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COMMENTS OF AN EXPERT: BIOMARKER EVIDENCE FOLLOWING EXPOSURE TO POLLUTANTS

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I. INTRODUCTION

LITIGATION has rapidly become trial by expert since the enactment of the Federal Rules of Evidence in 1975.[1] The Federal Rules generally broadened the standards for admissibility of evidence.[2] Specifically, Rule 702 authorizes judges to admit expert testimony on scientific matters if it "will assist the trier of fact . . . ."[3] Moreover, Rule 703 allows judges to admit expert opinion based on otherwise inadmissible evidence when the facts or data on which the opinion is based are "of the type reasonably relied upon by experts in a particular field."[4] The Third Circuit has emphasized that Rule 703 requires the reliability of data to be determined by experts in the relevant discipline, rather than the court.[5] This approach heightens the importance of the expert's role in litigation. Expert testimony admitted under this Rule is submitted to the jury for determination as to its validity.

In the area of toxic tort litigation, the scientific evidence offered by the expert can be vital to proving injury. In particular, experts in immunology claim that evidence of abnormal human

† Dr. Zahalsky holds a Ph.D. in microbiology from New York University and is an immunology professor at Southern Illinois University at Edwardsville. His consulting firm, Immunox Research, Inc., specializes in providing scientific consultation for litigation. P.R. McConnachie holds a Ph.D and is a researcher at Immunox. He is President of Immunotest. The admissibility of expert witness testimony was the underlying theme of the *Journal's* symposium. Dr. Zahalsky delivered an address at the symposium overviewing his experience as an expert witness in the area of toxicology.

1. *See* FED. R. EVID. 702 advisory committee's note (proposed amendment) ("The use of [expert] testimony has greatly increased since enactment of the Federal Rules of Evidence."); *see also* Jack B. Weinstein, *Improving Expert Testimony*, 20 U. RICH. L. REV. 473 (1976) (almost all federal cases tried today involve expert testimony).

2. *See* Weinstein, *supra* note 1, at 477.

3. FED. R. EVID. 702.

4. FED. R. EVID. 703. *See also* Christophersen v. Allied-Signal Corp., 939 F.2d 1106 (5th Cir. 1991) (en banc) (per curiam) (expert opinion should be excluded when based on underlying facts so unreliable that opinion would not assist trier of fact).

5. *See In re* Japanese Elec. Prod. Antitrust Litig., 723 F.2d 238, 276 (3d Cir. 1983). The court must, however, make a factual determination as to what facts or data experts in the field rely on. *Id.* at 277.

response to toxic exposure is provided by biomarkers of organ damage or dysfunction. Biomarkers are "[m]easurable alterations in cells or cell products caused by an abnormal effect on a particular organ system . . . . [M]easurable implies some knowledge of the accuracy and precision of the methods used to detect the change."[6] On that basis, expert opinion based on biomarker results may be reported out as being both reliable and valid and, consequently, admissible at trial. This is why the specialized knowledge of the expert witness is vital.

It is the role of the expert witness to determine from biomarkers, or other means, whether toxic exposure has caused organ damage or dysfunction. Even the most reputable experts may, however, disagree as to whether methods used to detect change are, in fact, reliable and valid. This is illustrated in the case of *In re Paoli Railroad Yard PCB Litigation*.[7]

The original *In re Paoli* case was a consolidation of thirty-eight suits brought against the Southeastern Pennsylvania Transportation Authority by neighbors and workers in the Paoli Railyard for improper storage of polychlorinated biphenyls (PCBs).[8] Plaintiffs claimed that they suffered injuries proximately caused by exposure to the high levels of PCBs found in the area surrounding the Paoli Railyard.[9] Their entire case depended on expert testimony which attempted to link PCB exposure to causation.[10] The defendants moved for summary judgment, arguing that the plaintiffs' expert testimony was not based on facts or data reasonably relied upon by experts in the field.[11] The district court weighed the expert testimony offered by the plaintiffs against that of the defendants. The court was persuaded by the

6. *See* SUBCOMMITTEE ON BIOMARKERS OF ORGAN DAMAGE AND DYSFUNCTION FOR THE RENAL HEPATOBILIARY AND IMMUNE SYSTEMS, CENTER FOR DISEASE CONTROL/AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY, SUMMARY REPORT, *Biomarkers of Organ Damage or Dysfunction for the Renal Hepatobiliary and Immune Systems* 1 (1990) [hereinafter SUMMARY REPORT].

7. 706 F. Supp. 358 (E.D. Pa. 1988), *rev'd*, 916 F.2d 829 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991).

