

Twenty-first Century Toxicogenomics Meets Twentieth Century Mass Tort Precedent: Is There a Duty to Warn of a Hypothetical Harm to an “Eggshell” Gene?

Thomas Parker Redick*

I. INTRODUCTION

This article will focus on the potential liability of manufacturers of genotoxic compounds and radiation sources for genetic harm to consumers. In particular, I will address the potential for recovery of “fear of cancer” damages caused by alleged genotoxic harm, which involves a documented physical injury to a gene that has no clinical adverse effect (but may develop into cancer in the future). While there will be breakthroughs in public health policy through the intelligent and informed use of toxicogenomics — toxicological data that utilizes genomics to identify genes that are susceptible to injury from certain toxic substances, radiation, or other causes — the initial stages of toxicogenomic data collection could prove very risky to companies who do not warn of newly discovered genotoxic adverse effects of their products.

The United States has recognized the importance of toxicogenomics by establishing the National Center for Toxicogenomics (NCT) within the National Institutes of Environmental Health Sciences (NIEHS) — the umbrella organization taking genomic data and applying it to environmental toxins.¹ NIEHS is acutely aware of the potential impact that toxicogenomic data could have on consumers concerned about the risks of environmental toxins. This new data will present a challenge of epic proportions in effective hazard communication.

We will have a large amount of data that will be complex and confusing for awhile. We don’t want interest groups and the press using the data prematurely to frighten the American public or to misinterpret the data — we want the data used wisely. We want to be able to agree on what some of the scientific issues are and maybe organ-

* Thomas Parker Redick chairs the technology risk management practice group at Gallop Johnson & Neuman, L.C. in St. Louis, Missouri (www.gjn.com) and is Vice Chair of the Committee on Toxic Tort and Environmental Litigation for the American Bar Association’s Section on Environment, Energy & Resources (ABA SEER) (tpredick@gjn.com). Christina Galdos Bernstein at Maas, Miyamoto and Bernstein in San Diego, and Natasha L. Drew of Keller & Heckman in Washington, D.C. provided research assistance. I would also thank ABA SEER for permission and acknowledge prior publication of case law analysis cited in this paper in ABA SEER Committee newsletters.

1. See NAT’L INST. ENVTL. HEALTH SCI., SUMMARY DESCRIPTION OF THE NATIONAL CENTER FOR TOXICOGENOMICS, <http://www.niehs.nih.gov/dert/programs/tg-sum.htm> (last visited Feb. 20, 2003).

ize an “environmental court” or blue ribbon panel of experts to look at the data as they are being developed and interpret the information for the public and for policy makers.²

NIEHS has begun discussions with industry concerning what to do with the volume of new toxicogenomic information NIEHS will generate in the next ten years. NIEHS has indicated an interest in generating partnerships and friendships with various interested industries.

In the next decade and throughout the twenty-first century, evidence generated by the mapping of the human genome will expose many new links of causation that traditional epidemiology has left untouched.³ With research providing more refined analytical tools for identifying those who are susceptible and the alleged causes of their diseases, companies marketing hazardous compounds and potentially genotoxic products (including those emitting seemingly harmless non-ionizing radiation, such as electromagnetic fields) will need to monitor the literature carefully for potential adverse effects on genetically susceptible sub-populations. As this article will discuss, existing product liability law in some jurisdictions could hold the defendant marketing a product liable for harm caused to genetically susceptible persons, if that harm was reasonably foreseeable and a warning was feasible to deliver.

It is also clear that the regulatory system in the United States may not provide much protection for companies who fail to warn the genetically susceptible. Regulators who are made aware of a potential harm to the genetically susceptible will be compelled to act by *media* reports of human injury. This compulsion could lead to the sudden withdrawal of products, even if the vast majority of users find the product to be highly beneficial. The courts in the United States will be asked to make some difficult judgment calls on policy grounds, including:

- 1) Should the potential for injuries to a small subclass of potential users be sufficient grounds to deny the marketing of a product as a matter of existing environmental regulation (which does not mandate zero risk but allows “one-in-a-million” levels of carcinogenicity to slip through)?
- 2) If the answer to the foregoing question is “not necessarily,” then will a decision be made to market products with no warning to the genetically susceptible (who will not know that they are genetically susceptible without taking a genetic test, making

2. NAT'L ADVISORY ENVTL. HEALTH SCI., MINUTES OF THE NATIONAL ADVISORY HEALTH SCIENCES COUNCIL MAY 21, 2001 (report of the NIEHS director, Dr. Kenneth Olden), <http://www.niehs.nih.gov/dert/council/2001/may2001.htm> (last visited Feb. 20, 2003).

3. For a good medical text on genetic epidemiology independent of toxicogenomics (i.e., “alternative cause” genetic disorders), see *THE GENETIC BASIS OF COMMON DISEASES* (Richard A. King et al. eds., 2d ed. 1992).

it infeasible to warn)? Will this create a liability risk for the company involved?

The second issue illustrates the basic dilemma presented by toxicogenomic information in the context of a failure to warn. While toxicogenomic data from NIEHS will identify a class of users at risk, it will not identify each member of the class. As a result, companies will be in the distinctly uncomfortable position of knowing, to a reasonable degree of scientific certainty, that their product may be harming a small group of users.

If there is a significant threat of harm, a company faced with that knowledge will also have to analyze the potential for awards of punitive damages based upon their “conscious disregard” for the consequences of marketing their product (and the rights of this subclass of genetically susceptible users). In many cases, companies will make the decision to forego marketing products that may actually be very beneficial to the vast majority of users. This decision may occur in advance of any regulatory decision to recall the product. While some companies may be surprised to hear that they should act before regulators, this is the legacy left by a quarter century of jury verdicts determining federal regulatory standards to be a mere minimum level of protection.

In making this determination, companies should assess their product in light of the state of the science of toxicogenomics (i.e., has the hypothetical harm been adequately validated) and the state of the ever-changing law on: (1) medical monitoring or “cancerphobia” recovery and (2) the standard defenses in product liability law. I will review those defenses in the context of toxicogenomic data, addressing the “doubling risk” defense, the idiosyncratic reaction defense, the “state of the art” defense, and some recent motions on “general causation” using *Daubert/Frye*⁴ principles for excluding experts. I will conclude that the role of the courts in defining policy on toxicogenomics may prove paramount, as regulatory agencies struggle with the balancing of risks to a very few against the benefits to many.

The courts will become involved at two levels: (1) Pre-market surveillance of toxicogenomic risks — as the overseers of regulatory policy with power to strike down standards that are either inadequate or overly protective of the hypothetically genetically susceptible, and (2) Post-market surveillance — as gatekeepers for scientific evidence introduced in litigation alleging that a genetically susceptible person was actually harmed by a compound (including genetic injury that

4. *Weisgram v. Marley Co.*, 528 U.S. 440 (2000) (reasserting need to exclude unfounded expert opinions); *Gen. Elec. Co. v. Joiner*, 522 U.S. 136 (1997) (evaluating expert exclusion rulings under the deferential “abuse of discretion” standard); *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579 (1993) (establishing federal district courts as “gatekeepers” for expert testimony).

leads to an increased risk of getting cancer or other diseases in the future).

Judicial post-market surveillance may prove to be the superior form of "precaution" for compounds that present significant benefits and carry remote, highly hypothetical risks to small subclasses of people. In our current media-driven culture, however, where public health policies shift with the winds of public opinion, finding the optimum benefit of toxicogenomic knowledge may be difficult. To paraphrase Alexander Pope, a little knowledge is a dangerous thing; drink deeply, or not at all.⁵

This admonition does not apply solely to the courts and our regulators. When it comes to toxicogenomics, practicing lawyers will find that it is fairly easy to become completely swamped in the complexity of toxicogenomics, genetic epidemiology, and related scientific disciplines. It is not just the science itself, but the fact that the toxicogenomic approach brings mass torts down to the *individual* level. For those courts and attorneys that untangle this web of toxicogenomics (which breaks everything down to the level of individuals, subdividing groups of plaintiffs by genetic traits), the reward may be judicial opinions at the trial court level approaching the thousand-page mark.⁶

II. TOXICOGENOMICS: HOW TO HANDLE THE FIRST HUNDRED HYPOTHESES

As NIEHS and NCT begin to generate hypothetical links between genetic harm and toxic substances, companies producing the products in question will need to reassess their obligation to warn of adverse health effects. Workers who are exposed to levels previously deemed safe may need to reassess their likelihood of having the genetic susceptibility that NIEHS has uncovered. For their employers, difficult questions will arise about whether workers should be allowed to remain in a potentially risky position in the workplace.⁷ One employer took matters into its own hands, in a misguided effort to protect its workers from harm, only to find itself facing stiff fines.⁸

5. See ALEXANDER POPE, PASTORAL POETRY, AND AN ESSAY ON CRITICISM (Emile Audra & Aubrey L. Williams eds., 1961).

6. See, e.g., *In re Hanford Nuclear Reservation Litig.*, No. CY-91-3015-AAM, 1998 WL 775340 (E.D. Wash. Aug. 21, 1998) (containing 700 pages of dense scientific analysis).

