

Understanding Tort Law Impacts Created by Scientific Advances of Human Biomonitoring and Genetic Biomarkers

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I. Introduction

Biomarkers and biomonitoring have both become a major focus of current research into environmental exposures and risks. The two concepts are related—they both involve measurements of parameters in the blood or other tissues of the body to evaluate exposure or risk to toxic substances. Biomarkers involves biological changes, usually at the molecular or cellular level, that result from an environmental exposure, while biomonitoring involves measuring levels of the toxic substance itself or its metabolites in the body.

While the primary focus of biomarkers and biomonitoring to date has been in research to better evaluate and measure exposure effects, these two types of data also have the potential to fill critical evidentiary gaps in toxic tort litigation. This type of litigation is often limited by the current inability to associate particular exposures with subsequent health consequences in a specific individual. The consequence of this ignorance is the need to rely on crude and often misleading assumptions and presumptions that frequently result in unjust outcomes, whether for manufacturers of harmless products that are unfairly saddled with expensive liabilities, or seriously injured citizens who are denied fair compensation because they cannot prove sufficiently that a particular exposure caused their injury. By providing an evidentiary link between exposures and health effects, biomarkers and biomonitoring have the potential to shine objective scientific illumination on whether a specific toxic exposure likely did or not contribute to a particular individual's injuries.

This paper explores the potential uses of biomarkers and biomonitoring in toxic tort litigation, and the scientific, legal, policy, and ethical challenges presented by these applications. It first discusses recent scientific advances in the development and validation of biomarkers and biomonitoring, and how the data from these tools can be used to inform estimates of toxic exposures and risks. It then identifies potential applications of biomarkers and biomonitoring in toxic tort litigation, drawing where available on existing cases and relevant precedents. The article then concludes by addressing several broader policy issues relating to the use of biomarkers in the litigation context, including the admissibility of biomarker and biomonitoring evidence under the new legal standards for scientific evidence, as well as other practical and normative issues that will be presented by the use of such data in litigation.

II. Background on Biomarkers and Biomonitoring

A. Biomarkers

Biomarkers are measurable changes in cells or tissues resulting from toxic exposures that can be used as a quantitative or qualitative measure of exposure or response to that exposure. *See* Anthony P. Decaprio, *Biomarkers: Coming of Age for Environmental Health and Risk Assessment*, 31 *Env'tl. Sci. & Tech.* 1837, 1842 (1997). Typically, biomarkers are classified into three broad categories measuring (i) susceptibility, (ii) effect, or (iii) exposure. National Research Council (NRC), *Biological Markers in Environmental Health Research*, 74 *Env'tl. Health Perspect.* 3, 3 (1987). A critical feature of all three types of biomarkers is that they provide important information about a specific individual rather than the population as a whole. Biomarkers

can therefore be useful for identifying symptomatic or pre-symptomatic persons who have been exposed to or are affected by a toxic substance, as well as to evaluate disease progression and estimate the risk of future disease in such persons. Over the past two decades, tremendous progress has been made in the theoretical understanding and practical application of biomarkers, many of which involve the use of genetic or molecular information. There are several different types of molecular and genetic biomarkers, briefly reviewed below.

One major type of biomarker is a DNA adduct, where a toxic substance or its metabolites binds with DNA to form a stable and characteristic chemical complex. V.K. Bhatnagar & G. Talaska, *Carcinogen Exposure and Effect Biomarkers*, 108 *Toxicology Letters* 107, 108 (1999). The formation of a DNA adduct can be an initial step in the mutation process, although not all adducts necessarily result in mutation. Several hundred different carcinogen-DNA adducts have been identified to date, with many carcinogens forming distinct patterns of adducts with respect to type and location on the DNA macromolecule. Christopher P. Wild & Paola Pisani, *Carcinogen DNA and Protein Adducts as Biomarkers of Human Exposure in Environmental Cancer Epidemiology*, 22 *Cancer Detection & Prevention* 273, 276–77 (1998). Adducts can provide an accurate molecular dosimeter of exposure, and are able to measure extremely low levels of exposure that might previously go undetected. Herman A. Schut & Kathleen T. Shiverick, *DNA Adducts in Humans as Dosimeters of Exposure to Environmental, Occupational, or Dietary Genotoxins*, 6 *FASEB J.* 2942 (1992); Paul A. Schulte, *Contribution of Biological Markers to Occupational Health*, 20 *Am. J. Ind. Med.* 435, 436 (1991).

Although they are a potentially useful biomarker of exposure or effect, DNA adducts have several important limitations, including (i) they usually last a short duration, ranging from several minutes to several months, thereby requiring sampling close in time to the actual exposure; (ii) significant differences in inter-individual rates of adduct formation occur; and (iii) the difficulty of sampling from tissues such as the lung or liver where disease may occur. Salama A. Salama, Milagros Serrana and William W. Au, *Biomonitoring Using Accessible Human Cells for Exposure and Health Risk Assessment*, 436 *Mutation Res.* 99 (1999).

Other biomarkers include various types of chromosomal aberrations, metabolic changes such as enzyme induction or inhibition, increased cell proliferation in tissues (hyperplasia), and genetic mutations. DeCaprio, *supra*, at 1840. For example, several important human carcinogens induce their own characteristic “mutational fingerprints” at precise sites in specific genes, such as the important tumor suppressor gene *p53*. Curtis C. Harris, *p53: At the Crossroads of Molecular Carcinogenesis and Risk Assessment*, 262 *Science* 1980 (1993). Thus, the detection of a characteristic genetic change might indicate the initiation of the cancer process, as well as the specific cause of that event.

An emerging new technology with significant potential applications in toxic tort litigation is the evaluation of gene expression patterns using DNA microarrays, which is part of what is often referred to as “toxicogenomics.” Exposure to a toxic substance, like any other perturbation, results in characteristic changes in gene expression in cells, by which some genes that are normally inactive in a particular tissue are turned “on” and expressed whereas other genes that are normally expressed are now suppressed. Spencer Farr & Robert T. Dunn, *Concise Review: Gene Expression Applied to Toxicology*, 50 *Toxicological Sci.* 1, 1 (1999). These gene expression changes may sometimes be the cause or in other cases the consequence of the early stages of a toxic response. Christine Debouck & Peter N. Goodfellow, *DNA Microarrays in Drug Discovery and Development*, 21 (Suppl.) *Nature Genetics* 48, 49 (1999).

Gene expression changes can be analyzed by collecting and characterizing messenger ribonucleic acid (mRNA) using a DNA microarray (sometimes also referred to as a gene chip or DNA chip). A DNA microarray consists of a set of many different single-stranded genetic sequences fixed to a substrate, such as a glass slide or membrane, in a defined pattern. The mRNA from cells exposed to a toxic substance can then

be collected, dyed and allowed to bind with the fixed single-stranded DNA on the microarray. The pattern of binding can reveal which genes have been turned on and off in the exposed cells. The use of DNA microarrays to study global gene expression provides “a tool of unprecedented power for use in toxicology studies.” Emile F. Nuwaysir, *et al.*, *Microarrays and Toxicology: The Advent of Toxicogenetics*, 24 *Molecular Carcinogenesis* 153, 158 (1999).

Gene expression changes measured by microarrays have the potential to provide a more sensitive, characteristic, and earlier indicator of a toxic response than typical toxicological endpoints such as morphological changes, carcinogenicity, or reproductive toxicity. Nuwaysir, *et al.*, *supra*, at 154–55. Microarray data promise greater specificity because while “there are a limited number of cellular, organ, and organismal manifestations of chemically-induced toxicity, the possible number of gene expression patterns for encoding those manifestations is enormous.” Farr & Dunn, *supra*, at 2. Many different toxic agents may be capable of causing the same toxicological endpoint, *e.g.*, a liver tumor, in many cases by different mechanisms, whereas each chemical will produce a unique gene expression profile, thus providing a higher resolution tool with much greater specificity than simply monitoring the toxicological endpoint. Charles P. Rodi, *et al.*, *Revolution Through Genomics in Investigative and Discovery Toxicology*, 27 *Toxicological Pathology* 107, 109 (1999). Microarrays also permit evaluation of all toxicological endpoints in a single assay, whereas traditional toxicological methods generally require separate studies for carcinogenicity, mutagenicity, reproductive toxicity, teratogenicity, immunotoxicity, neurotoxicity, and endocrine disruption. W.D. Pennie & I. Kimber, *Toxicogenomics; Transcript Profiling and Potential Application to Chemical Allergy*, 16 *Toxicology in Vitro* 319, 320 (2002).

