temporal relationships are important in evaluating results from laboratory tests – specifically, whether the timing of the exposure and the onset of disease in the experiments is consistent with the latency period of the disease. The duration of the exposure to a controlled chemical concentration is also essential in determining how long of an exposure is required at a certain concentration to cause a response. These issues are aptly illustrated in *Cavallo v. Star Enterprises*.[110] Plaintiff Cavallo was diagnosed

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[103] *Id.* at 607.

[104] *Id.*

[105] *Id.*

[106] *Id.* at 606 (citing Testimony of Dr. David Ozonoff, 5/21/01 Tr. at 85-86).

[107] *Id.* at 608.

[108] *See id.*

[109] *See id.* at 607

[110] Cavallo v. Star Enter., 892 F. Supp. 756, 764 (E.D.Va. 1995).

with sinusitis, conjunctivitis, and pulmonary dysfunction after she was exposed to gas fumes from AvJet airplane fuel that spilled near a restaurant she was visiting.[111]

During the trial, both parties agreed that Cavallo had been exposed to a concentration of AvJet fumes at roughly 61 mg/m^3 for 5-30 minutes.[112] Cavallo's toxicologist, Dr. Monroe, cited several epidemiological studies that he had relied upon in reaching his conclusion that Cavallo's illness was linked to the fume exposure.[113] The first, the Molhave study, involved individuals who were exposed to 22 volatile organic compounds indoors for 2.75 hours at 5-25 mg/m^3.[114] The AvJet fuel only contained 7 of the compounds.[115] In the Molhave study, the exposure resulted only in short-term effects, such as irritation of the eyes, nose, and throat.[116] None of the individuals in that study suffered any lasting effects.[117] The next study, the Koren study, was very similar to the Molhave study, in that 14 people were exposed to virtually the same 22 compounds as in the Molhave study at a concentration of 25 mg/m^3 for 4 hours.[118] Again, no lasting effects were reported.[119] Finally, the expert cited an article where two Navy pilots were exposed to an "excessive" amount of fuel vapors during a one-hour flight.[120] The fumes became so nauseating that the pilots had to perform an emergency landing.[121] Both of pilots suffered a burning sensation in their eyes, and one suffered from headache and nausea.[122] Both pilots returned to duty within 4 days and did not suffer any long-term effects.[123]

The *Cavallo* court pointed out that the expert had failed to explain how he had derived his conclusion that the AvJet fuel was capable of causing severe long-term sinus and respiratory effects when the tests he relied upon only confirmed short-term irritation.[124] The court noted that "the reported physical effects were of brief duration" and that:

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[111] *Id.* at 758.

[112] *Id.* at 764.

[113] *Id.* at 765.

[114] *Id.*

[115] *Id.* at 766.

[116] Lars Molhave et al., *Human Reactions to Low Concentrations of Volatile Organic Compounds*, 12 ENV'T INT'L 167 (1986).

[117] *Cavallo*, 892 F. Supp. at 765.

[118] Hillel S. Koren et al., *Exposure of Humans to a Volatile Organic Mixture III: Inflammatory Response*, 47 ARCHIVES ENVTL. HEALTH 39 (1992).

[119] *Cavallo*, 892 F. Supp. at 765.

[120] Henry O. Porter, *Aviators Intoxicated by Inhalation of JP-5 Fuel Vapors*, 1990 AVIATION, SPACE, & ENVTL. MED. 654 (1990).

[121] *Cavallo*, 892 F. Supp. at 766.

[122] *Id.*

[123] *Id.*

[124] *Id.*

> Dr. Monroe does not explain why the short-term effects noted there are consistent with the long-term effects claimed here. While Rule 702 does not necessarily mandate that the expert find a study linking the *exact* chemicals at the *exact* exposure levels with the *exact* illnesses at issue, it does require that the expert demonstrate a scientifically valid basis for projecting the findings of a study identifying a different chemical-illness relationship to the proffered causal theory.[125]

Indeed, while the test subjects from the epidemiological studies experienced similar initial symptoms as Cavallo, namely eye, nose, and throat irritation shortly after exposure, none suffered any lasting effects. Conversely, Cavallo's symptoms continued for several years.[126] The plaintiff's expert established that a chemically similar substance was capable of causing temporary sinus irritation, but because the expert was unable to explain how these studies showing short-term sinus irritation could be applied in some way to determine if the fuel could cause long-term sinusitis and pulmonary dysfunction, his testimony was held inadmissible because it did not help the trier of fact to determine the issue of whether or not AvJet fuel was capable of causing sinusitis or pulmonary dysfunction.[127]