7. See *Int'l Union v. Johnson Controls Inc.*, 499 U.S. 187 (1991) (holding that paternalistic company policy barring opportunities to women of child-bearing age to prevent harmful lead exposure violated Title VII, gender discrimination).

8. See Press Release, U.S. Equal Employment Opportunity Comm'n, EEOC Settles ADA Suit Against BNSF for Genetic Bias (Apr. 18, 2001), <http://www.eeoc.gov/press/4-18-01.html> (Burlington Northern allegedly conducted secret genetic tests of workers to keep them from toxicogenomic injury, violating rights of genetic privacy and committing unlawful genetic discrimination while trying to protect workers.).

First, a word about the technology platform that NCT will be using. There is a new class of products that allow “high throughput” screening for chemicals. Using “chips” that sort genetic material through various means, NCT will pick up genetic traits of interest that may be impacted by toxins. The technology is based on the use of DNA “microarrays,” small glass chips containing thousands of corresponding gene sequences that can probe the genetic activity of genes that were exposed to chemicals and drugs. This use of microarrays involves methodology that will be in need of validation over time.⁹

Second, careful attention should be paid to the emergence of toxicogenomic biomarkers for disease or exposure to toxins. Biomarkers can come in a variety of different forms. As NCT explains on its website, animal tests are notoriously limited in their applicability to human metabolisms, but toxicogenomics opens up the door to defining exactly which mechanisms in animals are affected by a toxin.¹⁰ If similar genetic mechanisms are in place in humans, then the risk can be documented with greater certainty than before (and ruled out in many cases for animal studies that were not confirmed by human epidemiology).¹¹

These toxic linkages could create possible “signatures” indicating damage in plaintiffs’ genes:

Careful data analysis could identify similar patterns in different species, leading to a “signature” for a given pathway of toxicity. Once signatures are identified using large scale, global microarray analysis, it will then be possible to develop smaller, multi-chemical and multi-pathway arrays that can be used to assess the potential toxicity of chemicals in a rapid, prospective manner. This would result in better interspecies extrapolation, greater confidence in animal models, reduction in the number of animals needed for testing, faster testing, and most importantly, insights into pathways of toxicity and their mechanisms.¹²

The use of the term “signature” in relation to “toxic pathways” should be more than enough to capture the attention of every toxic tort attorney in the United States.

A thorough review of the NCT’s website is recommended for readers interested in the technical details of toxicogenomics: the NCT defines and interprets the meaning of toxicogenomics for the lay audience.

9. See NAT’L INST. OF ENVTL. HEALTH SCI., MICROARRAY GROUP OF THE NATIONAL CENTER FOR TOXICOGENOMICS, <http://dir.niehs.nih.gov/microarray/home.htm> (last visited Apr. 4, 2003).

10. See SUMMARY DESCRIPTION OF THE NATIONAL CENTER FOR TOXICOGENOMICS, *supra* note 1.

11. NAT’L INST. OF ENVTL. HEALTH SCI., BIOMARKERS FACILITY CORE, <http://www.niehs.nih.gov/centers/fac-core/unc-fac3.htm> (last visited Apr. 4, 2003).

12. NAT’L INST. OF ENVTL. HEALTH SCI., THE NATIONAL CENTER FOR TOXICOGENOMICS, Sept. 5, 2000, <http://iccvam.niehs.nih.gov/methods/invidocs/NCTPaper.pdf>.

NCT's "Environmental Genome Project" will identify genes important in making people susceptible to environmentally induced diseases.¹³ They are funding studies linking genes to environmental toxins.¹⁴ Teams of "epidemiologists, biostatisticians, ethicists, molecular biologists experienced in using high through-put technologies, and toxicologists and/or other environmental health scientists" will undertake "molecular epidemiology studies of environmentally induced diseases, such as asthma, [and other respiratory diseases], birth defects, autoimmune diseases, and cancer" — to find a suspected genetic impact of chemicals, which may be posted on the Internet shortly after discovery.¹⁵

As new hypotheses emerge for genetic susceptibility, new toxic pathways will appear in the scientific literature as hypotheses. This may occur long before the scientific community is willing to accept these as indicators of environmentally-induced disease. Lawyers and carefully chosen experts will nevertheless take hypothetical genetic susceptibilities into court for the consideration of juries. A study should be undertaken to determine whether these hypotheses are leading to (1) precautionary regulatory decisions about products, or (2) jury verdicts or major settlements of toxic tort litigation arising from a hypothesis of genetic susceptibility.

III. GENOMICS AND THE PREVENTION OF HARM

The focus of toxicogenomic research is necessarily on prevention of harm — by knowing toxic pathways, steps can be taken to prevent exposures leading to harm. Some of the first great success stories in toxicogenomics will emerge from the clinical trials of new drugs that pose a risk of adverse effects to certain genetically susceptible individuals. As those genes for susceptibility are detected, the protocol for administering the drug will add a genetic test for screening out the genetically susceptible.

Against this backdrop, the question arises — where do we draw the line for such genetic screening? Should all pharmaceuticals have similar screening? All chemicals? If not, would the law of strict product liability find such companies failing to conduct the necessary testing liable for failing to warn?

13. NAT'L INST. OF ENVTL. HEALTH SCI., ENVIRONMENTAL GENOME PROJECT, <http://www.niehs.nih.gov/envgenom/> (last visited Feb. 20, 2003).

14. See NAT'L INST. OF ENVTL. HEALTH SCI., PLANNING GRANTS FOR MOLECULAR EPIDEMIOLOGY IN THE ENVIRONMENTAL GENOME PROJECT, <http://grants.nih.gov/grants/guide/rfa-files/RFA-ES-01-005.html> (last visited Feb. 20, 2003) [hereinafter PLANNING GRANTS].

15. *Id.* For an example of such a study, see University of Washington Genome Center Repository of Candidate-Gene Polymorphisms for Environmental Genome Project (EGP), <http://www.genome.washington.edu/projects/egpsnps/> (last visited Feb. 20, 2003).

A. *Genomics and Medicine Set the Stage for the Duty to Warn*

The mapping of the human genome will provide immediate benefits in the treatment of cancer. In addition to illuminating the mechanisms for cancer (which will assist experts in proving medical causation from environmental influences), genomic data will be used to screen out genetically susceptible individuals who might have an adverse reaction to a drug.¹⁶

This newfound ability to trace specific causation of idiosyncratic genetic harm *before* it occurs would clearly pose a paradigm shift of epic proportions for the duty to warn of hazardous substances. Throughout the history of chemical regulation and litigation, the latency period and complexity of cancer causation precluded action by chemical companies on specific causation of harm to individuals. After epidemiological causal evidence was clear, then companies knew enough to merit a warning. Now that the state of the art technology for tracing cancer causation is moving toward a model that allows prophylactic action to stop specific adverse events, the question of “when to warn” takes on a new dimension.

While genetic testing to avoid harm to the genetically susceptible may be feasible to implement in clinical trials, the cost of testing all the persons possibly exposed to radiation or chemicals marketed widely in the U.S. would be prohibitive. As a result, many companies that market or use potentially genotoxic chemicals or radiation (including electromagnetic, non-ionizing forms) will be faced with the potential threat of liability for “failing to warn” the genetically susceptible of a potential threat to their health.

For those companies willing to incur the cost, the biotechnology industry’s new branch — toxicogenomic testing services — will step forward to assist in the detection of toxicity at an early stage in product development. Unfortunately, however, there is no guarantee that persons at risk would willingly submit to genetic testing. Without a genetic test, those who are susceptible will remain ignorant of that risk.

A more likely scenario, under the current legal precedents in place in many jurisdictions, will be the payment of medical monitoring awards — in cash — to plaintiffs who claim that their minimal exposure to chemicals caused detectable and compensable harm to their genes (harm that could lead in the future to cancer if they are not carefully monitored for cancer’s onset). It is this particular avenue of recovery that this paper will address. In a brave new world where

16. See *Nat’l Inst. of Health, Before the Senate Health, Educ., Labor and Pensions Comm.*, 107th Cong. (2001) (testimony of Francis Collins, M.D., Ph.D., Director, National Human Genome Research Institute), <http://www.hhs.gov/asl/testify/t010725b.html> (last visited Feb. 20, 2003).

genetic harms can be detected, will new fears of future cancer lead plaintiffs to allege a failure to warn of known toxicogenomic risks?