Yet another advantage of studying gene expression changes to assess toxicity is that such alterations can occur almost immediately following exposure, whereas the clinical manifestation of toxicity may take days, months, or even years to develop. Farr & Dunn, *supra*, at 1. Because these toxicological endpoints are the end result of earlier molecular events that can be monitored by microarrays, it is possible to screen for toxicity much more quickly and earlier using microarrays than with traditional toxicological methods. Rodi, *et al.*, *supra*, at 107. Moreover, because they represent an earlier step in a toxic response, gene expression changes will be detectable in a larger percentage of the exposed animal or human population than will ultimately go on to develop clinical disease, thereby providing a more statistically robust measure of effect. For these reasons, gene expression changes assayed using DNA microarrays have the potential to provide both an earlier and more sensitive biomarker of a toxic response.

Of particular interest is the rapidly growing body of evidence demonstrating that specific chemicals or classes of chemicals with similar toxicological properties produce a characteristic gene expression “fingerprint” or signature profile. Initial “proof-of-principle” experiments have successfully identified the identity or toxicological mechanism of chemicals based on their gene expression profiles. Hisham K. Hama-deh, *et al.*, *Prediction of Compound Signature Using High-Density Gene Expression Profiling*, 67 *Toxicological Sci.* 232 (2002). The finding that it is possible to discern exposure to an individual chemical based on unique gene expression changes suggests that it may be possible to use microarrays to measure exposure or toxic responses to specific chemicals in individuals or populations. Nuwaysir, *et al.*, *supra*, at 157. This and other toxicogenomic methods will likely have important potential applications for toxic torts.

Before it can have practical application, a biomarker must be adequately characterized and validated to establish that it accurately and consistently measures exposure or predicts disease. NRC, *supra*, at 6–7. A large number of potential biomarkers have been identified and are at various stages in their development and validation. Most of these biomarkers are not yet ready for practical application, although some have been validated and are in current use. Many complications remain, especially in accounting for such factors as

intra- and inter-individual variations in biomarker responses, interactions between different biomarkers or susceptibilities, variations in biomarker response over ranges of exposures, and correlating human and animal biomarker responses. Frederica Perera, *The Potential Usefulness of Biological Markers in Risk Assessment*, 76 *Envtl. Health Perspect.* 141, 143–44 (1987). A critical characteristic of all biomarkers is their duration, as many biomarkers only measure recent exposures. Yet, despite these challenges, rapid progress is being made in the development and validation of biomarkers, and this new technology is already beginning to transform our understanding of, and strategies to address, toxic effects.

B. Biomonitoring

The most straightforward exposure marker is the presence of the toxic agent or its metabolites in the human body. The length of time in which such agents remain in the body varies considerably depending on the substance involved. Approximately 270 substances can presently be identified in the body through biomonitoring. Carl F. Cranor, *Do You Want to Bet Your Children's Health on Post-Market Harm Principles? An Argument for a Trespass or Permission Model for Regulating Toxicants*, 19 *Vill. Envtl. L.J.* 251, 254 (2008).

Biomonitoring has been used to demonstrate exposure in for a variety of substances in a variety of settings. For example, in response to widespread illegal use of a pesticide in homes, the State of Mississippi utilized biomonitoring to efficiently allocate resources to those families that had the greatest exposure as determined by a measurement of a metabolite of the pesticide within the urine of those exposed. R. Jackson, *et al.*, *Will Biomonitoring Change How We Regulate Toxic Chemicals?*, 30 *J.L. Med. & Ethics* 177, 178 (2002). It has also been used to determine workplace exposure to cigarette smoke in casino workers through a measurement of cotinine, a metabolite of tobacco smoke, in order to reinforce state regulatory actions. *Id.* at 180–81 (2002).

III. Potential Applications in Toxic Tort Litigation

Biomarkers and biomonitoring have potential applications in toxic tort litigation in demonstrating exposure, proving causation, and creating new causes of action. Some biomarkers (*e.g.*, genetic polymorphisms) may also be useful in demonstrating the susceptibility of a plaintiff, but are not addressed here. See accompanying paper by Bernard Taylor. In each of these applications, both biomarkers and biomonitoring have the potential to provide objective scientific data that is woefully lacking in most current toxic tort cases.

A. Exposure

A threshold issue in toxic tort litigation is that the plaintiff must demonstrate sufficient exposure to the toxic agent that allegedly caused his or her injury. Many courts require the plaintiff to not only prove that exposure occurred, but also require some degree of quantification of that exposure. As one federal court of appeals stated, “there must be evidence from which the fact finder can conclude that the plaintiff was exposed to levels of that agent that are known to cause the kind of harm that the plaintiff claims to have suffered.” *Wright v. Williamette Industries, Inc.*, 91 F.3d 1105, 1107 (8th Cir. 1996). In other types of personal injury litigation, such as cases involving allegedly harmful medical devices or pharmaceuticals, proving exposure is usually not a problem, because the exposed individual knowingly and deliberately undertook a carefully measured exposure (by implanting a medical device or administering a pharmaceutical). In toxic tort cases involving, for example, alleged injuries from groundwater contamination or from an accidental explosion at an industrial facility, it is much more difficult to demonstrate and quantify exposure.

Toxicological biomarkers of exposure and biomonitoring data have the potential to provide objective evidence of individual exposure (or lack thereof). Courts have already indicated their receptivity to the

application of these types of data. For example, citizens living near the Three Mile Island (TMI) nuclear facility attempted to use chromosomal biomarkers to demonstrate and quantify exposure to a plume of radiation allegedly released during the 1979 TMI accident. The plaintiffs lacked adequate direct or modeling evidence of exposure, which the court described as the “critical issue” in the case. *In re TMI Litigation*, 193 F.3d 613, 622 (3d Cir. 1999), *cert. denied*, 120 S.Ct. 2238 (2000). The plaintiffs therefore sought to prove exposure based on evidence of an increased frequency of dicentric chromosomes in the lymphocytes of citizens living near the facility. The court held that this use of biomarkers was “an accepted method, not simply for determining if the subject of the analysis was irradiated, but also for estimating radiation dose to the individual.” *Id.* Notwithstanding its finding that “[r]adiation dose estimation based on dicentric enumeration is a valid and reliable scientific methodology,” the court rejected the evidence in that particular case because the “validity and reliability decrease as the time gap between the alleged irradiation and the dicentric count increases” and the plaintiffs had waited fifteen years to assay dicentric chromosomes in the allegedly exposed population. *Id.*

This judicial holding, while not helpful to the plaintiffs in that specific case, nevertheless does establish the more general proposition that chromosomal rearrangements can be used in the proper context as biomarkers to both establish and quantify exposure in litigation. Other types of biomarkers, such as changes in gene expression, are also likely to be offered as biomarkers of exposure in future cases. See Gary E. Marchant, *Genomics and Toxic Substances: Part I - Toxicogenomics*, 33 *Envtl Law Rep.* 10071 (2003). As the TMI case demonstrates, the temporal relationship between the exposure event and the subsequent assay for biomarkers will be a critical issue for producing a valid exposure estimate and hence judicial acceptance. Other important issues will be the specificity and sensitivity of the biomarker assay, and inter-individual variations in biomarker levels for a given exposure. Gary E. Marchant, *Toxicogenomics and Toxic Torts*, 20 *Trends in Biotech.* 329 (2002).

Similarly, biomonitoring data can be an effective tool for demonstrating exposure. It has been used in litigation to determine exposure for many toxic substances including dioxin, lead, polychlorinated biphenyl, and others. *Avila v. Willits Env'tl. Remediation Trust*, 633 F.3d 828, 837 (9th Cir. 2011); *Palmer v. Asarco Inc.*, 2007 WL 2302584 (N.D. Okla. Aug. 7, 2007); *Rubanick v. Witco Chem. Corp.*, 242 N.J. Super. 36, 72, 576 A.2d 4, 22 (N.J. Super. Ct. App. Div. 1990), judgment modified and remanded, 125 N.J. 421, 593 A.2d 733 (1991). In some cases, the biomonitoring data was used by plaintiffs to establish exposure, whereas in other cases biomonitoring was used to discredit some toxic tort claims for lack of exposure. See *Gass v. Marriott Hotel Services, Inc.*, 558 F.3d 419, 426 (6th Cir. 2009). Consequently, biomonitoring has significant value in focusing judicial resources on legitimate claims involving significant exposures.