8. *Id.* at 361. PCBs are toxic chemical compounds manufactured for over 40 years for use in electrical insulation and heating and cooling units. RONNY J. COLEMAN & KARA HEWSON WILLIAMS, HAZARDOUS MATERIALS DICTIONARY 118 (1988). PCBs had been used for decades in the railroad transformer cars serviced at the Paoli Railyard. *In re Paoli*, 706 F. Supp. at 361.

9. *In re Paoli*, 706 F. Supp. at 361-62.

10. *Id.* at 369-70. Experts testifying on behalf of plaintiffs included: (1) Dr. Albert Allen, who had a doctorate in environmental chemistry; (2) Dr. Deborah Barsotti, a toxicologist with a doctorate in pathology; and (3) the author of this article, Dr. Zahalsky, who has a doctorate in microbiology. *Id.*

11. *Id.* at 376.

defendants' expert testimony that there was no causal link between PCB exposure and plaintiffs' injuries and excluded the majority of the plaintiffs' expert opinion under Rule 703.[12] Consequently, the district court granted summary judgment on the grounds that the plaintiffs failed to meet their burden of proof as to causation.[13]

On appeal, the Third Circuit reversed this decision and held that the district court's evidentiary ruling was to be set aside for "fail[ure] to give plaintiffs an adequate opportunity to present their factual and legal contentions on the evidentiary issues" relating to causation.[14] *In re Paoli* demonstrates that the question of reliability of an expert's opinion may be dispositive to the outcome of a toxic tort case when causation is at issue.

As an expert, I am aware of the difficulties in proving with a reasonable degree of scientific certainty that toxic exposure caused organ damage when there are no overt signs. My experiences as an expert in immunology form the basis for the observations and comments in this Article. The Article will discuss the role of measurement as used by the expert and the expert's usage of biomarkers. The Article then focuses on the magnified effects that exposure to toxins has on children as evidenced by studies utilizing biomarkers.

II. BIOMARKERS AS A MEASURING DEVICE

A. The Role of Measurement as Used by Experts

Measurement provides data on which an expert can base a reliable and valid opinion for admission in a court.[15] Measurement does not imply statistical treatment of the data to a level of statistical significance. Statistical significance is a confidence statement, and in practice we may or may not achieve it. But, statistical significance is neither a requirement nor a statement of reasonable probability, and measurement of data without statistical significance is by itself a means of determining reasonable probability.

12. *Id.* at 366.

13. *Id.* at 375.

14. 916 F.2d 829, 836 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991). In addition, the appellate court held that the district court "ruled on an inadequate factual record and it failed to adequately articulate the basis for its rulings." *Id.* *See also* Rubanick v. Witco Chem. Corp., 542 A.2d 975 (N.J. Super. 1988), *rev'd*, 576 A.2d 4 (N.J. Super. Ct. App. Div. 1990), *modified*, 593 A.2d 733 (N.J. 1991) (trial court improperly excluded expert witness testimony).

15. *See supra* notes 4-6 and accompanying text.

Specifically, the role of measurement is to provide the expert with reliable and valid data which may *then* be interpreted to support or refute an opinion of etiology or cause, of the presence of disease or progression to a disease state, of interventions or treatments, and of future needs through biomonitoring and examination.[16] The burden borne by the opinion maker is to make an interpretation of probability in a responsible and accountable manner. This burden does not command certainty, but demands a reasonable degree of scientific probability. This standard permits, indeed encourages, the testing of alternatives to yield the more likely or more probable outcome.

Legal notions of causation, however, differ from these scientific causal concepts. In tort law, the legal test is that wrongful conduct must be the proximate cause of the harm. Legal scholars traditionally base causation theories on deductive reasoning. Scientists, on the other hand, use causal concepts to set up hypotheses. The method by which they test these hypotheses usually involves inductive reasoning and probabilistic evidence.[17] Thus, a scientific explanation is framed in terms of causality, but the evidence to support the explanation need not involve a deductively framed causal chain. These differing approaches present a difficulty for courts in handling evidence based on scientific notions of causation. The difficulties are exaggerated in hazardous waste litigation.[18] Legal notions demand traceable causal links in chain of events; scientific notions rely on evidence of reasonable probability to prove causation.[19] A reasonable probability of a hazardous substance causing injury may not satisfy the legal notion of proximate cause.[20] Rule 703 provides the court with a means of resolving this conflict by setting a scientific standard on which the court can rely.