B. *Chemical Regulation and Genetic Harm From Toxic Substances*

The first question that must be addressed, as we evaluate the risks of cancerphobia litigation arising from toxicogenomic data, is the type of genetic harm that can be documented. As a brief tour of the World Wide Web will show, genomics will not just be used to cure diseases, but also to track down the chemical culprits that are allegedly *causing* diseases. This impending deluge of toxicogenomic data may transform existing legal frameworks for environmental regulation and toxic tort liability. Those companies and other stakeholders with interests in chemical health effects will increasingly use toxicogenomic data in “mechanistic” approaches to existing toxic substances (e.g., to reclassify substances as known carcinogens, as recently occurred to dioxin).¹⁷

This regulatory decision has been soundly criticized for allowing federal agencies far too much discretion in branding particular chemicals as known carcinogens.¹⁸ Despite this brewing dispute over the ability of regulatory agencies to use mechanistic approaches to classifying carcinogenic compounds, it appears certain that an increasing number of genetic tests will be developed for specific chemical interactions. In fact, such tests for biomarkers may be marketed long before scientific studies prove the hypothetical link to disease.

As a result, the genetic revolution in medicine may be preceded by a genetic revolution in medical causation for toxic tort plaintiffs. Litigation may drive faster acceptance of a gene/chemical hypothesis by the regulatory community with medical literature and regulatory action trailing far behind the science performed in pursuit of mass tort rewards.

IV. TOXICOGENOMICS AND THE MASS MEDIA: ERIN BROCKOVICH’S BLUE GENES

If new toxicogenomic data suggests harm to “eggshell genes” (i.e., genetic susceptibilities), plaintiffs’ attorneys in the U.S. may increasingly file mass tort “fear of cancer” lawsuits against chemical companies, alleging that genetically susceptible potential subclasses

17. See, e.g., *Tozzi v. U.S. Dep’t of Health & Human Servs.*, 271 F.3d 301, 311 (D.C. Cir. 2001) (endorsing the use of a mechanistic approach to proving dioxin has carcinogenic properties and holding that the Secretary of Health and Human Services did not act arbitrarily in finding dioxin to be a “known” carcinogen without epidemiology to support that decision).

18. See Alan Charles Raul & Julie M. Zampa, *Deeper Judicial Scrutiny Needed for Agencies’ Use of Science*, LEGAL BACKGROUND (Washington Legal Foundation, Washington, D.C.), Jan. 25, 2002 (providing a critique of “mechanistic” approach to causation).

were not warned of potential harm. Their experts might also make use of genetic testing to establish biomarkers in damaged genes.¹⁹ Pairing a biomarker with a susceptible genotype, genetic tests could reveal alleged DNA damage.²⁰

If NIEHS needs a preview of the media's treatment of the "toxicogenomic gene of the month club" that may arrive with the publication of their toxicogenomic hypotheses, they need only stop by the video store and rent *Erin Brockovich*²¹ for the evening. In this Academy-award-winning film, the word "genes" appears twice — once for the defense and once for the plaintiffs. As will often occur in real life, neither side has any scientific foundation to say that the cancer in question was caused by toxicogenomic impact.

First, the defense attorney in the movie smugly informs Erin Brockovich (as played by Julia Roberts) that the health problems the plaintiffs are suffering from were caused by diet or "bad genes" — reflecting genetic "alternative cause" theories. Unfortunately for defense counsel, in the cases that followed the settlement featured in the film, the defense theory of "bad genes" ran aground upon a discovery referee's decision to limit the scope of discovery to the medical records of family members within the first degree of genetic relation.²² Such a narrow scope precluded the thorough inquiry into family history that a genetic alternative cause defense required.²³ As new genetic causes of ordinary, everyday, non-toxicogenomic health problems are revealed by genomic data, defense attorneys will increasingly turn to genetic theories to demonstrate an alternative cause for the alleged injury.

Genes make their second cameo appearance when Erin Brockovich's academic toxicology expert tells her that the compound in question "gets in your genes; you pass it on to your kids." This particular genetic theory was actually adjudicated against Erin's clients in the litigation that followed the settlement featured in the film. Judge Rothschild of Los Angeles County Superior Court dismissed all pre-

19. See, e.g., Howard Marks, *Electromagnetic Forces From Overhead High-Voltage Transmission of Electricity: Establishing Causation Using Toxicological and Epidemiological Evidence Under a Post-Daubert Standard*, 13 J. ENVTL. L. & LITIG. 163, 180-83 (1998).

20. *Id.*

21. ERIN BROCKOVICH (Jersey Films 2000).

22. The author lost a motion to compel genetic evidence from second-degree relatives (e.g., grandfather) from plaintiffs involved in the Hinkley and Kettleman litigation against Pacific Gas & Electric (PG&E) in a motion heard by Discovery Referee Howard Weiner in March 2000 in *Aguayo v. Betz* (L.A. County Super. Ct). The opinion was not recorded.

23. The tactical implications of raising a "genetic alternative cause" defense can be daunting. For practicing attorneys in search of guidance on genetic testing and expert testimony, see Thomas Parker Redick & Christina Galdos Bernstein, *Genetics and Epidemiology Evidence in Environmental Regulation and the Courtroom: Beware the Genome Gnomes*, 2002 SPECIAL COMM. ON SCI. & TECH. NEWSL., A.B.A. SEC. ON ENERGY, ENV'T & RESOURCES 10, available at <http://www.abanet.org/environ/committees/sciencetech/newsletter/may02/redick.html> (last visited Feb. 20, 2003).

conception plaintiffs (whose claims were based on genetic damage to parental egg or sperm) on summary judgment.²⁴ In an unpublished appellate decision, the court of appeals affirmed the dismissal of all “pre-conception” plaintiffs on the grounds that public policy and current science could not permit the claims to go forward.²⁵ As a matter of law, the compound in question did not get into anyone’s genes, nor was it passed on to the children involved.

Toxicogenomics could help to push the boundaries of science into “intergenerational” liability waters in the future. Courts are ill-equipped to handle intergenerational claims, however, given the daunting policy-making and scientific challenges. Courts will presumably hesitate before daring to open the litigation floodgates to multiple generations of claimants with the inevitable evidentiary challenge inherent in litigating a cancer case that alleges causation based on conduct that occurred many decades in the past (e.g., through exposures to a parent or grandparent).

In the courts, where mass torts are often filed based on hypothetical scientific evidence, the media also plays a role in promoting certain hypothetical harms long before they are recognized by leading scientists in the particular field of inquiry.²⁶ The Brockovich litigation (which is still ongoing despite the bankruptcy filing of Pacific Gas & Electric) illustrates how a company can be held liable for “cancerphobia” damages for failing to warn of a hypothetical risk of cancer with the news media drumming up plaintiffs.

While the power of media investigation can be invaluable in uncovering wrongs, it can also lead to unintended consequences when the hype of a good story outpaces the science behind the lawsuit. As Justice Stephen Breyer stated in his book, *The Vicious Circle*, our environmental regulatory system is imperfect in its tendency to overreact to certain risks and underreact to others.²⁷ This process, which Justice Breyer calls “the vicious circle,”²⁸ too often leads to misallocated regulatory resources. Moreover, plaintiffs’ attorneys routinely argue to juries and judges, whenever compliance with regulatory standards are interposed as a defense in chemical exposure cases, that such standards provide a *minimum* level of protection that often (1) is based on outdated scientific evidence, (2) is biased by industry influ-

24. Thomas Parker Redick, *Genetics and Epidemiology in Environmental Regulation and the Courtroom: Beware the Genome Gnomes*, at <http://www.gjn.com/FSL5CS/pressroom/pressroom91.asp> (last visited Mar. 3, 2003) (discussing the unreported case of *Adams v. Pacific Gas & Electric*).

25. *Id.*

26. See, e.g., “Erin Brockovich,” *Affirmed*, WALL ST. J., Apr. 6, 2000, available at <http://www.fumento.com/brocklett.html> (last visited Jan. 13, 2002).

27. See STEPHEN BREYER, *BREAKING THE VICIOUS CIRCLE: TOWARD EFFECTIVE RISK REGULATION* (1993).

28. *Id.*

ences, and (3) at its very best, fails to take into account the more susceptible elements of the population (e.g., children, zygotes, the elderly, the immune-compromised, women, and the unwittingly careless).

As a result of these imperfections in the regulatory and judicial systems, toxicogenomics is entering a world that seems ripe to engage in media-driven controversies over alleged harm to hypothetically genetically susceptible persons. In particular, the prospect of uncovering links to harm that is done to children seems certain to ring bells in media establishments around the U.S. The essential ingredients for a good story will be found wherever there is a scientific expert willing to point to some hints of the hypothetical harm in scientific literature, which will be used to suggest that the corporation in question acted in “conscious disregard” of genetically susceptible persons.