Biomonitoring has a significant advantage over traditional environmental methods in establishing exposure in toxic tort cases, as with other contexts, because those traditional methods often rely on inferences such as local variation in concentration, individualized activity patterns (time spent outdoors, hand-to-mouth frequency etc.). Albert C. Lin, *Beyond Tort: Compensating Victims of Environmental Toxic Injury*, 78 *S. Cal. L. Rev.* 1439, 1475 (2005); Jackson, *et al.*, *supra*, at 178–79. Furthermore, environmental sampling estimates of individual exposure have questionable reliability, as they rely on measurements of soil, air, dust, water, etc., to determine the level of exposure of an individual or community. Because these measures are indirect, there is the possibility that they are not true measures of an individual’s exposure. In fact, in some cases the predicted exposure from environmental measurements has been found to be dramatically different than the exposure measured via biomonitoring. Jackson, *et al.*, *supra*, at 179 (predicted blood and urine levels of toxicants frequently are markedly different than biomonitoring levels).

For example, researchers at the University of Michigan studying dioxin discovered that dioxin exposure as measured in the participants’ blood serum was unrelated to the presence of contaminated soil or

house dust. §9:5 Biomonitoring, PLIREF-PLL s 9:5. This study highlighted the fact that differences between predicted exposure and actual dose can be critical. Consequently, defense attorneys in toxic tort litigation should be cognizant of the possibility that that predicted exposures determined through environmental measurements may vary significantly from the actual dose. See *Gates v. Rohm & Haas Co.*, 265 F.R.D. 208, 223–25 (E.D. Pa. 2010) (finding that expert's use of an "advantageous average" utilizing the high exposure estimates was inappropriate for class certification purposes).

However, the detection of a toxic substance in the blood stream is not always sufficient to establish relevant exposure in toxic tort litigation. Some toxins exist naturally in the environment at a normal background level, and there are residual levels of various manmade pollutants in environmental media from a variety of current and historical sources. For example, cyanide is known to exist in many the seeds of various fruits. A plaintiff alleging cyanide exposure would need to establish that the presence of cyanide in her blood is greater than the background level of cyanide in the environment or risk an adverse summary judgment. See *In re Paoli R.R. Yard PCB Litig.*, 35 F.3d 717, 778 (3d Cir. 1994) (requiring blood tests to show exposure greater than background levels to survive summary judgment).

Biomonitoring can also potentially establish the background exposure levels for the general population which can be used for a baseline for determining exposed individuals or groups. Lin, *supra*, at 1472. Of course, establishing such background exposure levels for the general population would require a substantial sample of the population, but some states have already begun to address this problem by implementing a state-wide biomonitoring program for select substances. California Environmental Contaminant Biomonitoring Program (CECBP), [http:// www.cdph.ca.gov/programs/Biomonitoring/pages/default.aspx](http://www.cdph.ca.gov/programs/Biomonitoring/pages/default.aspx) (accessed May 20, 2011). California passed a biomonitoring act in 2006 that targets specific chemicals. *Id.* If this program is successful it will help to establish background exposure rates and will also highlight those areas with particularly high exposure rates. Jennifer Girod & Andrew R. Klein, *Personalized Medicine and Toxic Exposure*, 9 Hous. J. Health L. & Pol'y 163, 170 (2009); 4 *L. of Toxic Torts* §29:11 (2011). It is not clear to what extent background exposure rates derived from states, such as California, can be generalized to states that lack such geo-specific data. On one hand, the rates provide some information where it is otherwise lacking. On the other hand, the data may be irrelevant because it doesn't reflect the geographic characteristics of relevant area. However, background exposure levels from different areas combined with low disease rates for conditions associated with the specific chemical may help provide some evidence of a safe exposure rate. Reactive litigation may result in those communities that are found to have higher than normal exposure to a specific chemical if the source of the contamination can be discovered.

The descriptive statistic used to describe the background exposure in the general population is a reason for concern. If the background exposure level is the average or mean exposure of the general population, then it is important to keep in mind that approximately half of the population will always be above this figure by definition. Many of these people will be above the average even absent any tortuous contact of other parties. There will always be variation of exposure within the population due to individual differences such as proximity to locations with naturally high concentrations of the relevant substance or behavioral differences such as increased hand-to-mouth activity. See Jackson, *et al.*, *supra*, at 179.

Although biomonitoring can substantiate or rebut claims of exposure in many circumstances, it is important that biomonitoring cannot resolve all exposure problems. This is especially true in cases involving past exposure. See *Wicker v. Consol. Rail Corp.*, 371 F. Supp. 2d 702, 719 (W.D. Pa. 2005). Different chemicals behave differently in the body. Some chemicals have a long half-life (the time it takes for the amount of the substance to be cut in half) and are eliminated from the body. Consequently, these chemicals can be detected through biomonitoring even long after the exposure to the chemical ended. Some chemicals are even seques-

tered in adipose tissue and may be difficult to detect. Those chemicals with a short half-life are more troublesome because they are often eliminated from the body rapidly. If biomonitoring of these chemicals occurs too late, they will not be detected at all, particularly in cases where acute exposure is charged. Thus, without other evidence of exposure (such as the presence of a biomarker) plaintiff will have a difficult time establishing exposure. §9:5 Biomonitoring, PLIREF-PLL s 9:5. However, this is not a problem for chemicals with a long half life, such as dioxin, which can be detected through biomonitoring even if the exposure occurred two decades prior to testing. *Id.*

B. Causation

The second, and usually most onerous, impediment that a toxic tort plaintiff must overcome is to demonstrate causation. The causation inquiry has two steps. The first step, general causation, inquires whether the toxic agent that the plaintiff was exposed to is capable of causing the health problems afflicting the plaintiff. The second step, specific causation, asks whether that exposure actually did cause the health effects in the individual plaintiff. Biomarkers, and to a lesser extent biomonitoring data, can be useful for both inquiries, but are likely to be most significant for the specific causation inquiry.

The primary application of biomarkers for general causation will be to provide a linkage between a toxic agent and toxicological endpoint that have not been directly substantiated in standard toxicological studies. Often plaintiffs lack any data showing a direct association between the specific agent they were exposed to and the particular health effect they are alleging was caused by that exposure. By necessity, they often attempt to rely instead on data showing that the agent causes other, related health effects (*e.g.*, a tumor in a different organ of the body) or that a similar agent (perhaps from the same family of chemical compounds) does cause the specific health effect at issue. Courts generally reject such indirect data, ruling that a plaintiff must produce evidence showing a direct linkage between the specific exposure and particular health endpoint at issue in that case.

Biomarkers have the potential to provide such a connection. For example, a plaintiff with a kidney tumor may be able to rely on evidence showing that the toxic agent in question causes liver tumors if there is evidence that the agent produces similar biomarkers (*e.g.*, DNA adducts, gene expression changes, or proteomic markers) in both the liver and kidney, and the liver biomarkers are in some way related to the liver tumors. The common biomarker in the liver and kidney might allow the plaintiff to extrapolate the tumor findings in the liver to the kidney. Similarly, if a plaintiff has been exposed to an agent (compound A) that causes an elevated biomarker in the lung but has not been associated with any toxicological endpoint in a published study, the plaintiff may be able to rely on evidence showing that a related compound B causes the same biomarker elevation in the lung and the toxic endpoint present in the plaintiff. While this biomarker “bootstrapping” to prove general causation has yet to be considered by courts, several judicial statements and holdings suggest that courts might be amenable to such arguments. If so, it would greatly expand the universe of potential combinations of toxic agents and toxicological endpoints for which plaintiffs will be capable of demonstrating general causation.