The methods of science are *not* methods of proof. They are, as practiced, and as adopted by our legal system, the methods and inquiries that are meant to convey *reasonable probability*. The words that raise the level of scientific suspicion include: always, never, totally, absolutely, and completely. As scientists, we are not *sure*, but we are not speculating either. We are not concre-

16. *See infra* note 34.

17. *See* Troyen A. Brennan, *Causal Chains and Statistical Links: The Role of Scientific Uncertainty in Hazardous-Substance Litigation*, 73 CORNELL L. REV. 469, 481-82 (1988).

18. *Id.*

19. *See generally id.* at 478-91.

20. *Id.* at 471, 491.

tized into unmodifiable positions, but we are not amoeboid either. We are, at our best, sorters and excluders, weighers of evidence and interpreters. And, in the end, honorable men and women of the professions, in the laboratory, clinic, scientific forums, or courtroom, may honorably disagree as to the probable meaning of a set of data or cluster of findings or profile of biomarker measurements. Our shared burden is to continue to test the reliability of our probability statements. The investigator or expert who is committed to relying *solely* on historic evidence, statistical inference, or descriptive epidemiologic findings which do not have the *power* to test an alternative hypothesis is the person who is not yet committed to the methods and practices that may yield evidence of probable cause.

B. Federal Government Recognition of Using Biomarkers

The use of Biomarkers in Environmental Health Science is illustrated by a recent United States Public Health Service (P.H.S.) summary report. In the preface of their report dated August 27, 1990, the P.H.S. Center for Disease Control/Agency for Toxic Substance and Disease Registry (CDC/ATSDR) Subcommittee on Biomarkers of Organ Damage and Dysfunction made the following statements:

> The potential for adverse health effects caused by exposure to environmental pollutants is one of the most pressing concerns of modern society. The adverse effects of some toxic exposures are immediately evident. Other toxic exposures occur at levels that do not cause acute illness but may cause unrecognized biologic changes and an increase in the prevalence of certain chronic diseases. The challenge of environmental health laboratory science is to determine the extent of toxic exposure, identify preclinical changes, monitor affected populations, and aid in attempts at intervention before disease processes become irreversible.
>
> Without overt disease or specific symptoms, the only way to identify sub-pathophysiological changes in a particular organ system is to look for alterations in the cells and metabolic products of the tissues that make up that system. For purposes of this document, measurements that detect sub-alterations will be termed biomarkers of organ damage or dysfunction. Although

> many tests for organ damage and dysfunction are performed routinely in clinical laboratories, their use in population studies for public health epidemiology are often different from the way they are used in normal medical practice. Conversely, tests that are not used routinely by clinical pathologists may be useful or even essential to epidemiologists. . . .
>
> The primary purpose of the subcommittee was to evaluate currently available laboratory tests for their suitability in measuring human organ-specific biomarkers. Tests were selected on the basis of the public health importance in detecting adverse health effects caused by exposure to toxic substances . . . .
>
> The public health goal of using biomarkers in studies at sites of potential toxic exposure is to be able to inform a population whether biomarker test results suggest an increased risk of morbidity or mortality due to toxic exposure in that population.[21]

The possibilities for the actual use of biomarkers in assessing human health was summarized by the Subcommittee as follows:

> [B]iomarkers can be used to identify: 1) susceptibility to the toxic effects of environmental pollutants; 2) exposure to such toxicants; and 3) biologic effects of exposure. Susceptibility markers are measurable indicators of biologic factors that influence the probability of disease. Exposure markers are measurable indicators that can occur after the body is exposed to toxicant(s). The most obvious example of an exposure marker is the measured level of a toxicant in an organism.
>
> . . . [W]e will limit consideration to markers of the third category: the biologic effects of toxic exposure and organ damage. Such responses may range from transient and reversible changes with virtually no health effects to permanent changes that are associated with increased morbidity and mortality.[22]

Clearly, the Subcommittee recognizes and advocates the expert's use of biomarkers. Since the spectrum of change in health encompasses metabolic fluctuations within physiological limits

21. SUMMARY REPORT, *supra* note 6, at i.
22. *Id.* at 1-2.

through cell and tissue pathology *without* overt symptoms of disease to clinically apparent illness, we are faced with the need to follow (i.e., monitor) the progression of cell and organ dysfunction and dysregulation from subclinical through pre-clinical to clinical overtness. Hence, the role of the expert in detecting and monitoring organ dysfunction and dysregulation is crucial.