V. FEAR OF CANCER CLAIMS IN THE AGE OF TOXICOGENOMICS

Cancer fears have been compensable for many years in various jurisdictions for incidents involving intentional acts.²⁹ Long before the biological mechanisms of carcinogenesis were well understood, fear of cancer claims made their appearance in the occasional case.³⁰ Typically, a person’s likelihood of developing cancer or other future illnesses as a result of toxic exposure is difficult to predict, as many forms of cancer involve long latency periods and development depends on interrelation of many factors.³¹

Commentators saw the deluge coming and cautioned against arbitrary decisions based on bad facts.

It is difficult to go a week without news of toxic exposure. Virtually everyone in society is conscious of the fact that the air they breathe, water, food and drugs they ingest, land on which they live, or products to which they are exposed are potential health hazards. Although few are exposed to all, few also can escape exposure to any.³²

29. See, e.g., *Alley v. Charlotte Pipe & Foundry Co.*, 74 S.E. 885, 886 (N.C. 1912) (stating that cancer fear is a “Sword of Damocles” hanging by a thread over plaintiff).

30. See, e.g., *Ferrara v. Galluchio*, 152 N.E.2d 249 (N.Y. 1958).

31. Since the inception of the modern era in environmental law, the occasional commentator has suggested that up to 90% of cancers could have *some* link to environmental and dietary factors. See J. Higginson, *Importance of Environmental Factors in Cancer*, in ENVIRONMENTAL POLLUTION AND CARCINOGENIC RISKS 15, 17 (1976) (defining environmental as not being caused by genetics — includes both naturally occurring and man-made carcinogens). With the courts finding tiny comparative fault percentages sufficient to establish “causation” in some cases, toxicogenomics opens up the potential for a wide array of products to be implicated in cancer causation. See, e.g., *Rutherford v. Owens-Illinois, Inc.*, 941 P.2d 1203 (Cal. 1997).

32. Terry Morehead Dworkin, *Fear of Disease and Delayed Manifestation Injuries: A Solution or a Pandora’s Box?*, 53 *FORDHAM L. REV.* 527, 576 (1984).

With advances in diagnostic research involving the genetic triggers for cancer and the explosion of mass torts cases involving asbestos, however, “fear of cancer” cases began to emerge in the toxic tort arena.³³

The seminal case opening the door to medical monitoring for fear of cancer based upon genetic damage from a hazardous chemical is *Ayers v. Jackson Township*.³⁴ In *Ayers*, over 300 plaintiffs alleging exposure to toxic substances in drinking water (leading to a “genetic switch” ready to turn cancerous in the future) were allowed to recover medical monitoring costs based on a largely unquantified excess risk substantiated by expert opinion about a reasonable likelihood of future illness.³⁵

As the permissible scope of recovery for fear of future illness expanded along with the research allowing expert opinions to create a reasonable fear of future illness, courts began expressing concern about opening the floodgates of litigation should such claims become widely available. As a result, the Supreme Court of California, in *Potter v. Firestone Tire & Rubber Co.*,³⁶ made a policy decision: (1) to allow broad recovery for medical monitoring (with minimal and largely unspecified medical causation standards) where defendant acted with fraud or malice, while it simultaneously (2) limited recovery for future risks based on *negligent* conduct causing chemical exposure and resulting emotional distress lacking any physical injury.³⁷

The *Potter* decision involved exposure to residents living near a disposal site that was improperly used for disposal of Firestone’s hazardous waste. From 1963 to 1980, Firestone operated a tire manufacturing plant near Salinas. In 1967, Firestone contracted with Salinas Disposal Service (SDS) and Rural Disposal, two companies operating the Crazy Horse Landfill. Firestone agreed to deposit its industrial waste in canisters provided by SDS located at the plant site, and SDS agreed to haul the waste to the Crazy Horse site.³⁸

At the outset of their contractual relationship, SDS informed Firestone that it did not allow dumping of toxic wastes at the landfill because groundwater would be contaminated. Firestone gave assurances it would not send toxics to the landfill; however, its plant manager still sent large quantities of liquid toxic waste to the landfill.³⁹

In May of 1977, Firestone’s plant engineer in charge of environmental matters sent a memo to department heads about the proper

33. See, e.g., *Devlin v. Johns-Manville Corp.*, 495 A.2d 495 (N.J. Super. Ct. Law Div. 1985) (discussing fear of asbestos-related cancer).

34. 525 A.2d 287 (N.J. 1987).

35. *Id.* at 308-15.

36. 863 P.2d 795 (Cal. 1993).

37. *Id.* at 800-01.

38. *Id.* at 801.

39. *Id.*

disposal of liquid wastes, detailing legal disposal methods under California law. When compliance with proper procedures proved too costly, noncompliance became widespread. In 1984, the owners of property near the landfill discovered toxic chemicals in their home water wells and sued Firestone, seeking medical monitoring and damages for emotional distress, based upon their fear of future cancer.⁴⁰

The California Supreme Court in *Potter* set forth the following tests for fear of cancer claims:

[I]n the absence of a present physical injury or illness, damages for fear of cancer may be recovered only if the plaintiff pleads and proves that:

- (1) as a result of the defendant's negligent breach of a duty owed to the plaintiff, the plaintiff is exposed to a toxic substance which threatens cancer; and
- (2) the plaintiff's fear stems from a knowledge, corroborated by reliable medical or scientific opinion, that it *is more likely than not* that the plaintiff will develop cancer in the future due to toxic exposure.⁴¹

As an exception to the general rule, in the absence of physical injury or illness, damages for negligently inflicted emotional distress may be recovered without meeting the "more likely than not" threshold if the plaintiff pleads and proves that:

- (1) as a result of the defendant's negligent breach of a duty owed to the plaintiff, he or she is exposed to a toxic substance which threatens cancer;
- (2) the defendant, in breaching its duty to the plaintiff, acted with oppression, fraud or malice as defined in Civil Code section 3294; and
- (3) the plaintiff's fear of cancer stems from a knowledge, corroborated by reliable medical or scientific opinion, that the toxic exposure caused by the defendant's breach of duty has significantly increased the plaintiff's risk of cancer and has resulted in an actual risk of cancer that is significant.⁴²

The court further stated that medical monitoring "costs are a compensable item of damages in a negligence action where the proofs demonstrate, through reliable medical expert testimony, that the need for future monitoring is a reasonably certain consequence of the plaintiff's toxic exposure and that the recommended monitoring is reasonable."⁴³

The standard of "more likely than not" (i.e., 51% probability of future disease) for mere negligence is a very difficult one to meet given current scientific limits on predicting causation in particular individuals. Even with the advent of toxicogenomics, the risk of cancer

40. *Id.*

41. *Id.* at 816 (emphasis added).

42. *Id.* at 818.

43. *Id.* at 800.

actually occurring from genetic damage caused by carcinogens may never rise to over 50%. For example, the risk level for long term tobacco use, which has many known carcinogens, is generally considered to be less than 50%.⁴⁴

This 51% barrier to proof does not apply, however, in the context of the “malice” exception to the *Potter* doctrine, which allows recovery of medical monitoring for mere “significant risk” (a concept not well-defined in the decision or subsequent cases).

Once the plaintiff establishes that the defendant has acted with oppression, fraud or malice, the plaintiff must still demonstrate that his or her fear of cancer is reasonable, genuine and serious in order to recover damages. In determining what constitutes reasonable fear, . . . it is not enough for a plaintiff to show simply an ingestion of a carcinogen or a significant increase in the risk of cancer. In addition, the plaintiff must show that his or her actual risk of cancer is *significant* before recovery will be allowed (footnote omitted). Under this reasoning, a plaintiff’s fear is not compensable when the risk of cancer is significantly increased, but remains a remote possibility.⁴⁵

While the plaintiffs asked for “doubling risk”⁴⁶ as the standard for what is significant, the court in *Potter* did not define its scientific standard for “significant risk.”

The *Potter* court also discussed at length the public policy concerns underlying its decision to deny easy recovery for mere negligent failure to warn. Recognizing the “indisputable fact that all of us are exposed to carcinogens every day,” the court first noted that all of us are potential fear of cancer claimants.⁴⁷ Therefore, the more likely than not limit for mere negligence helps address the tremendous societal cost of otherwise allowing emotional distress compensation to a potentially unlimited class of plaintiffs.

A second policy concern weighing in favor of the 51% threshold was the unduly detrimental impact that unrestricted fear of cancer liability would have in the health care field. In particular, the supreme court recognized amicus curiae California Medical Association’s point that “access to prescription drugs is likely to be impeded by allowing recovery of fear of cancer damages in negligence cases without the imposition of the heightened threshold.”⁴⁸ This explicit recognition of the benefits to many, despite harm to a few, may prove helpful in cases featuring idiosyncratic reactions (i.e., a rare toxicogenomic

44. For example, the author has observed public health advertising billboards in Illinois that estimated the risk of tobacco-related death from such use at 3-to-1 odds.