The greatest utility of biomarkers in toxic tort litigation is likely to be in demonstrating specific causation. Specific causation is the “Achilles’ heel” of many plaintiffs’ claims because of the scientific difficulty in proving that a specific exposure caused disease in a particular individual. The only cases in which specific causation is not a major challenge is those involving “signature” diseases that are caused primarily or exclusively by a particular agent, such as mesothelioma caused by asbestos or clear cell adenocarcinoma caused by the drug DES. In most other causes, many toxic agents as well as other environmental exposures (*e.g.*, foods, medicines, lifestyle factors, disease vectors) and intrinsic factors (*e.g.*, genetic susceptibility) are capable of

causing or contributing to the cause of the disease manifested in the individual plaintiff. Standard “black box” toxicology that looks at increased rates of disease in a population in response to a particular exposure is simply incapable of determining the cause of disease in a particular individual. Courts thus resort to methods such as differential diagnosis or statistical presumptions to adjudicate specific causation, which are based on conjecture rather than direct evidence of causation.

Biomarkers have the potential to provide direct evidence to link a specific exposure with health endpoints in an individual plaintiff. Specifically, strong evidence of specific causation will be provided by a finding that chemical-specific biomarkers of effect are elevated in a plaintiff who has been exposed to that agent and has developed disease known to be caused by that agent. Conversely, defendants can use the absence of biomarkers expected from such an exposure to refute any linkage to the plaintiffs’ disease.

An example of the use of biomarkers to support causation is a federal appellate court decision overturning a trial court’s dismissal of a case brought by parents of a young child claiming she had been harmed by exposure to formaldehyde from a new dresser. The trial court dismissed the case based on its finding that the parents had not made a sufficient showing that the dresser’s emissions of formaldehyde caused the child’s health problems, but the appellate court reversed and allowed the case to go forward based in part on evidence that the child had antibodies in her blood indicating a recent exposure to formaldehyde. *Bednar v. Bassett Furniture Manufacturing Co.*, 147 F.3d 737 (8th Cir. 1998). In another case, a plaintiff smoker who developed adenocarcinoma was able to establish that tobacco smoke was the probable cause of his tumor by introducing expert evidence that he had deletions in three specific chromosome regions involving tumor suppressor genes that are more common in smokers with adenocarcinoma than in non-smokers with adenocarcinoma. *Tompin v. American Tobacco*, 2001 WL 36113663 (N.D. Ohio 2001).

Only biomarkers that are specific for a specific toxic agent or family of compounds will be useful for demonstrating specific causation. For example, some mutagenic chemicals produce a chemical-specific spectra of mutations that can be used as a biomarker of exposure to that chemical. M. Patlak, *Fingering Carcinogens with Genetic Evidence*, 31 *Envtl. Sci. Tech.* 190A (1997). Similarly, gene expression changes may be able to provide a chemical-specific “fingerprint” of exposure to a particular toxicant. M.J. Aardema & J.T. MacGregor, *Toxicology and Genetic Toxicology in the New Era of “Toxicogenomics”: Impacts of “-omics” Technologies*, 499 *Mutation Res.* 13 (2002). In contrast, some biomarkers such as many chromosomal rearrangements are generally not agent-specific, and in such cases are unlikely to be helpful in proving or disproving specific causation.

A series of cases involving benzene exposure and leukemia demonstrate the potential utility and shortcoming of a biomarker, in this case specific chromosomal; rearrangements, in proving or rebutting causation. There are several types of leukemia, some of which are often associated with specific types of chromosomal rearrangements. Both plaintiffs and defendants have attempted to utilize these associations to support their defense or claims. A defendant employer successfully used the absence of a characteristic chromosomal rearrangement to defend against a claim on behalf of a deceased worker that occupational exposure to benzene caused his worker’s acute myelogenous leukemia (AML). *Expert Testimony: Jury Returns Verdict for Oil Company After Testimony on Missing Disease Marker*, 22 *Chem. Reg. Rep. (BNA)* 193 (1998) (reporting jury verdict in *Wells v. Shell Oil Co.*, DC ETexas, jury verdict 3/2/98). While it was undisputed that benzene is capable of causing AML, the jury delivered a verdict for the defendant after its expert testified that benzene only causes AML with specific cytogenetic markers—breaks in the 5th and 7th chromosomes—which were not present in the worker’s DNA. Although successful in this Texas case, the identical defense was rejected in a subsequent West Virginia case on the ground that the cytogenetic marker theory is “nothing more than an untested, unsupported hypothesis cloaked in the aura of scientific knowledge.” *Benzene: Defense Experts’*

Opinions Inadmissible, Not Based on Reliable Methodology, 22 Chem Reg. Rep. (BNA) 613 (1998) (discussing *Lavender v. Bayer Corp.*, W. Va. Cir. Ct., No. 93-C-226-K, 5/29/98). In the converse case, an attempt by a plaintiff to argue that his AML was caused by benzene as evidenced by breaks in chromosomes 5 and 7 was recently rejected by a California jury. See *Jury Finds for Shell in Benzene Wrongful-Death Case*, 29 No. 5 Westlaw J. Toxic Torts 3 (April 20, 2011) (reporting jury verdict in *Head, et al. v. Shell Oil Co.*, No. BC358265, Cal. Super. Ct., L.A. County, jury verdict Feb. 10, 2011).

More recently, a plaintiff who developed acute promyelocytic leukemia (APL) used expert testimony that benzene causes a specific type of chromosomal rearrangement (in this case a translocation between chromosomes 15 and 17) that is characteristic of APL. The district court rejected this testimony as unreliable, but the First Circuit Court of Appeals over-turned the decision and held that the expert could testify on this evidence. *Milward v. Acuity Specialty Products Group, Inc.*, ___ F.3d ___, 2011 WL 982385 (1st Cir., Mar. 22, 2011). In another case, a family alleged that benzene from a local landfill caused their daughter's acute lymphoblastic leukemia (ALL), and based their causation argument in part on expert testimony that the child had chromosomal aberrations typical of those caused by benzene. Although accepted by the lower courts, the Texas Supreme Court rejected such testimony as conclusory. *City of San Antonio v. Pollock*, 284 S.W.3d 809 (Tex. 2009).

Because specific causation will generally require biomarkers of effect, another contentious issue in such inquiries will be the tissue in which the biomarker is measured. For many toxicological endpoints, the target organ (*e.g.*, the liver or brain) cannot be easily assayed for biomarkers. Researchers often use surrogate tissues (*e.g.*, white blood cells) to assay for biomarkers. J.D. Groopman & T.W. Kensler, *The Light at the End of the Tunnel for Chemical-Specific Biomarkers: Daylight or Headlight?*, 20 Carcinogenesis 1 (1999). Parties are likely to dispute whether a biomarker measured in a more easily accessible surrogate tissue is an adequate surrogate for the target organ under the legal standards for causation.

Yet another area of likely dispute in using biomarkers to prove specific causation is the issue of whether the biomarker response detected in the individual plaintiff is indeed diagnostic for causation. Biomarkers are generally identified and validated in populations rather than individuals, and the baseline levels and changes in any single individual could be affected by a variety of intrinsic (*e.g.*, genetics) and extrinsic (*e.g.*, diet or medications) factors. Thus, even when a biomarker of effect that may suggest specific causation is detected in an individual plaintiff, the opposing party will likely seek to cast that finding into question by suggesting other exposures or factors that might explain the reported finding.

Unlike biomarkers, which can reveal cellular and subcellular changes indicative of a particular chemical, biomonitoring can only provide indirect evidence of causation. Lin, *supra*, at 1473. The first step in establishing causation through biomonitoring is to establish general causation, that is, that the measured chemical (or a metabolite thereof) is capable of causing injury or illness (general causation is not as significant with regard to biomarkers because the very changes that establish a biomarker may be indicative of a disease process). Even when a chemical is found to be capable of injury or illness causation requires evidence that it was the specific chemical detected via biomonitoring that caused (or might cause) the injury to the plaintiff and was only present in the plaintiff's body but for the actions of defendant.

Establishing this specific causation is difficult for a number of reasons. First, current technology does not permit identification of the source of the chemical found through biomonitoring. For example, a plaintiff in New York attempted to demonstrate exposure to toxic mold through biomonitoring tests for specific antibodies; however, the judge discounted the evidence because of a lack of evidentiary foundation that fungal exposures could produce the antibodies measured through the biomonitoring. *Fraser v. 301-52 Townhouse Corp.*, 13 Misc. 3d 1217(A), 831 N.Y.S.2d 347 (N.Y. Sup. Ct. 2006). In Texas, a judge took note that

chemicals in the plaintiff's blood were not exclusive to the defendant's business and could have come from numerous sources. As a result, the case was thrown out for want of causation. *Feria*, 2004 WL 500869 (2004).