Dr. Monroe's theory that an exposure at 61 mg/m^3 for 5-30 minutes was sufficient to cause Cavallo's chronic illness was further refuted by existing evidence from the defendant regarding the duration of exposure necessary at a certain concentration level to cause the plaintiff's illness. The defendant's expert, Dr. Rodricks, explained that "Threshold Limit Values (TLV) have been established by the American Conference of Governmental Industrial Hygienists for petroleum compounds related to aviation fuel."[128] These studies were conducted to determine a safe exposure level to which "workers may be repeatedly exposed day after day without adverse health effects."[129] The court stated that, "the TLVs for aviation fuel, 'which are designed to protect workers exposed 8 hours [per] day on a chronic basis,' exceed the worst-case concentration to which Ms. Cavallo may have been exposed (61

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[125] *Id*. at 766-767.

[126] *Id.* at 755, 765.

[127] Dr. Monroe attempted to combat this temporal discrepancy by concluding that Cavallo developed RUDS (Reactive Upper Airways Syndrome) from her exposure to the fumes, and that this made her especially sensitive to certain household chemical compounds. He relied on a study where "[a]ll the patients had an initial chemical exposure, which was followed by multiple physical and mental complaints in response to subsequent exposure to a variety of odorous organic chemicals." *Id.* at 768 (citation omitted). However, the court refuted his reasoning since the studies did not involve any exposure to AvJet or any similar fuels or chemical compounds and no dose-response relationship was identified for any of the chemicals involved. *Id.*

[128] *Id.* at 769

[129] *Id*. at 769.

mg/m^3) on one evening by a factor of more than 10."[130]

According to the testimony given by the defendant's expert, Star Enterprise employees were exposed to AvJet fumes on a regular basis at a presumably higher concentration than the plaintiff and none of them suffered any of the lasting long-term effects that affected Cavallo.[131] The plaintiff's expert, who was unable to explain how a brief exposure from a distance could cause the plaintiff's chronic illnesses, did not dispute this assessment.[132] He opined that an exposure of 5-30 minutes at a concentration of 61 mg/m^3 was sufficient to cause the plaintiff's condition.[133] However, the studies upon which he relied varied in duration of exposure from one hour at the minimum in the Porter study to four hours maximum in the Koren study.[134] The plaintiff's expert did not test a concentration of 61 mg/m^3 of AvJet or any similar compound for a period of 5-30 minutes, nor did he attempt to explain how he ascertained the toxicity of that amount from evidence of short-term irritation in a more prolonged exposure at a lesser concentration.[135] His opinion that a 5-30 minute exposure at 61 mg/m^3 was sufficient to cause Ms. Cavallo's chronic illnesses was unsupported by the evidence he provided and was speculative at best.[136]

B. Specific Causation

The next step of the causal chain requires the expert to testify that the suspected cause, which the expert has already proved to be capable of causing the plaintiff's injury, did in fact cause the plaintiff's injury. This requires the expert to conduct a differential diagnosis to "rule in" likely causes, based upon a doctor's physical examination of the patient and a review of the patient's medical history, and to "rule out" all other causes until only the most likely cause remains.[137]

1. "Ruling In": Reliance upon Temporal Relationships and Statistical Data in Differential Diagnosis

The concept of temporal relationships has a different meaning in determining specific causation than it does in determining general causation. For general causation, temporal relationships in laboratory tests of the chemical in question are analyzed to determine if an exposure leads to the onset of the disease in the same manner that the disease normally develops.[138]

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[130] *Id.*

[131] *Id.*

[132] *Id.*

[133] *Id.*

[134] *Id.* at 765.

[135] *Id.* at 769.

[136] *See id.*

[137] *See id.* at 771.

[138] *See id.* at 764.

For specific causation, temporal relationships are analyzed in the context of the plaintiff's specific exposure, specifically whether the amount of time between the plaintiff's exposure and development of symptoms is short, thus indicating a greater likelihood of causation.[139] In this context, temporal relationships are illustrated by the premise that, because X walked past a spill of chemical Y and developed illness Z four days later, Y caused illness Z in X.