45. *Potter*, 863 P.2d at 818 (emphasis added).

46. See Section IV-A *infra*.

47. *Potter*, 863 P.2d at 811-12.

48. *Id.* at 812.

harm). It also stands as a judicial recognition of the threat to innovation in pharmaceuticals that “fear of future disease” cases pose.

The third policy concern considered is that allowing recovery to all victims who may reasonably fear cancer could ultimately work to the detriment of those who sustain actual physical injury and develop cancer as a result of toxic exposure. If the same recovery of \$800,000 allowed to four plaintiffs in *Potter* were similarly allowed in large class actions, the numbers for this one type of injury alone would be staggering.⁴⁹

A fourth reason given by the supreme court focused on predictability and consistency of results. Here, the court noted that the more likely than not probability limitation establishes a sufficiently definite and predictable threshold for recovery to permit consistent application from case to case. Such a definite threshold may also contribute to early resolution or settlement of claims.⁵⁰

Finally, the court recognized that the more likely than not standard may foreclose compensation to individuals with genuine and objectively reasonable fears (i.e., those who have undergone genetic testing and know themselves to be at risk from exposure to the compound in question). As a result, it is sometimes necessary to “limit the class of potential plaintiffs if emotional injury absent physical harm is to continue to be a recoverable item of damages in a negligence action.”⁵¹

While the court limited claims arising in *negligence*, it left the door open for any “significant” risks – including harm to a genetically susceptible subclass – that can prove a reckless or intentional failure to warn them, or a similarly reckless violation of regulations.

VI. TOXICOGENOMICS AND TYPICAL TOXIC TORT DEFENSES

Companies considering whether they have a duty to warn of a toxicogenomic hypothesis should evaluate the potential claims in light of existing defenses to toxic tort liability.

A. *The “Doubling Risk” Defense*

In recent years, epidemiology and the law have combined to create the doubling risk concept.⁵² This is the defense attorney’s bright

49. *Id.* at 813-14.

50. *Id.*

51. *Id.* (citing *Thing v. La Chusa*, 771 P.2d 814 (Cal. 1989)).

52. Doubling risk means that if the background is 10 per 1 million, and the risk doubles from exposure to 20 in 1 million, then the risk has doubled and all 20 people before the court have a 50/50 chance of being the one who was injured by chemicals (but only 10 are really sick from chemical exposure). This is arbitrary, since a relative risk at 15 would not let *any* recover because all might be background cancers (a cluster). It also gives a windfall to the 10 people above who are part of the background, the legal equivalent of a lotto ticket. With the advent of

line for medical causation in tort law epidemiology. Many courts have embraced the idea.⁵³ As noted above, plaintiffs' attorneys in *Potter* endorsed this standard for recovery under the malice exception's "significant risk" standard.

As a result, both defense experts and experts for plaintiffs will increasingly be moving toward use of genetic susceptibility data in proving toxic tort causation, to avoid application of the "doubling risk" standard for pretrial screening of toxic tort claims. A recent article in *Jurimetrics* by Sander Greenland and James Robins points toward a new approach that plaintiffs' experts could take in establishing causation, using "genotype stratification" to establish medical causation for susceptible groups.⁵⁴ This appears to be a clever way to avoid a doubling risk defense to claims where medical causation is based on small increases in cancer risk because the courts generally require at least two times the background risk for a disease before they recognize increased risk under the more likely than not standard for medical causation.

Greenland and Robins suggest in a hypothetical that a relative risk of 2 may be subdivided into separate risk groups of 3 and 1.5 using toxicogenomic evidence. These experts point out that some subgroups making up the study population would be at 3 times relative risk, while others would be at 1.5 (under the doubling risk requirement). Greenland and Robins suggest that it would be unfair and arbitrary that some recover and others do not, simply because we do not fully understand the mechanism of causation.⁵⁵

Doubling risk as a judicial sorting device is admittedly crude, since a genetically susceptible person might fall through the cracks.⁵⁶ Doubling risk motions can reward the unworthy in some cases, while denying recovery to the worthy in other cases. For example, doubling risk would require, for a group of 100,000 persons, some proof that a background incidence of 100 cancers has doubled to 200 probable cancers in the exposed population. The reason for this is simple — the

genotype stratification, however, there are now tools for finding causation in a more precise manner (so that the eleventh through fifteenth persons would be compensated — but not the other ten who are background).

53. The case law relating to the use of epidemiology to prove causation is varied and complex. For a thorough review of the case law, see FREDERICK T. SMITH, *DAUBERT AND ITS PROGENY: SCIENTIFIC EVIDENCE IN PRODUCT LIABILITY LITIGATION* (2000).

54. Sander Greenland & James M. Robins, *Epidemiology, Justice, and the Probability of Causation*, 40 *JURIMETRICS J.* 321, 335 (2000). Greenland and Robins, who disclose their roles as plaintiffs' toxic tort experts in footnote five of their article, reason that "upon stratification by a given genotype, this ratio becomes 3 at each genotype level" in concluding that the subclass of genetically susceptible can be revealed as harmed through their analytical techniques. *Id.*

55. *Id.*

56. This may lead some courts to use doubling risk as only one factor to consider, with other factors entering in to permit causation to be proved even where doubling risk is lacking. See, e.g., *In re Joint E. & S. Dist. Asbestos Litig.*, 52 F.3d 1124, 1134 (2d Cir. 1995).

court will not know which of the persons with cancer before it are imposters if there are only 150 cancers. About 100 of these cancers will be part of the “background incidence” of cancer, while 50 were possibly caused by the chemical in question. The odds of one person having the cancer caused by the chemical will be much less than 50%, not within the “preponderance of evidence” standard for proof.

With genetic susceptibility evidence, however, an expert can employ genotype stratification and separate the genetically susceptible into a subclass. From a group of 100,000 persons, there might be twenty-five genetically susceptible persons who can show excess risk (2x background) from chemical exposure. These people can show doubled risk if the class is narrowed by excluding those who are not genetically susceptible. Thus, even if the risk is still marginal (i.e., just above the doubling risk for the genetically susceptible), it represents a risk that would have been lost in the haystack of the 100,000 people. As a result, this refinement in doubling risk analysis creates a fairer, more efficient system.

Genetic testing to establish a susceptible genotype could also be paired with the use of genetic tests revealing alleged biomarkers in damaged genes.⁵⁷ DNA damage has an increasingly long and controversial history in toxic tort litigation. Pairing the damage with a genetic susceptibility, plaintiffs would present expert testimony of both the eggshell gene and the biomarker that could break it. For example, a genetic deficiency in the ability to repair DNA could provide a plaintiff with sufficient evidence to challenge existing limitations on recovery for fear of cancer in some jurisdictions.⁵⁸

Since *Potter* did not set a standard for cancer fears being “significant” under the malice exception, the plaintiffs in that case asked the court for a “doubling risk” standard for viable medical monitoring claims. As a result, the future medical monitoring case law may see the endorsement of doubling risk for particular genetic subclasses, who would then be entitled to medical monitoring.

Before a new, potentially toxic product is marketed, the company marketing the product should conduct studies to determine if doubling risk is exceeded for a particular subgroup of persons who will be exposed.

57. See, e.g., Marks, *supra* note 16, at 181.

58. See, e.g., *Potter v. Firestone Tire & Rubber Co.*, 863 P.2d 795 (Cal. 1993) (holding that plaintiffs negligently exposed must meet fifty-one percent probability of cancer, while fraud or malice allows monitoring damages where there is merely a “significant” risk). For further analysis of the issues involved in endocrine disruption and medical monitoring case law, see Thomas P. Redick et al., *Fear of Endocrine Disruption in the Workplace*, 14 NAT. RESOURCES & ENV'T 231 (2000) (discussing defense of OSHA preemption to biomarker-driven fear claims).

B. *The Idiosyncratic Reaction Defense*

A genetic susceptibility that is neither known nor readily knowable at the time of exposure provides an opportunity for alleging the idiosyncratic reaction defense to negligence and strict liability claims. Under this defense, the proximate cause of the injury is attributed to the unforeseeable idiosyncrasy or allergy of the plaintiff, not the defendant's failure to warn. The idiosyncratic reaction defense can provide defendants with a theory to avoid or significantly limit their liability by arguing that plaintiffs' injuries occurred because a particular plaintiff was especially and unforeseeably sensitive to a substance, chromium. Under both negligence and strict product liability failure to warn theory, a defendant need only warn about dangers that it knew or should have known about.