Second, the mere presence of a foreign chemical in the blood does not necessarily mean that the chemical causes a disease. §9:5 Biomonitoring, PLIREF-PLL s 9:5. There are typically many physiological steps in between exposure to a toxic substance and causation. Jackson, *et al.*, *supra*, at 178. At a minimum, the substance must be shown to be toxic and in sufficient quantities to cause illness or injury. §9:5 Biomonitoring, PLIREF-PLL s 9:5. Thus, it would be prudent to compare the circumstances of each case to the epidemiological literature of the alleged toxic substance. *Id.* Of course, failure to demonstrate exposure at any level necessarily defeats causation. *Id.*

Finally, regulatory thresholds for toxic substances are not necessarily appropriate thresholds for causation in a tort case. Regulatory thresholds are essentially risk-benefit analyses. *Gates v. Rohm & Haas Co.*, 265 F.R.D. 208, 226 (E.D. Pa. 2010). In some circumstances, the regulatory threshold is a conservative measure, intended to maximize public safety. *Id.* Thus, because of the steps taken to ensure public safety, the regulatory threshold may be overly conservative, so exposures greater than the regulatory threshold may provide little information regarding causation. *Abarca v. Franklin County Water Dist.*, 1:07-CV-0388-OWW-DLB, 2011 WL 140371 (E.D. Cal. Jan. 5, 2011). It is therefore possible that exposures exceeding the regulatory threshold, even to a significant degree, may still be insufficient to establish causation. *Gates v. Rohm & Haas Co.*, 265 F.R.D. 208, 226 (E.D. Pa. 2010). In cases with conservative regulatory measures it would be prudent to reference the epidemiological literature to identify the concentrations of the toxic substance sufficient to establish causation.

Conversely, the regulatory threshold could be a liberal cost-benefit analysis that allows a certain degree of risk of injury in order to allow an activity that has a social benefit. In cases with a liberal threshold, it is possible that concentrations *below* the guidelines are sufficient to cause injury or illness. It has been suggested that even trace amounts of a substance may nonetheless be dangerous. James F. d'Entremont, *Fear Factor: The Future of Cancerphobia and Fear of Future Disease Claims in the Toxicogenomic Age*, 52 Loy. L. Rev. 807, 807–08 (2006). Some courts have been amenable to these “low dose” theories of causation. *Rhodes v. E.I. du Pont de Nemours & Co.*, 657 F. Supp. 2d 751, 764 (S.D.W. Va. 2009) *aff'd in part, appeal dismissed in part*, 636 F.3d 88 (4th Cir. 2011). However, person's advocating low dose theories of toxicity should supplement their position with epidemiological evidence.

Although the inherent difficulties in proving causation through biomonitoring, it does have one significant advantage to proving causation because it is empirical in nature. For example, the Human Toxome Project maintains a database that correlates adverse health effects with various chemicals. Human Toxome Project: Health Effects, <http://www.ewg.org/sites/humantoxome/healtheffects/> (accessed May 19, 2011). Biomonitoring, as a direct measurement of exposure, has a greater likelihood of providing better data for more accurate correlations. Thus, biomonitoring has some potential to focus litigation on the truly harmful substances and discredit those cases that rely on purely speculative data or junk science. Longitudinal surveillance, such as the biomonitoring program recently enacted in California, have the potential to find relationships between certain activities and health outcomes. Jackson, *et al.*, *supra*, at 180 (biomonitoring of lead through the late 1970s found a relationship between lead in gasoline and lead found in the blood stream).

C. New Causes of Action

A relatively new trend in toxic tort litigation is for plaintiffs who have been exposed to a toxic agent to file lawsuits seeking compensation for their latent risks that have not yet manifested into health problems. These latent risk claims are of three general types: (i) “increased risk” claims in which exposed plain-

tiffs seeks to recover for their asymptomatic increased risk of disease; (ii) “fear of disease” claims in which exposed plaintiffs seek compensation for their fear of developing a disease such as cancer, which they claim is an injury in and of itself; and (iii) “medical monitoring” claims in which plaintiffs seek to recover the future costs of periodic medical examinations to check for any developing disease. The motivation for bringing a claim under the first two theories (increased risk and fear of disease) is that the defendant company and relevant evidence may not be available if the plaintiff waits fifteen or twenty years for the manifestation of latent disease. Medical monitoring claims are based on the premise that frequent medical examinations may result in early detection and hence more effective treatment of emerging clinical disease.

Because virtually every citizen has been exposed to some type of toxic agent, courts have searched for limiting principles to prevent being flooded by latent risk claims, while permitting the most compelling claims to proceed. Thus, most courts have required a plaintiff bringing an increased risk or fear of disease claim to demonstrate a “present injury” as a prerequisite to pursuing such a claim. *Ayers v. Township of Jackson*, 525 A.2d 287, 287 (N.J. 1987); see Gary E. Marchant, Genetics and Toxic Torts, 31 *Seton Hall L. Rev.* 949 (2001). Many courts have also required a demonstration, and in some cases a quantification, of a sufficient magnitude of increased risk. *Bryson v. The Pillsbury Co.*, 573 N.W.2d 718 (Minn. Ct. App. 1998). Most plaintiffs exposed to toxic agents are unable to meet these threshold requirements using traditional toxicological data. Biomarker and biomonitoring data may help to support latent risk claims in several ways.

First, biomonitoring data can provide empirical evidence of increased exposure to support latent risk claims. For example, biomonitoring data may provide substantial assistance in claims alleging increased risk of injury. If increased exposure to a substance is positively correlated to an increased risk of sustaining an injury resulting from the exposure, then an accurate assessment of exposure achieved through biomonitoring will substantially assist the fact finder in evaluating the claim. Those plaintiffs with substantial exposure above the risk level will be entitled to a greater likelihood and magnitude of monetary relief than those plaintiffs only slightly above a risk level. Lin, *supra*, at 1488–89. Conversely, the fact finder might not choose to award any damages where the plaintiff fails to show a concentration of the toxic substance above the risk threshold.

Similarly, in fear of disease claims, biomonitoring can provide the fact-finder with empirical data it can use in evaluating the reasonableness of the plaintiff’s fears. James F. d’Entremont, *Fear Factor: The Future of Cancerphobia and Fear of Future Disease Claims in the Toxicogenomic Age*, 52 *Loy. L. Rev.* 807, 835 (2006). Where the biomonitoring data provides a good indication of the extent of exposure, the fact-finder will have objective data to use, in contrast to the traditional means which relies on speculative predictions by expert witnesses and subjective assessments by family members. See Mark A. Koppel, *Gilliam v. Roche Biomedical Laboratories : An Introduction to Fear-of-Disease Damages in Arkansas*, 48 *Ark. L. Rev.* 555, 555–63 (1995). In addition to filtering out bogus claims, biomonitoring can help support plaintiffs’ claims as well. Courts are rightfully wary of plaintiffs without a manifest injury. James F. d’Entremont, *Fear Factor: The Future of Cancerphobia and Fear of Future Disease Claims in the Toxicogenomic Age*, 52 *Loy. L. Rev.* 807, 835–36 (2006). Consequently, biomonitoring might buoy such a plaintiff’s claim if it can show substantial exposure, and therefore a legitimate concern about an increased risk.

Likewise, where a claim for medical monitoring requires a showing of exposure above and beyond the general population, biomonitoring can provide such evidence. §9:5 Biomonitoring, PLIREF-PLL s 9:5. Under a claim for medical monitoring the plaintiff must show that “the increased risk of disease makes it reasonably necessary for the plaintiff to undergo periodic diagnostic medical examinations different from what would be prescribed in the absence of exposure.” If the exposure is not significantly different than the average exposure, then it might not be reasonably necessary to undergo periodic examinations. §9:5 Biomonitoring, PLIREF-PLL s 9:5. In addition, risk assessment values can also provide some assistance. A federal

district court in West Virginia recently held that where biomonitoring reveals exposure levels below government risk assessment levels courts should not find that the exposure is sufficient to establish a claim for medical monitoring. *Rhodes v. E.I. du Pont de Nemours & Co.*, 657 F. Supp. 2d 751, 774 (S.D.W. Va. 2009) *aff'd in part, appeal dismissed in part*, 636 F.3d 88 (4th Cir. 2011). Defense should also be wary of exposure levels only slightly above the average for the general population as those elevated levels could be chance variation from the mean and unrelated to the defendant's conduct.