Indeed, in some cases, the time between the plaintiff's exposure and the onset of symptoms can be highly indicative of a causal relationship between the substance and condition. The *Cavallo* Court noted that, "if a person were doused with chemical X and immediately thereafter developed symptom Y, the need for published literature showing a correlation between the two may be lessened."[140]

However, many courts are highly skeptical of permitting a finding of specific causation based heavily on a temporal relationship in the absence of scientific data affirming general causation. In *Heller v. Shaw Industries, Inc.*,[141] the Third Circuit explained:

> The temporal relationship will often be (only) one factor, and how much weight it provides for the overall determination of whether an expert has 'good grounds' for his or her conclusion will differ depending on the strength of that relationship. For example, if there was a minor oil spill on the Hudson River on the same day that Heller began experiencing her symptoms in West Chester, Pennsylvania, and she recovered around the time the oil was cleaned up, a proper differential diagnosis and temporal analysis by a well-qualified physician such as Dr. Papano could not possibly lead to the conclusion that the oil spill caused Heller's illness.[142]

The Third Circuit in *Heller* reversed the district court's exclusion of the plaintiff's expert, Dr. Papano, who conducted a differential diagnosis and testified that certain Volatile Organic Compounds (VOCs) present in the carpet were responsible for causing the plaintiff's respiratory illnesses.[143] His testimony was based largely on the temporal relationship between the plaintiff's symptoms and the installation of the suspect carpet.[144] The court noted the division among the circuits regarding the reliance of medical experts on temporal analyses without published studies.[145] The court reasoned:

> *Daubert* and *Paoli* require a physician to rely on definitive published

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[139] *See id.* at 773.

[140] *Id*. at 774.

[141] Heller v. Shaw Industries., Inc., 167 F.3d 146 (3d Cir. 1999).

[142] *Id*. at 154.

[143] *Id.* at 158-59.

[144] *Id.* at 157-58.

[145] *Id.*("a number of courts, including our own, have looked favorably on medical testimony that relies heavily on a temporal relationship between an illness and a causal event.").

> studies before concluding that exposure to a particular object or chemical was the most likely cause of a plaintiff's illness. Both a differential diagnosis and a temporal analysis, properly performed, would generally meet the requirements of *Daubert* and *Paoli*.[146]

The *Daubert*/*Paoli* factors for admissibility were met in *Heller* because "differential diagnosis 'consists of a testable hypothesis,' has been peer reviewed, contains standards for controlling its operation, is generally accepted, and is used outside of the judicial context."[147] The court explained that, in the medical field

> experience with hundreds of patients, discussions with peers, attendance at conferences and seminars, detailed review of a patient's family, personal, and medical histories, and thorough physical examinations are the tools of the trade, and should suffice for the making of a differential diagnosis even in those cases in which peer-reviewed studies do not exist to confirm the diagnosis of the physician.[148]

Doctors do not necessarily routinely consider published studies and tests when performing their diagnoses. A doctor will review the patient's history and files, examine the patient, determine his or her symptoms, and make a judgment. The timing of the onset of the symptoms plays an important role in a physician's determination of the possible causes of those symptoms. However, if an expert is going to render a conclusion involving another field of science, he *must* follow the standards of that field of science in order for his opinion to be reliable. It would not be fair for a doctor to say under a less rigorous standard of examination and subsequent diagnosis that toluene caused Reactive Airways Dysfunction Syndrome (RADS) based mainly on a strong temporal relationship, when a toxicologist making the same judgment would have had to follow the standard of his field, which requires a determination of exposure levels and epidemiological data confirming the toxin's ability to cause the disease. Such a double standard would undermine the entire purpose of requiring extensive epidemiological proof of general causation, which is to show that the defendant's product or chemical could have even caused the plaintiff's injury in the first place.

Indeed, the Circuits are divided on whether a differential diagnosis based on a temporal relationship alone is sufficient to support a medical expert's testimony on causation. In contrast to *Heller*, the Fifth Circuit, in *Moore v. Ashland Chemical*,[149] held that "[i]n the absence of an established scientific connection between exposure and illness, or compelling circumstances such as those discussed in *Cavallo*, the temporal connection between exposure to

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[146] *Id*.

[147] *Id*. at 154-155 (quoting *In re* Paoli R.R. Yard PCB Litig. 35 F.3d 717, 742 n.8 (3d Cir. 1994)).

[148] *Id*. at 155.