One of the essential elements of negligence liability is knowledge of the dangers involved. If the manufacturer actually knows or should know, in the exercise of reasonable care, of the dangerous character of the product, it is liable for failure to warn under negligence principles. A manufacturer or seller is "negligent if he fails to warn the ignorant of the hidden danger" in a product when he knows that the product might be dangerous to some members of the population (even if the susceptible group is a small minority of society).⁵⁹

Other courts have similarly recognized that a manufacturer may only be subject to liability for negligent failure to warn when it has "actual knowledge that its product might cause harm to an identifiable class of sensitive users or if, based on the state of scientific knowledge, it is chargeable with such knowledge."⁶⁰ In *Adelman-Tremblay v. Jewel Cos.*,⁶¹ the plaintiff alleged injuries resulting from application of artificial fingernails with the defendant's kit. The Seventh Circuit, deciding the case under Wisconsin law, found that in a *majority of jurisdictions* in 1988 there was no duty to warn of the possibility of a rare and unusual allergic reaction.⁶² The inquiry should turn upon whether the defendant knew or should have known about the effect the product had on the plaintiff, and knowledge may be limited.

The rule barring the idiosyncratic consumer from recovery generally applies whether suit is brought under strict liability, breach of warranty, or negligence.⁶³ The unusual susceptibility of the consumer was traditionally recognized as a complete defense where the manu-

59. *Proctor & Gamble Mfg. Co. v. Superior Court*, 268 P.2d 199, 202 (Cal. Ct. App. 1954).

60. *See, e.g., Adelman-Tremblay v. Jewel Cos.*, 859 F.2d 517, 522 (7th Cir. 1988).

61. *Id.*

62. *Id.* at 521.

63. *Presbrey v. Gillette Co.*, 435 N.E.2d 513, 520 (Ill. App. Ct. 1982) (citing WILLIAM PROSSER, *LAW OF TORTS*, §§ 96, 102 (4th ed. 1971)).

facturer had no reason to know that a very few users of his product might be injured.⁶⁴

California's traditional idiosyncratic reaction defense is set forth in *Oakes v. E.I. Du Pont de Nemours & Co.*⁶⁵ The court in *Oakes* affirmed the trial court's grant of a demurrer where the complaint failed to allege that the defendant *knew or should have known* that its weed killer could cause a reaction in allergic people. In *Oakes*, the manufacturer included a warning on the product to avoid exposure. The warning in *Oakes* stated the following: "Caution! May cause irritation of eyes, nose, throat, and skin. Avoid breathing dust or spray mist. Avoid contact with skin, eyes and clothing."⁶⁶ The court found that the manufacturer was not required to include specific warnings of unknown potential risks or side effects.⁶⁷ The defendant facing evidence of genetic susceptibility could be found to have had a duty to warn of known or knowable risks of allergies, but they did not have a duty to warn of unknown or unknowable potential idiosyncratic reactions.⁶⁸

In *Gober v. Revlon*,⁶⁹ a Fourth Circuit case applying California law, the court found that a defendant manufacturer could be subject to liability if they knew (or should have known) about a potentially dangerous allergic reaction.⁷⁰ The *Gober* court's decision to find liability for a susceptible subclass is premised upon the knowledge of the manufacturer that a class of persons could be allergic and exposed to a toxin without being warned about the risk of allergic reaction.

Several recent decisions in Illinois appear to be consistent with the *Oakes* holding. In *Goldman v. Walco Tool & Engineering Co.*,⁷¹ the plaintiff, a parts inspector for Caterpillar, was exposed to a rust preventative oil when he placed his hand in a bag containing the oil while inspecting a part manufactured by defendant.⁷² The plaintiff claimed multiple injuries resulted from the contact. Defendant received the oil from Mobil in 55-gallon drums with warning labels affixed to the drums. Defendant then used the oil in the packaging of their parts but placed no label on either the parts' bags containing the oil or the box in which the bags were shipped.⁷³

64. *Id.*

65. 77 Cal. Rptr. 709 (Cal. Ct. App. 1969).

66. *Id.* at 711.

67. *Id.* at 713.

68. *Id.*

69. 317 F.2d 47 (4th Cir. 1963).

70. *Id.* at 50. This case was decided six years prior to *Oakes*. The *Gober* opinion is consistent with *Oakes* because both cases require that defendant knew or should have known of the potential idiosyncratic or allergic reaction in plaintiff.

71. 614 N.E.2d 42 (Ill. App. Ct. 1993).

72. *Id.* at 44.

73. *Id.* at 45.

At trial, the defendant's expert opined that the plaintiff's condition was the result of an idiosyncratic reaction and that his medical problems were ongoing and genetic.⁷⁴ The court distinguished this case from others involving the idiosyncratic reaction defense because this case involved an inherently dangerous chemical instead of an "over the counter" consumer product.⁷⁵ While the court did not substantially change its analysis, it also noted that in recent years the rule of non-liability for idiosyncratic reactions has been relaxed.⁷⁶ In ruling for the plaintiff, the court stated that the "duty to warn of a product's dangerous propensities is imposed upon a manufacturer or supplier where there is unequal knowledge, actual or constructive, and the defendant, possessed of such knowledge, knows or should know that harm might or could occur if no warning is given."⁷⁷

Illinois courts have traditionally found the idiosyncratic reaction defense viable.⁷⁸ In *Presbrey v. Gillette*,⁷⁹ the plaintiff claimed permanent injury from use of an antiperspirant manufactured by Gillette. The court held that the plaintiff was not entitled to recovery because the plaintiff's injury was an idiosyncratic reaction that would not occur in the average person. The manufacturer did not know, and it had no reason to know, that the plaintiff might be injured. Consequently, the court held that the manufacturer owed no prior duty to warn of a risk that was only remotely possible (i.e., unknowable) and unknown to the manufacturer.⁸⁰

An Oregon case, however, demonstrates the difficulties a defendant may have in prevailing on *summary judgment* when asserting the idiosyncratic defense. In *Jones v. General Motors Corp.*,⁸¹ the plaintiff claimed injuries from an air contaminant stemming from a leak in the passenger area of his car. General Motors argued, among other things, that they were not liable for the plaintiff's injuries because his reaction was idiosyncratic. The court held that the defendant's idiosyncratic reaction defense is "itself a factual question."⁸²

The idiosyncratic nature of a reaction may be difficult to establish on summary judgment, if the plaintiff is successful at creating an issue of fact (e.g., conflicting expert testimony about the idiosyncratic na-

74. *Id.* at 46-47. The defense expert based his opinion that the plaintiff's injuries were genetic on the results of allergy skin testing conducted on the plaintiff; counsel should be aware of a possible trend toward refusing this defense. *Id.*

75. *Id.* at 49.

76. *Id.* The court did not indicate how or in what manner the rule was relaxed.

77. *Id.*

78. *See, e.g.,* *Bear v. Power Air, Inc.*, 595 N.E.2d 77 (Ill. Ct. App. 1992); *Garcia v. Jiminez*, 539 N.E.2d 1356 (Ill. Ct. App. 1989); *Presbrey v. Gillette Co.*, 435 N.E.2d 513 (Ill. Ct. App. 1982).

79. 435 N.E.2d 513 (Ill. Ct. App. 1982).

80. *Id.* at 520.

81. 939 P.2d 608 (1997).

82. *Id.* at 617.

ture of the reaction). Thus, if there is any indication that genetic injury could plausibly be triggered by exposure to a toxic substance, there may be a fact issue requiring jury consideration. Over time, as more genetic links to chemicals are understood, genuine conflicts in expert testimony may increase, and the duty to warn subclasses known to be susceptible may increasingly be imposed as a result.

C. *The “State of the Art” Defense: ‘Tis Noble to Know What’s “Knowable”*

If a toxicogenomic harm was not known or knowable at the time the product was marketed and a plaintiff was foreseeably exposed,⁸³ the court must consider “state of the art” evidence. Where a product liability defendant can show that the product was tested to a reasonably accepted industry standard that reflected the existing state of the scientific expertise (i.e., the “state of the art”), this compliance with existing science can be raised as a defense when a future product risk causes harm. The policy reasons behind this are fairly clear — the courts are reluctant to make industry an insurer of products by holding companies liable for harms they could not have foreseen and corrected.

The California Supreme Court clarified the scope of the failure to warn theory of strict liability to allow state of the art evidence. In *Anderson v. Owens-Corning Fiberglas Corp.*,⁸⁴ the court held that “[t]he rules of strict liability require a plaintiff to prove only that the defendant did not adequately warn of a particular risk that was known or knowable in light of the generally recognized and prevailing best scientific and medical knowledge available at the time of manufacture and distribution.”⁸⁵ This holding clearly applies to toxicogenomic knowledge, which is merely the next step in scientific understanding of medical causation of injury. As a result, courts following California’s lead will initially consider toxicogenomic evidence of product harm to be insufficient to overcome a state of the art defense. However, this defense could fade as the toxicogenomic data becomes available at the time new products enter the market. Over time, the state of the art will include toxicogenomic evidence.