III. BIOMARKERS PROVE THE EFFECTS OF TOXIC EXPOSURE ON CHILDREN

When studies are done to determine if exposure to pollutants have caused organ damage, tests designed specifically for children are often not used. For instance, in *In re Paoli* an ATSDR study which surveyed the neighbors surrounding the railyard found that those residents who lived in areas with more PCBs in the soil had no more PCBs in their blood than the residents in other areas.[23] However, the ATSDR did not focus its investigations on children, although children are generally considered to be at greatest risk of injury from PCB exposure.[24] This is a common oversight in epidemiological studies.

Why are children likely to be more sensitive to toxic chemicals? Children expend more energy than adults and consequently eat more food, breathe more air, and drink more water per pound of body weight than an adult.[25] As a result, children are exposed to higher doses of toxins from the environment.[26] Since the dose of toxics per pound of body weight in a child is higher, children are more susceptible to injury from environmental toxins than adults.[27] Additionally, children are growing rapidly and certain toxins cause more damage to rapidly dividing cells.[28] The higher percentage of rapidly dividing cells in a child compared to an adult makes the child more vulnerable to toxins than adults.

Children are also more susceptible to toxic chemicals because some organ systems, particularly in the very young child, are immature.[29] A child's immune system for approximately the

23. 706 F. Supp. 358, 365 (E.D. Pa. 1988), *rev'd*, 916 F.2d 829 (3d Cir. 1990), *cert. denied*, 111 S. Ct. 1584 (1991).

24. *Id.*

25. Beverly Paigen, *Children and Toxic Chemicals*, 1986 J. PESTICIDE REFORM 2.

26. *Id.*

27. *Id.*; *cf.* Regan J.R. Smith, *Playing the Acid Rain Game: A State's Remedies*, 16 ENVTL. L. 255, 264 (1986) (lead from acid rain poses greater health risks to children).

28. Paigen, *supra* note 25, at 2.

29. *Id.*

first two years of life is formed and responsive, but immature. Children exposed to a toxin affecting the immune system will probably have more ear infections, more viral illnesses, more colds, more pneumonia, and more bouts of flu.[30]

A child's reproductive system is also more vulnerable to toxic agents, as has been shown in both animal studies and human experience where exposure to the chemical dibromochloropropane (DBCP) has been tested or known to occur.[31]

The rapid growth of children, though "mak[ing] them especially sensitive to chemical damage . . . also means that they can recover quickly."[32] Removal of children from sources of toxins can result in the children "catching up" as it were, to their peers.[33] The children whose data we have compiled were removed from the source of a toxin, but *the damage* they sustained appears to have remained. The compelling nature of these data hopefully will lead others, such as the ATSDR, to reconsider and reevaluate their comments regarding a level of dioxin which produces no adverse health effects.

IV. CONCLUSION

The American people and citizens of other countries have become increasingly aware of and knowledgeable about actual and potential exposure to pollutants in the air, waters, and surface materials of the daily environment. Following from such awareness has been the need for accurate and objective information on the health effects of inhaled, absorbed, and ingested pollutants. The emergence and validation of biomarkers that can be used to measure the extent and consequences of exposure to environmental pollutants has led to their use as markers of disease because markers can both discriminate among and describe stages within the continuum of subclinical, pre-clinical, and clinically overt disease.[34]

30. *Id.*

31. *Id.*

32. *Id.* at 5.

33. Paigen, *supra* note 25, at 5.

34. *See* NATIONAL RESEARCH COUNCIL, BIOLOGIC MARKERS IN PULMONARY TOXICOLOGY, SUBCOMMITTEE ON PULMONARY TOXICOLOGY, 91-103 (1989) (describing markers of inflammatory and immune responses to inhaled toxins). Although it may still be argued whether the presence of sensitizing cells and/or antibodies in the broncho-lavage fluid of patients exhibiting both hypersensitivity pneumonitis and berylliosis completely identifies the disease as having been caused by beryllium inhalation, the fact that beryllium does act as a hapten pro-

The burden of the expert is to use biomarkers to achieve just such discrimination and provide the treater with a quality and quantity of evidence that allows for intervention at the earliest time. Together, the opinions offered by the expert and relied upon by the treater share in the recognition that human damage from pollutants that results in body system dysfunction and dysregulation does not occur as an "all or none" response. Rather, the use of biologic markers reveals a progression to (or in) a disease state or recovery from a condition of disease. The opinions of the expert, therefore, *are* the data. Without the expert there is no data or evidence, therefore, the role of the expert is invaluable in verifying the effects of toxic exposure to pollutants.

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vides reasonable certainty that an immunological response is a predominant, hence probable causal feature of the pathogenesis of berylliosis.