Second, biomarkers may provide the requisite evidence of "present injury" necessary to sustain a latent risk claim. There is both scientific and legal disagreement about whether the presence of a biomarker is sufficient to indicate a present injury. For example, many changes in gene expression may simply indicate the body's reversible and adaptive response to a toxic exposure, while other gene expression changes may be a true indicator of real toxic injury. Carol J. Henry, *et al.*, *Use of Genomics in Toxicology and Epidemiology: Findings and Recommendations of a Workshop*, 110 *Env'tl. Health Perspect.* 1047 (2002). A recent expert review of DNA adducts concluded that "[i]n the absence of any other toxicological data, the formation of chemical-specific DNA adducts should be considered an adverse effect, *i.e.*, one which potentially compromises the organism." L.H. Pottenger, *et al.*, *Biological Significance of DNA Adducts: Summary of Discussion of Expert Panel*, 39 *Regul. Toxicol. Pharmacol.* 403 (2004). Yet, the same review observed that there are a number of examples of DNA adducts that do not appear to be associated with any detectable toxicological consequence.

While the courts are somewhat split on the significance to be accorded to asymptomatic biomarkers, at least some courts have recognized asymptomatic molecular changes that are part of the disease process as a sufficient present injury to support a latent risk claim. For example, the Southern District of New York held that "[t]here is no reason why MTBE-DNA adducts should not meet the physical manifestation requirement simply because they are 'subcellular.'" *In re MTBE Products Liability Litigation*, 2007 WL 4245893 (SDNY 2007). In a smoking case, the court upheld medical monitoring for plaintiffs at increased risk for lung cancer from smoking based on their experts' testimony that tobacco smoke caused subclinical damage to their lungs, including damage to the genes in the airway cells, explaining: "We must adapt to the growing recognition that exposure to toxic substances and radiation may cause substantial injury which should be compensable even if the full effects are not immediately apparent." *Donovan v. Philip Morris*, 2009 WL 3321445 (Mass. 2009). A handful of other cases have likewise recognized that subclinical biomarkers may constitute a present injury. *See, e.g., Brafford v. Susquehanna Corp.*, 586 F.Supp. 14 (D.Colo. 1984) (holding that plaintiffs exposed to uranium mine wastes had created triable issue of fact by alleging that they had incurred chromosomal damage which represented a present injury); *Werlein v. United States*, 746 F.Supp. 887, 901 (D.Minn. 1990) (up to trier of fact to determine whether chromosomal breakage allegedly caused by exposure to contaminated water was present injury). Thus, the availability of biomarkers that have been validated as a reliable marker of disease progression may cause some courts to relax their requirement of symptomatic disease to support a latent risk claim.

Other jurisdictions require symptomatic disease to satisfy the present injury requirement, primarily due to the difficulty up until now of objectively proving alleged subcellular injuries and concerns about flooding the courts with new claims. *See, e.g., Rainer v. Union Carbide Corp.*, 402 F.3d 608 (6th Cir. 2005) (asymptomatic uranium-enrichment plant workers who were shown to have an increased frequency of chromosomal aberrations (in ~ 8 percent of their cells vs. 1.3 percent for controls) have not suffered any symptoms of a clinical disease necessary to bring a claim); *Caputo v. Boston Edison Co.*, No. 88-2126-Z, 1990 WL 98694 (D. Mass. 1990) ("cellular damage does not rise to the level of physical injury as a matter of law"). For example, the Ninth Circuit Court of Appeals, in holding that "bodily injury" requires "pain or interference with bodily functions," stated that "not every alteration of the body is an injury. Thinking causes synapses to

fire and the brain to experience tiny electric shocks; fear stimulates the production of chemicals associated with the fight-or-flight response. All life is change, but all change is not injurious. Adopting plaintiffs' interpretation of bodily injury would render the term surplusage, as every exposure to radiation would perforce cause injury." *Dumontier v. Schlumberger Technology Corp.*, 543 F.3d 567 (9th Cir. 2008). Allowing claims based on biomarkers indicating subcellular damage would open a "floodgate" of litigation: "Based upon the average American's exposure to chemically processed foods, toxic fumes, genetically modified fruits and vegetables, mercury-laden fish, and hormonally treated chicken and beef, this might encompass a very large percentage of the total population." *Wood v. Wyeth-Ayerst Labs.*, 82 S.W.3d 849 (Ky. 2002).

A series of cases involving workers or residents who were exposed to beryllium and are seeking medical monitoring are presenting and deciding the issue of when a subclinical bodily response to a toxic exposure rises to the level of an injury recognizable by tort law. Beryllium can cause a severe, life-threatening immune-mediated disease called chronic beryllium disease (CBD). Before developing the full disease, at-risk exposed individuals can become immunologically sensitized to beryllium, a subclinical effect that can be detected by a blood test known as the Beryllium Lymphocyte Proliferation Test (BePLT). The general approach of the courts to date has been to limit medical monitoring to plaintiffs who can prove they have been sensitized to beryllium using the BePLT assay. *See, e.g., Pohl v. NGK Metals*, 936 A.2d 43 (Pa. Sup. 2007) (precluding claim for medical monitoring by residents living near a beryllium plant unless they tested positive in BePLT assay). However, at least one court has imposed an even more stringent standard and held that beryllium sensitization is not compensable injury that can support a medical monitoring claim. *Paz v. Brush Engineered Materials*, 555 F.3d 383, (5th Cir. 2009).

A second potential use of biomarkers in supporting novel claims is to assist plaintiffs in demonstrating and perhaps quantifying their increased risk. The detection of biomarkers of effect in the exposed plaintiff could qualitatively confirm the increased risk from the plaintiff's exposure, and if supported by adequate human studies, could even be used to quantify risk (as the court in the TMI litigation indicated, discussed above). Such a finding would also validate the plaintiff's fear of disease, whereas a finding of no increase in biomarkers would diminish such fears and discredit any associated legal claims.

Biomarkers of effect (or perhaps even exposure) could also be used to support medical monitoring claims in two respects. First, the detection of such biomarkers in an individual would verify that the disease process has commenced and that further periodic testing of that individual might be warranted. Biomarkers could also serve as the target as well as the justification for medical monitoring, in that the monitoring would focus on detecting biomarkers of effect in exposed individuals, which might justify increased preventive or prophylactic measures in those individuals. A requirement for a valid medical monitoring claim in most jurisdictions is that monitoring and diagnostic methods exist that make early detection and treatment of the disease both possible and beneficial. *Hansen v. Mountain Fuel Supply Co.*, 858 P.2d 970, 979 (Utah 1993). Biomarkers may satisfy this requirement by making possible early detection that may make treatment more effective.

In addition to latent risk claims, biomonitoring gives rise to two additional causes of action: toxic trespass and battery through exposure. Toxic trespass is similar to a trespass on real property. In a toxic trespass claim, claimants argue the presence of an unwanted foreign substance within the claimant's body is an invasion of the personal property of the body. Carl F. Cranor, *Do You Want to Bet Your Children's Health on Post-Market Harm Principles? An Argument for a Trespass or Permission Model for Regulating Toxicants*, 19 Vill. Envtl. L.J. 251, 299 (2008). In the past, speculative/predictive evidence that an unwanted substance is present in the claimant's body has generally not been sufficient to sustain the cause of action, so plaintiffs generally have not had much success with toxic trespass claims. However, advances in biomonitoring may provide more substantive proof that a foreign substance is present. 51 No. 2 *DRI For Def.* 28. If the foreign

substance is in substantial quantities, biomonitoring evidence may make courts more amenable to toxic trespass claims.

Just as in a claim for trespass on real property, toxic trespass theoretically does not require a showing of injury to sustain a claim. The mere presence of the foreign substance is the wrong that sustains the claim. Cranor, *supra*, at 255. Without a need to prove injury or even the potential for injury, toxic trespass has the potential to open a floodgate of litigation as biomonitoring becomes more ubiquitous.

Consequently, there is a substantial policy argument that toxic trespass claims should be carefully bounded by the courts. Requiring deliberate or wonton action from defendants as the cause of the foreign substance's presence might make a reasonable claim for trespass. However, if a claim for toxic trespass could be sustained through mere negligence, it might become unbounded in its reach. A person with a cold might be liable if he infects a coworker. A person with a pollinating tree in her backyard might be liable for aggravating the allergies of a passerby. Taken to an extreme, an unhygienic person might be liable to those that inhale the molecules creating his aroma.