Moreover, some defendants may seek to introduce toxicogenomic evidence on their own initiative, if only to limit liability to a subclass of susceptible plaintiffs. Courts will presumably continue to

83. Many courts have recognized a “post-sale” duty to warn of newly discovered risks of products released without an adequate warning (where it is feasible to do so). See Kevin R. Boyle, Note, *The Expanding Post-Sale Duty of a Manufacturer: Does a Manufacturer Have a Duty to Retrofit Its Products?*, 38 ARIZ. L. REV. 1033 (1996).

84. 810 P.2d 549 (Cal. 1991).

85. *Id.* at 558.

allow defendants this option. Defendants would use toxicogenomic evidence as a shield to rule out causation, while plaintiffs might be denied the sword of toxicogenomic data to prove causation in particular cases.

The passage of time could also help to limit the scope of a duty to warn. In *Artiglio v. Corning Inc.*,⁸⁶ the California Supreme Court held that too many years had elapsed between Dow Chemical's seminal toxicology research and activities on behalf of Dow Corning and the plaintiffs' alleged injuries. In *Artiglio*, plaintiffs argued that Dow Chemical, a bulk supplier that conducted early research on the silicone later used for breast implants, owed them a duty because Dow Chemical negligently undertook some efforts to ensure the safety of all of Dow Corning's silicone products. The court disagreed and found that Dow Chemical owed the plaintiffs no duty of care because the silicone research they did conduct was not of such breadth and magnitude to create a duty, and it occurred decades before the harm.⁸⁷ Summary judgment for the defendant was upheld.

While the *Artiglio* decision featured a bulk supplier that was not on the front lines in marketing and testing the breast implants, there could be broader use of this decision outside the bulk supplier context. For genetic susceptibilities that are hypothetical and probabilistic in nature, long periods of time may pass between the first date when an ostensible gene for susceptibility is identified and the dates when disease is manifest and proof of causation is less probabilistic and more certain. After several human generations have come and gone, and data has accumulated confirming or disproving various hypothetical links, genetically supported proof of causation may become the dominant mode of proving causation in chemical exposure cases.

A well-documented review of potential adverse impacts can record this uncertainty and the enormous cost of warning the genetically susceptible. This review, twenty years hence, could provide evidence for a future summary judgment motion by the defense. As a result, proactive actions taken today to detect or rule out a duty to warn of toxicogenomic effects (including an offer of free genetic testing to those who are potentially susceptible) could foreclose future claims of a failure to warn the genetically susceptible, if those actions are well-documented.

86. 957 P.2d 1313 (Cal. 1998).

87. *Id.* at 1320.

D. “Substantial Factor” Causation: Contrasting California and Arizona

With the standards for “substantial factor” causation reaching into the lower regions of epidemiological risk and scientific certainty, strategic steps taken to rule out a duty to warn the genetically susceptible could become even more sensible over time.

The Ninth Circuit’s decision in *Kennedy v. Southern California Edison Co.*,⁸⁸ the “nuclear fleas” case, illustrates the potential for existing causation standards to create fertile ground for arguments based on “genotype stratification” theories. In a case involving alleged health effects from nuclear fleas (tiny particles of radioactive material) that allegedly packed a toxicogenomic punch, the Ninth Circuit applied California law to establish a medical causation standard for a radioactive substance.⁸⁹ This wrongful death case arises from alleged radiation exposure from a nuclear power plant that allegedly caused Ellen Kennedy to develop terminal chronic myelogenous leukemia (CML), a rare blood cell cancer. The plaintiffs asserted that CML resulted from negligence on the part of Southern California Edison Company (Cal Edison) that led to her exposure to radiation at the San Onofre Nuclear Power Plant. Additionally, the plaintiffs sued Combustion Engineering, Inc., under a products liability cause of action, for the alleged faulty production of nuclear fuel rods. The theory of the case was that Joe Kennedy, Ellen Kennedy’s husband, inadvertently brought home microscopic particles of radioactive material, known as nuclear fleas, from the power plant on his clothing, hair, tools, etc. The plaintiffs alleged that nuclear fleas, which contained radiation dosages in excess of the maximum allowable by federal regulations, caused Mrs. Kennedy’s fatal cancer.⁹⁰

First, the court held that the district court erred in refusing to give a jury instruction under *Rutherford v. Owens-Illinois, Inc.*,⁹¹ in this single-defendant hazardous substance case. While this case involved two defendants, the court treated Cal Edison and Combustion Engineering as a single defendant with respect to the issue of alternative causes. While both defendants raised the defense that there were alternative possible causes of Mrs. Kennedy’s cancer, neither argued that the other was an independent source of causation. The court found that with a *Rutherford* instruction, the jury could have found

88. 219 F.3d 988 (9th Cir. 2000).

89. *Id.*

90. *Id.* at 991-92.

91. 941 P.2d 1203 (Cal. 1997). The court explained that a *Rutherford* instruction shifts the burden of proof to defendants; it was first used in asbestos cases tried on a products liability theory to prove that their products were not a legal cause of the plaintiff’s injuries, provided the plaintiff first establishes that (1) plaintiff was exposed to toxic products defendant manufactured or sold and (2) exposure to asbestos fibers generally could cause injury. *Id.* at 1206.

more than a “negligible probability” that Mrs. Kennedy’s cancer was caused by radiation from the plant. However, the jury instructions, as given, stated that radiation from the plant need only have “contributed” to Mrs. Kennedy’s risk of developing cancer. The court read *Rutherford* as requiring more. The court found that the plaintiffs’ burden was to demonstrate that the exposure in reasonable medical probability was a substantial factor in contributing to the risk of cancer.⁹²

Second, the court held that the district court erred in dismissing claims under California product liability law. The plaintiffs presented evidence that the radioactive fuel fleas were released from Combustion Engineering’s apparently defective fuel rods. Combustion Engineering argued that it was entitled to summary judgment on strict liability because this was an “isolated” transaction — it never marketed the fuel rods to the public and could not have foreseen that the rods would injure a non-employee of the plant like Mrs. Kennedy.

The court disagreed. It found that the record suggested that Combustion Engineering had supplied thousands of fuel rods on a continuing basis to the plant and several other nuclear plants. Therefore, Combustion Engineering’s enterprise differed entirely in both quality and degree from the *ad hoc* and infrequent activities to which the “isolated transaction” exception has been previously deemed applicable. Based on *Elmore v. American Motors Corp.*,⁹³ the court concluded that Combustion Engineering could have foreseen that the spouse of a nuclear-plant worker might fall within the foreseeable zone of danger posed by Combustion Engineering’s products. As a result, it was error for the court to decide the issue as a matter of law.⁹⁴

The *Kennedy* case appears to state a broad notion of substantial factor causation. If applied to future cases involving genetic evidence, the standard for substantial factor causation could prove both detrimental to alternative cause arguments (since it will apparently be trumped by minor co-causal factors) and could allow the genetically susceptible plaintiff to argue for substantial factor causation based on slim percentage increases in background risk.

In contrast to the expansive view of causation taken in *Kennedy*, a superior court in Arizona addressing causation for the effects of TCE (an industrial solvent) applied “but for” causation to deny the plaintiffs’ experts the opportunity to testify in a landmark *Daubert/Frye* motion that drew national attention. In *Lofgren v. Motorola*,

92. *Kennedy*, 219 F.3d at 993-95.

93. 451 P.2d 84, 89 (Cal. 1969).

94. *Kennedy*, 219 F.3d at 1000-03.

Inc.,⁹⁵ the plaintiffs alleged various theories to attempt to link their health problems, including cancers, to exposure to TCE. The court held that their experts did not have adequate scientific evidence to meet the “but for” causation standard in Arizona.⁹⁶ Presumably evidence meeting the “but for” standard would also have to hurdle the next level of proximate cause — i.e., where the foreseeability of harm is so remote, the courts decline to afford relief.

VII. “GENERAL CAUSATION” MOTIONS UNDER *DAUBERT*/*FRYE* STANDARDS

The impacts of genetic testing data flowing from the mapping of the human genome are already beginning. Any toxic tort counsel that retains cutting edge or world-class experts will find them making reference to emerging genetic theories in epidemiology, toxicology, and biostatistics. Over time, the evidence generated by the mapping of the human genome will expose many new links of causation that traditional epidemiology could not reach. The biotechnology industry will find new markets for its diagnostic tests.⁹⁷ A new class of experts will provide the key to tracing new causation pathways, exonerating some suspects and implicating other suspects. Properly applied, using sound scientific techniques, toxicogenomic data could bring order to a chaotic, inefficient system of chemical regulation and liability. Improperly applied, it could increase the number of cases alleging “junk” science.⁹⁸

In federal courts in the United States, the Supreme Court has issued a series of decisions that make it quite clear that sound scientific methodologies are required to support an opinion that a chemical caused a particular disease.⁹⁹ The *Daubert* doctrine was recently given a resounding 9-0 affirmance in a case reversing a trial court’s decision to admit a series of fire causation experts.¹⁰⁰ The gatekeep-

95. No. CV 93-05521, 1998 WL 299925 (Ariz. Super. Ct. June 1, 1998).

96. *Id.* at *3.