[149] Moore v. Ashland Chemical Inc., 151 F.3d 269 (5th Cir. 1998).

chemicals and an onset of symptoms, standing alone, is entitled to little weight in determining causation."[150] In *Moore*, an expert witness testifying on the cause of the plaintiff's RADS relied upon the short time between the plaintiff's exposure to chemical fumes and the onset of his symptoms, as well as the contents of the defendant's MSDS, which linked "short vapor exposure" to blood, liver, lung, kidney, and nervous system damage.[151] However, the expert had no scientific evidence linking the chemical in question, toluene, to RADS, much less any data about the minimal level of exposure to toluene vapors necessary to cause RADS.[152] Accordingly, the court concluded that:

> [n]one of *Daubert*'s factors to assess whether the opinion was based on sound scientific principles was met. Dr. Jenkins' theory had not been tested; the theory had not been subjected to peer review or publication; the potential rate of error had not been determined or applied; and the theory had not been generally accepted in the scientific community. In sum, Dr. Jenkins could cite no scientific support for his conclusion that exposure to any irritant at unknown levels triggers this asthmatic-type condition.[153]

These cases can be factually distinguished to some extent. Courts seem to agree that where a temporal relationship is extremely demonstrative of causation, the amount of epidemiological data required may be decreased, as common sense would dictate. Similarly, where a temporal relationship is weak, most courts require the expert to provide scientific data on general causation. It is in the middle area, where evidence of a temporal relationship suggests a possibility of causation, where the circuits are divided on whether or not a medical expert must provide epidemiological studies and other scientific data.

2. "Ruling Out" Alternative Causes to Show Actual Cause

Once the expert has "ruled in" all of the possible causes of the plaintiff's condition, the expert must then "rule out" all of the other causes until only the most likely cause remains.[154] This process can become convoluted when multiple causes are present and difficult to disprove. How does an expert distinguish between a plaintiff's long history of smoking, family history of cancer, and constant exposure to potentially toxic smoke? It is important to recognize here the difference between the admissibility of the expert's testimony and the plaintiff's ability to meet the burden of proof. With regard to specific causation, the plaintiff must prove that it is more likely than not that

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[150] *Id.* at 278.

[151] *Id.* at 277.

[152] *Id.* at 279.

[153] *Id.*

[154] *See* Cavallo v. Star Enter., 892 F. Supp. 756, 771 (E.D. Va. 1995), *aff'd* on this ground, *rev'd* on other grounds 100 F.3d 1150 (4th Cir. 1996).

the defendant's agent in fact caused his injury.[155] The relevancy requirement Federal Rule of Evidence 401 requires expert testimony to demonstrate that a contested fact is more likely with the addition of that evidence than it would be without the evidence. Thus, an expert's testimony is admissible if it is the product of a properly-performed differential diagnosis and if it makes the issue of causation more probable than it would be without the testimony.

The First, Third, and Fourth Circuits agree that an expert's testimony may be admissible where the expert determines more than one cause after properly performing a differential diagnosis in ruling in potential causes and summarily ruling out other causes, despite the expert's failure to rule out all other causes. The First Circuit in *Baker v. Dalkon Shield Claimants Trust*[156] reversed the district court's exclusion of the expert testimony proffered by the defendant, which rebutted the plaintiff's expert's testimony establishing the defendant's contraceptive as the sole cause of plaintiff's pelvic disease.[157] The court stated that the defendant's alternative explanation that Baker's previous chlamydia infection was "self-evidently relevant to the case at hand; it offers a scientific explanation directly pertinent to the central issue in the case, namely, whether the Dalkon Shield IUD caused Baker's injury . . . . Rule 401 merely requires that evidence make a contested fact more likely than it would be without the evidence . . . ."[158]

Thus, for example, if John Jackson's expert conducted a differential diagnosis and ruled in the factory smoke and Jackson's exposure to second-hand smoke as possible causes and was unable to rule out either possible cause, the expert's testimony would still be admissible because his testimony makes the issue of causation due to factory smoke more likely than it would have been without that testimony. The fact that other causes exist does not affect admissibility because expert testimony showing the defendant's toxic agent's independent capability to cause the plaintiff's illness is inherently relevant to the issue of the defendant's causation and makes the issue of causation by the defendant's alleged toxin more likely to be true than without the testimony.