The claim of battery for harmful or offensive exposure to chemicals is related to toxic trespass. The theory behind a battery by exposure claim is that exposure to a foreign substance resulting from the action of another can rise to the level of an offensive or harmful contact. Courts have shown some reluctance to the extension of the tort of battery to mere chemical exposure. *McClenathan v. Rhone-Poulenc, Inc.*, 926 F. Supp. 1272, 1282 (S.D.W. Va. 1996); *Rhodes v. E.I. du Pont de Nemours & Co.*, 657 F. Supp. 2d 751, 773 (S.D.W. Va. 2009) *aff'd in part, appeal dismissed in part*, 636 F.3d 88 (4th Cir. 2011). In *McClenathan*, the court rejected an exposure battery claim because there was no showing of intention to cause harm or offense on the part of the actor. *McClenathan*, 926 F. Supp. at 1282. In *Rhodes*, the court rejected the claim because the plaintiffs failed to show harm from the alleged exposure, and subjective evidence of offense was not dispositive to show that the exposure was sufficiently offensive to sustain a charge of battery. *Rhodes v. E.I. du Pont de Nemours*, 657 F. Supp. 2d at 773. However, the court suggested that the presence of a biomarker suggesting that the exposure had caused a structural or functional alteration of a body part might be sufficient to show the requisite harm. *Id.* Though courts have not explicitly invalidated claims of battery by exposure, they have shown significant reservation and have made it clear that the mere presence of a foreign substance in the body of the plaintiff is not sufficient to sustain a claim for battery. *Id.*

IV. Potential Obstacles and Complications

This section reviews several key challenges for the use of biomarkers and biomonitoring data in toxic tort litigation.

A. Premature Use of Data

Litigation has several attributes that will create strong incentives for the premature use of unvalidated biomarkers. First, litigation decision-makers do not have the luxury enjoyed by regulatory agencies of being able to wait to make a decision until adequate data are available (or to change their position if necessary in light of subsequent information), as lawsuits generally proceed according to an ordered schedule that marches inevitably to a final decision. Second, because litigants usually only have one "bite at the apple," they have every reason to deploy any piece of evidence that could possibly support their case. Third, litigation frequently involves high stakes and strongly-held positions, which again makes parties and their attorneys eager to use any evidence that may be helpful to their case. Fourth, lawsuits are decided by lay decision-makers, whether they be judges or juries, who usually lack scientific training and expertise, and thus who may be

vulnerable to being misled into accepting dubious biomarker evidence by a wily expert. Finally, the lack of other direct evidence of specific causation in most toxic tort cases often leaves parties little choice but to use whatever biomarker evidence might be available, regardless of how well (or little) it is validated.

Similarly, with respect to biomonitoring data, advances in the detection of substances within the body have occurred more rapidly than scientific studies on toxicity. §9:5 Biomonitoring, PLIREF-PLL s 9:5. Consequently, biomonitoring is currently able to detect many substances in the body which have unknown toxicity. Nevertheless, a plaintiff may seek to influence a jury by presenting such biomonitoring data, even though the toxicological data do not support the likely juror inference that such results indicate an increased risk.

For all these reasons, it is inevitable that some litigants will seek to rely on biomarker and biomonitoring evidence prematurely. There have been other examples of dubious scientific concepts being successfully employed, at least initially, such as the claims put forward by “clinical ecologists” of “chemically induced AIDS,” which was subsequently discredited in position statements adopted by leading scientific societies. See, e.g., E. Marshall, *Immune System Theories on Trial*, 234 Science 1490 (1986). Such examples suggest that both the legal system and the scientific community need to be vigilant against improper or premature introduction of biomarker and biomonitoring evidence into toxic tort litigation.

B. Admissibility

A biomarker should be adequately validated before it is used in litigation. Validation involves demonstrating the specificity, sensitivity, and reproducibility of the biomarker response. Anthony P. Decaprio, *Biomarkers: Coming of Age for Environmental Health and Risk Assessment*, 31 *Envtl. Sci. Tech.* 1837 (1997). The validation should also verify that the biomarker is consistently linked with a clinical endpoint (*i.e.*, toxicological injury). In litigation, the threshold inquiry into whether a biomarker has been adequately validated to be used in a lawsuit will generally be determined by the trial judge in deciding whether the biomarker evidence can be admitted into evidence.

In 1993, the U.S. Supreme Court issued its *Daubert* decision which fundamentally transformed the standard for admitting scientific and other technical evidence in federal courts. *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579 (1993). *Daubert* requires judges to act as “gatekeepers” for scientific evidence introduced into a lawsuit, by pre-screening such evidence to ensure that it is reliable and relevant before it can be presented to a jury. The Supreme Court provided a non-exclusive list of four factors a trial judge should consider in determining whether proffered scientific evidence is reliable, including whether the evidence: (i) can and has been empirically tested; (ii) has a known rate of error; (iii) has been peer-reviewed and published; and (iv) is generally accepted within the relevant scientific field. In response to this new admissibility standard for scientific evidence, trial courts have been much more stringent in admitting scientific evidence, which often has the consequence of dismissing a case if the party bringing the lawsuit (who thus has the burden of proof) lacks scientific evidence that is admissible.

The *Daubert* criteria for scientific reliability comport well with the validation requirements of biomarkers, in that they require evidence to be testable and tested with a known rate of error, peer reviewed and published, and generally accepted. Nevertheless, a trial judge faced with dueling experts disagreeing about whether a particular biomarker is adequately validated and meets the *Daubert* criteria may have a difficult time deciding whether to admit the evidence. The authors of many scientific studies reporting positive biomarker associations tend to emphasize (perhaps in some cases over-emphasize) the importance of their findings, and these statements published in credible scientific journals will certainly be presented to the judge even if most scientists do not believe that the particular biomarker is adequately validated for the purpose for which it is being introduced in litigation.

An illustrative example of the premature acceptance of a biomarker by the courts was the claim that silicone breast implants resulted in the production of antinuclear antibodies and/or silicone antibodies, and that the elevated levels of those biomarkers in women with silicone breast implants supported an association between the implants and rheumatologic disease. Some of the initial court cases permitted such evidence to be presented, and this biomarker evidence was apparently quite influential in large jury awards to plaintiffs with implants. *Hopkins v. Dow Corning Corp.*, 33 F.3d 1116 (9th Cir. 1994). Over time, however, scientific bodies such as the Institute of Medicine of the U.S. National Academy of Sciences challenged the reliability and relevance of such biomarkers. Subsequent judicial opinions began rejecting the admissibility of such evidence of elevated biomarkers under the *Daubert* criteria. *Allison v. McGhan Medical Corp.*, 184 F.3d 1300 (11th Cir. 1999); *Clegg v. Medical Engineering Corp.*, 2004 WL 471694 (Fla. Cir. Ct., Feb. 25, 2004).

At the same time, the strict standards for the admission of new scientific evidence under the *Daubert* regime may impede the use of novel biomarkers that may be scientifically valid but have not yet been widely accepted or appreciated in the scientific community. As one court recently noted, “[t]horny problems of admissibility arise when an expert seeks to base his opinion on novel or unorthodox techniques that have yet to stand the tests of time to prove their validity.” *McCulloch v. H.B. Fuller Co.*, 61 F.3d 1038 (2d Cir. 1995). Judges applying the strict scrutiny of scientific evidence that has become the norm following *Daubert* may be skeptical, perhaps unduly so, of emerging new biomarkers such as gene expression assays. This roadblock is likely to be only temporary, however, until one or more courts find that particular biomarkers are adequately validated and meet the *Daubert* criteria, at which point such biomarkers are likely to quickly become widely used in litigation.

In trying to decide whether particular biomarkers are adequately validated and therefore admissible under *Daubert*, trial judges will look for authoritative scientific criteria or standards for the validation of biomarkers by governmental agencies or scientific bodies. Yet, despite the frequent use of the term “validation” in the scientific literature, there is no consensus on the definition of validation or the “rules of evidence” for determining whether a biomarker has been validated (36). The lack of any such definitive criteria at the present time will complicate the judicial task, and will surely produce inconsistent and suspect court decisions.