97. NIEHS is actively encouraging collaborations with the biotechnology industry: “Partnerships with the biotechnology industry are encouraged to bring new technological advances in genomic and informatic sciences to the practice of epidemiology.” See PLANNING GRANTS, *supra* note 14. Given the high stakes of a case featuring significant damages, the biotech industry might find premium returns on niche products targeting suspected disease pathways. Participants in Cooperative Research and Development Agreements (CRADAs) may reap significant returns. See AM. ASS’N FOR THE ADVANCEMENT OF SCI., *Genome Issue*, 279 SCI. No. 5338, Oct. 24, 1997.

98. See generally PETER W. HUBER, *GALILEO’S REVENGE* (1991).

99. *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579 (1993). On remand, the appeals court considered medical causation in detail. *Daubert v. Merrell Dow Pharm., Inc.*, 43 F.3d 1311 (9th Cir. 1995) [hereinafter *Daubert II*]. For an epidemiological study to show causation under a preponderance standard, “the relative risk of limb reduction defects arising from the epidemiological data . . . will, at a minimum, have to exceed ‘2.’” *DeLuca v. Merrell Dow Pharm., Inc.*, 911 F.2d 941, 958 (3d Cir. 1990), *aff’d*, 6 F.3d 778 (3d Cir. 1993).

100. See *Weisgram v. Marley Co.*, 528 U.S. 440 (2000).

ing role of the trial courts in keeping out spurious expert testimony is clearer than ever.

Plaintiffs' counsel would argue that there are some chinks in this *Daubert* armor where district courts appear to have let some dubious medical opinions in under a medical judgment exception to the scientific methodology requirements in *Daubert II*.¹⁰¹ In state courts, moreover, a patchwork quilt of decisions often allows doctors to present their medical experience-based opinions with minimal methodological foundation.¹⁰² California, because it follows the *Kelly-Frye*¹⁰³ test of general acceptance for scientific opinions, has a line of cases that are not in accordance with the *Daubert II* decision on medical causation.¹⁰⁴

In the context of environmental mass torts, however, the courts of California have inherent power to require plaintiffs to make a prima facie case of actual injury before they require the court to engage in a long process of hearing evidence about injuries. In *Cottle v. Superior Court*,¹⁰⁵ the following order was affirmed on appeal: "The court tentatively ordered the exclusion of 'all evidence, by lay or expert witnesses, that plaintiffs have or will suffer any particular injury or illness based on exposure to toxic substances in the Dunes' unless plaintiffs could demonstrate by May 31, 1991, that viable claims for personal injury existed."¹⁰⁶

Courts facing thousands of claims will generally use case management methods to require plaintiffs to show "general causation" — that the compound in question could possibly cause cancer (or other alleged effect) at the doses in question.¹⁰⁷ This level of analysis sets aside the specific facts of particular plaintiffs, which complicate the question of causation considerably (e.g., they may have various alternative causes at issue for the harm they claim).¹⁰⁸

The adversarial process of tort litigation can lead juries to stray far afield from established scientific consensus, particularly in those

101. *Daubert II*, 43 F.3d 1311.

102. For a useful analysis of how *Daubert* has been applied by the states, see <http://faculty.lsu.edu/ccorcos/biblio/daubertrialcourts.htm> (last updated Jan. 13, 2003).

103. *Frye v. United States*, 293 F. 1013 (D.C. Cir. 1923); *People v. Kelly*, 549 P.2d 1240 (Cal. 1976).

104. See *People v. Ward*, 83 Cal. Rptr. 2d 828 (Cal. Ct. App. 1999). California does not subject expert medical opinion to the *Frye* test; it reserves *Frye* scrutiny for new technologies, not experience-based opinion testimony. See *id.* at 831.

105. 5 Cal. Rptr. 2d 882 (Cal. Ct. App. 1992).

106. *Id.* at 885.

107. See, e.g., *Lore v. Lone Pine Corp.*, No. L-3306-85, 1986 N.J. Super. LEXIS 1626 (N.J. Super. Ct. Law Div. Nov. 18, 1986). For a critique of the use of *Lone Pine* orders, see John T. Burnett, *Lone Pine Orders: A Wolf in Sheep's Clothing for Environmental and Toxic Tort Litigation*, 14 FLA. ST. U. J. LAND USE & ENVTL. L. 53 (1998).

108. See, e.g., *In re Hanford Nuclear Reservation Litig.*, No. CY-91-3015-AAM, 1998 WL 775340 (E.D. Wash. Aug. 21, 1998) (granting motion on general causation for majority of plaintiffs claiming exposure to downwind radiation and hexavalent chromium).

state courts or federal circuits that allow medical opinions in without adequate regard for gatekeeper principles prevailing in federal courts. In some states that recognize both medical monitoring claims and the “medical judgment” exception to *Daubert*’s “gatekeeper doctrine,” a physician expert may be allowed to propose the functional equivalent of a broad health insurance program (in the form of a medical monitoring award) payable in large part to his own medical group. If the floodgates are manned by physicians with an incentive to divert financial resources for medical monitoring to their own practices, this inherent bias could lead to runaway awards.

As noted above, epidemiology and the law have combined to create the doubling risk concept. To cross this threshold, plaintiffs are sometimes asked to prove that their risk is at least two times the background incidence of the disease allegedly caused by a chemical. In most toxic tort cases, the court will require an initial showing of general causation (i.e., that scientific evidence shows an increased risk with valid scientific studies to support that conclusion). In many cases, doubling risk will get the standard. Once general causation is shown, specific proof of each plaintiff’s case (“specific causation”) can be addressed through discovery and trial.¹⁰⁹

For example, the defense expert would demonstrate that the increased cancer risk for that 90% of exposed persons is simply too low for the court to even consider medical causation.¹¹⁰ The remaining 10% of plaintiffs would have proved only general causation, i.e., that they had enough exposure to be *considered* for specific causation. In many cases, modern epidemiology is insufficient in its specificity to demonstrate which of the various persons who have a greater than 2.0 relative risk could have cancer that was caused by the chemical exposure.

For companies trying to decide whether a warning is feasible, use of the doubling risk standard could provide a tool for initiating analysis of the duty to warn. If the genetically susceptible subgroup can be identified, and a warning is feasible (e.g., website notifications), then warnings may be deemed necessary, with perfect hindsight, in some

109. See Nicklas Akers & Nate Scott, *Admissibility of Epidemiological Evidence Under Daubert*, THE JUDICIAL GATEKEEPING PROJECT, at <http://cyber.law.harvard.edu/daubert/ch6.htm> (last visited Feb. 21, 2003); cf. Dave Hitt, *The Facts: Epidemiology 101*, <http://www.davehitt.com/facts/epid.html> (last visited Feb. 23, 2003).

110. The tangled history of the medical monitoring claims made for exposure to radiation from the Hanford Nuclear Reservation provides a recent and extensive exploration into the screening mechanisms employed by “state of the art” in epidemiology. See, e.g., *U.S. Dep’t. of Health and Human Servs., Before the Permanent Senate Subcomm. on Investigations Comm. on Gov’t Affairs*, 105th Cong. (1998) (testimony of Barry L. Johnson, Ph.D., Assistant Surgeon General, Assistant Administrator of the Agency for Toxic Substances and Disease Registry), <http://www.atsdr.cdc.gov/test-09-16-98.html> (last visited Feb. 21, 2003); Trisha Pritikin, *Errors Found in Hanford Thyroid Disease Study*, Jan. 2000, at <http://www.napf.org/articles/pritikin-hanford-errors.html>.

future lawsuit. The failure to warn today could open the door to a lawsuit tomorrow.

VIII. CONCLUSION

It is clear that the use of toxicogenomic data will be making many appearances in the courts and in debates over regulatory policy toward chemicals and radiation. There is no question that toxicogenomic evidence will sometimes be used without a solid scientific basis, as genome experts extend the boundaries of science into areas that are hypothetical (i.e., "junk science"). With creative plaintiffs' attorneys guiding them, toxicogenomic experts could create a fearful new world where many people fear microscopic, largely hypothetical interactions of genes and chemicals.

For many, this fear of genes could lead to unintended adverse consequences. Decisions to sell a home near a waste facility or not to have children for fear of passing some genetic harm to them could be based on a largely unfounded fear manufactured by experts and counsel for purposes of litigation and money damages. In that sense, the toxicogenomic revolution could bring a Pandora's box scenario, releasing some unpleasant adverse consequences. Properly applied, however, toxicogenomic data will shine light on previously dark areas of medical causation, and bring everyone involved closer to the truth.