In *Westberry v. Gislaved Gummi AB*, the Fourth Circuit, citing the Third Circuit, noted that "[t]he alternative causes suggested by a defendant 'affect the weight that the jury should give the expert's testimony and not the admissibility of that testimony' . . . unless the expert can offer 'no explanation for why she has concluded [an alternative cause offered by the opposing party] was not the sole cause,'"[159] The expert's opinion is irrelevant when he is presented with an alternative cause and he cannot give any reason why this

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[155] *See id.*

[156] Baker v. Dalkon Shield Claimants Trust, 156 F.3d 248 (1st Cir. 1998).

[157] *Id.* at 253

[158] *Id.*

[159] Westberry v. Gislaved Gummi AB, 178 F.3d 257, 265 (4th Cir. 1999) (citing Heller v. Shaw Indus., 167 F.3d 146, 156-57 (3d Cir. 1999)).

alternative cause is not the sole cause. For this situation to occur, the expert must be unable to give any reason why the purported cause was capable of causing the plaintiff's injury. In such a case, the expert's testimony would not make his or her proffered cause more likely to be true than without it.

IV. CONCLUSION

The different conclusions reached in evaluating scientific data and expert testimony in toxic tort litigation after *Daubert* demonstrates a marked confusion among the Federal Circuits. However, there are some axioms that are generally accepted among the circuits regarding the admissibility of such evidence. First, "[t]he ultimate goal of admissibility is helpfulness to the trier of fact."[160] Second, "an expert opinion must be based upon reliable methodology and must reliably flow from that methodology and the facts at issue – but it need not be so persuasive as to meet the party's burden of proof or even necessarily its burden of production."[161]

To meet admissibility requirements for specific causation, an expert must conduct a differential diagnosis after ruling in the suspected toxin and testify that the toxin was the cause of the plaintiff's disease, even if other potential causes exist that the expert cannot rule out.[162] The courts allow an expert to base his opinion on a properly-performed differential diagnosis. Federal Rule of Evidence 401 only requires an expert's testimony to make a contested fact more likely than it would have been without the testimony. An expert can comply with Rule 401 by proving the toxin's ability to cause the plaintiff's specific injury, regardless of what other potential causes exist.

The rules requiring an expert to conduct experiments proving that a chemical is capable of causing a plaintiff's injury, to quantify the plaintiff's duration and concentration of exposure, and to evaluate the plaintiff's exposure to the minimum dose-response level are essential to a court's evaluation of an expert's testimony on general causation, especially where the expert relies on complicated scientific experiments as the basis for the opinion. Experts often perform tests involving similar, but structurally different chemicals upon other species and explain how these results can be extrapolated to humans in a reliable manner.

Experts also conduct epidemiological studies and determine the statistical probability that a chemical is capable of causing a plaintiff's injury. Many courts routinely look to guidelines authored by the EPA and other regulatory agencies and traditionally followed by epidemiologists and toxicologists for guidance in determining whether these experiments were conducted in a reliable manner.

However, some courts have warned against relying upon regulatory

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[160] United States v. Velasquez, 64 F.3d 844, 850 (3d Cir. 1995).

[161] *Heller*, 167 F.3d at 152.

[162] *See In re* Agent Orange Product Liability Litigation, 597 F. Supp. 740, 781 (E.D.N.Y. 1984), *aff'd* 818 F.2d 145 (2d Cir. 1987).

positions in making inferences of causation. Judge Weinstein, in *In re Agent Orange Product Liability Litigation*, explained:

> The distinction between avoidance of risk through regulation and compensation for injuries after the fact is a fundamental one. In the former, risk assessments may lead to control of a toxic substance even though the probability of harm to any individual is small and the studies necessary to assess the risk are incomplete; society as a whole is willing to pay the price as a matter of policy. In the latter, a far higher probability (greater than 50%) is required since the law believes it unfair to require an individual to pay for another's tragedy unless it is shown that it is more likely than not that he caused it.[163]

While it is certainly true that a plaintiff would not be able to meet his or her burden of proof by a preponderance of the evidence if he or she was only able to show a minimal statistical causal correlation between the agent in question and his disease, courts use regulatory guidelines mainly to evaluate the reliability of the expert's methodology in compiling epidemiological and toxicological results. The expert must be able to show that the chemical in question, at the concentration level to which the plaintiff was exposed, was capable of causing the plaintiff's specific injury. This requires an expert to first provide test results that prove that a chemical can cause the specific disease in question in humans or animals.[164] After determining the chemical's ability to cause the disease, the expert quantifies the plaintiff's exposure and compares it to the amount determined through testing to be capable of causing the disease.