Biomonitoring, in particular, faces a potential admissibility challenge because of the inherent difficulty to identify the source of the chemicals discovered in the body. §9:5 Biomonitoring, PLIREF-PLL s 9:5. Biomonitoring evidence is only relevant on the condition that the substance identified in the body originated from the defendant. F.R.E 104. Consequently, plaintiffs should be prepared to make a preliminary showing of evidence sufficient to link the chemicals discovered through biomonitoring to the defendant.

C. Privacy of Litigants

Judicially compelled assays for some biomarkers and biomonitoring data may present privacy issues to the extent that they involve sensitive personal medical information that could, if improperly disclosed, result in stigma, embarrassment, or discrimination against litigants. In some cases, the harm may not be caused by the perceptions or actions of others, but simply because the litigant evaluated for biomarkers or biomonitoring data may have preferred not to know information about their own susceptibility or increased risk that is revealed by the assays. Bioethicists have recognized a right “not to know” details of one’s own health status or predispositions. C.M. MacKay, *Discussion Points to Consider in Research Related to the Human Genome*, 4 *Human Gene Therapy* 477 (1993).

Yet, the traditional rule in toxic tort and similar litigation is that when a plaintiff files a lawsuit seeking health-based damages, the plaintiff has placed his or her own health status in controversy, and the party who has been sued has the right to compel reasonable and relevant medical testing of the plaintiff. In federal

courts, for example, the trial judge has discretion to compel medical tests requested by an opposing party unless the judge finds such tests to be unnecessary or unreasonable. Mark A. Rothstein, *Preventing the Discovery of Plaintiff Genetic Profiles by Defendants Seeking to Limit Damages in Personal Injury Litigation*, 71 Indiana L.J. 877 (1996).

It is not difficult to imagine that an insurer or employer might view such information negatively and based on that perception, consciously or unconsciously discriminate against the plaintiff. For example, an insurance company may treat the evidence of early disease progression as a preexisting condition not entitled to insurance coverage, even though the condition was asymptomatic at the time of testing and would never have been revealed but for the litigation-related testing. Biomarkers of exposure present the least privacy concerns, but even with these biomarkers, evidence of significant exposure to a very hazardous agent would indicate an increased risk of disease which could again lead to discrimination against a plaintiff in insurance, employment and other contexts.

Notwithstanding these privacy concerns, it will often be necessary to compel the testing of a plaintiff for biomarkers (or absence thereof) because as discussed above biomarkers have the potential, for example, to provide very useful and relevant information for determining exposure, causation, and risk in litigation. Indeed, plaintiffs are likely to increasingly obtain and rely on such biomarker information themselves when it is helpful to their case. Opposing parties should not be precluded from seeking similar information when it is helpful to their case.

There will nevertheless be a need for courts to be vigilant of the need to protect plaintiffs' privacy rights against unnecessary, irrelevant, or overly broad requests for compelled biomarker testing. Plaintiffs' attorneys also have an ethical obligation to notify their prospective clients that filing a personal injury lawsuit may subject them to intrusive and unwanted medical testing. A party ordered to undergo biomarker evaluation who is concerned about the privacy of his or her medical information could seek a protective order from the court, which is a court-imposed confidentiality directive that requires sensitive information uncovered in litigation to be kept under seal and not disclosed outside of the trial proceedings.

D. Doctrinal Implications

Many uses of biomarker and biomonitoring data in toxic tort litigation will likely promote fairer and more scientifically defensible outcomes. In some cases, however, new biomarker or biomonitoring data have the potential to dramatically alter the legal system and legal doctrine. An example is claims for latent risk. Most of these claims, which involve lawsuits by individuals who are at increased risk from a toxic exposure but have yet to manifest any clinical symptoms, are precluded today by demanding evidentiary requirements imposed by the courts. Biomarker evidence has the potential to overcome many of these evidentiary barriers, such as by demonstrating an "existing injury" or making it easier to quantify increased risk. Since a large percentage of the general public has had a significant exposure to one or more toxic agents (even if a relatively small proportion will actually develop disease as a result), the courts may be flooded with tidal waves of latent risk lawsuits if biomarker evidence succeeds in overcoming the existing evidentiary barriers. Legal and legislative decision-makers will then be confronted with difficult policy choices on whether and when to allow latent risk claims, which have the potential to fundamentally transform the dynamics of the legal system.

Because biomonitoring in conjunction with epidemiological data can potentially generate quantifiable risk data, it is possible to shift toxic tort claims to a risk based compensation system. Albert Lin proposes such a system. Under his system, compensation is awarded based on the expected costs of harm to the exposed person determined by weighing the increased probability of harm created through exposure and the potential costs of the injury should it occur. Lin, *supra*, at 1439–40. Lin acknowledges that it would be

nearly impossible for anyone to be fully compensated if they eventually develop the illness because of the difficulty of showing a 100 percent chance of developing the disease. However, Lin argues that by restricting the awards to medical expenses, partial awards would still allow those exposed to obtain medical insurance to cover the development of future illnesses should they occur. *Id.*

Biomonitoring is gradually replacing predictive measures of exposure (such as soil concentrations, and estimations of hand-to-mouth activity) because it allows for an empirical determination of the actual exposure dose. §9:3 Medical Monitoring Claims, PLIREF-PLL s 9:3. Thus, evidence in toxic tort claims may be experiencing a shift toward a preference for biomonitoring data. As biomonitoring evidence becomes more common and reliable, courts are becoming increasingly more reliant on it. *Rowe v. E.I. duPont de Nemours & Co.*, CIV. 06-1810 (RMB), 2008 WL 5412912 (D.N.J. Dec. 23, 2008). For example, in *McManaway*, the court requested that the disclosure of any biomonitoring data from the plaintiffs, and further requested that the plaintiffs explain how the fact-finder could conclude that the alleged injuries occurred as a result of exposure if the biomonitoring results should demonstrate insufficient exposure. *McManaway v. KBR, Inc.*, 265 F.R.D. 384, 389 (S.D. Ind. 2009).

In some cases, judges seem to make negative inferences where a plaintiff fails to submit biomonitoring evidence where it is available. *See Cord v. City Of Los Angeles*, B167756, 2004 WL 2189182 (Cal. Ct. App. Sept. 30, 2004); *Nickerman v. Remco Hydraulics, Inc.*, C 06-2555 SI, 2007 WL 1793772 (N.D. Cal. June 19, 2007). If this trend continues, plaintiffs that do not obtain biomonitoring evidence of exposure without good reason (*i.e.* the short half life of a chemical might make biomonitoring tests for past exposure pointless) could face a negative inference that no exposure actually took place.

V. Conclusion

Biomarkers and biomonitoring data will increasingly be used in toxic tort litigation. Indeed, such data are likely to become the norm in toxics tort lawsuits in adjudicating both exposure and causation. As one court decision recently suggested, the expectation will be that parties seek to utilize such data, and when they don't, their arguments will be seen as suspect: held "[T]here are biological tests (biomarkers) that measure the levels of chemicals in the body to reveal whether these levels can exceed expected or accepted levels. ... [B]ecause no such tests were performed on Mr. Cord, 'it is impossible to determine to a medical certainty' whether Mr. Cord's exposure, absorption or toxicity to benzene or other chemicals exceeded normal and expected levels. In other words, existing tests were available to measure whether Mr. Cord in fact had excessive exposure to benzene and other chemicals, but plaintiffs' experts did not use them." *Cord v. City of Los Angeles* (Cal. App. Sept. 30, 2004).

Not only will the existing types of biomarkers and biomonitoring data be used more frequently, but new and perhaps more informative types of biomarkers now being developed in the research context will start to be applied in litigation contexts. For example, toxicogenomics, which measures cellular changes in gene expression, protein levels, and metabolites, among other parameters, is likely to increasingly be used in toxic tort litigation. Gary Marchant, *Genomics and Toxic Substances: Part I - Toxicogenomics*, 33 *Env'tl. Law Rep.* 10071 (2003). As a recent report from the National Research Council (the research arm of the US national Academies of Science) noted, "Both plaintiffs and defendants are likely to seek to use toxicogenomic data for various purposes in future toxic tort litigation" National Research Council, *Applications of Toxicogenomic Technologies to Predictive Toxicology and Risk Assessment* (2007). As the frequency and types of biomarker and biomonitoring data used or potentially used in toxic tort cases expands, attorneys and judges will be challenged to keep up to date with this rapidly shifting scientific terrain.