This method of determining general causation is recognized by guidelines authored by agencies such as the EPA and the IARC as important in determining which substances pose an increased risk of carcinogenicity to humans. The EPA recognizes that the goal of its guidelines is to determine whether a substance poses an increased risk of carcinogenicity in humans.[165] This determination does not require that the substance is shown to be more likely than not a carcinogen; it only requires that there be an increased risk to individuals exposed to the agent compared to that of unexposed individuals. In light of this, Judge Weinstein was right to say that the guidelines do not necessarily stand for a way to evaluate conclusively whether or not a particular substance can be proven "more likely than not" to be capable of causing a specific disease.

Nonetheless, such guidelines are not incapable of meeting such a burden of proof. The *Magistrini* court explained that relative risk is measured by a ratio

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[163] *Id.*

[164] If these tests are conducted on animals, the expert must reliably explain how he or she concluded that the positive correlation in the animal tests could equate to a positive correlation in humans, which is often done through an examination of the physiological similarities and absorption rates between the two species.

[165] *See* 51 F.R. 33993.

depending on the increased percentage of risk:

> Relative risk is commonly calculated by dividing the risk of developing a disease observed in an exposed group by the risk observed in an unexposed, but otherwise similar group. If the risks of the unexposed and exposed are the same, then the relative risk estimate is 1.0 . . . . Thus, a relative risk of 1.0 means that the agent has no effect on the incidence of disease . . . . [T]he threshold for concluding that an agent was more likely than not the cause of an individual's disease is a relative risk greater than 2.0.[166]

The guidelines recognize that a particular risk coefficient equates to a certain percentage of increased risk in humans from exposure to the chemical.[167] Thus the regulatory guideline is capable of helping a court determine, based on statistical percentages and risk coefficients that the expert calculates, whether a chemical more likely than not is capable of causing the plaintiff's specific injury.

Moreover, it is not inconsistent with *Daubert*, *Kumho Tire*, and Federal Rule of Evidence 702 for an expert to rely on statistical percentages, risk coefficients, and other probabilistic evidence in formulating an opinion on causation. *Daubert* requires an expert's testimony to be sufficiently reliable, which means it must be "scientifically valid."[168] To be scientifically valid, an expert's opinion must be "ground[ed] in the methods and procedures of science."[169] It is very uncommon for a toxicologist or epidemiologist to be able to predict with absolute certainty whether a particular substance is carcinogenic or otherwise dangerous to humans. As such, toxicologists and epidemiologists commonly rely on statistical percentages as a means of determining whether there is an increased risk of cancer or other illnesses from exposure to the toxin. This methodology is a hallmark of their respective professions. Therefore, it should be recognized by the courts as an appropriate methodology for an expert to rely upon.

Finally, and most importantly, permitting an expert to rely on such statistical probabilities allows many toxic tort plaintiffs to bring cases that they would not otherwise be able to bring due to their inability to prove causation. In this regard, the purpose of Justice Blackmun's opinion in *Daubert* has come to fruition for the benefit of toxic tort litigants. In *Daubert*, Justice Blackmun recognized "the 'liberal thrust' of the Federal Rules and their 'general approach of relaxing the traditional barriers to "opinion" testimony.'"[170] Restrictions on the use of probabilistic evidence are clearly at odds with Justice

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[166] Magistrini v. One Hour Martinizing Dry Cleaning, 180 F. Supp. 2d 584, 591 (D.N.J. 2002) (citing MICHAEL D. GREEN, ET AL., REFERENCE GUIDE ON EPIDEMIOLOGY, *in* REFERENCE MANUAL ON SCIENTIFIC EVIDENCE at 384 (Fed. Judicial Ctr. ed., 2d ed.2000)).

[167] *Magistrini*, 180 F. Supp. 2d at 591 (citing GREEN, *supra* note 166).

[168] Daubert v. Merrell Dow Pharms., 509 U.S. 579, 590 (U.S. 1993).

[169] *Id.*

[170] *Id*. at 588.

Blackman's "liberal thrust" declaration. In reality, such restrictions close the door on the lawsuits of many potential plaintiffs who may have been injured, including our old friend John Jackson. Even though Jackson may have a difficult time proving that it was more likely than not that the factory smoke was capable of causing and did cause his lung cancer because of his family history of cancer and his wife's history of smoking, the admission of statistical evidence showing an increased risk of cancer from the factory smoke will give him his day in court to try to prove his case.