

**The Use of  
Toxicology in Tort Litigation**  
**A Survey of Federal and State Jurisdictions**

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## INTRODUCTION

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This monograph reflects the increasing use of toxicology in tort litigation, as litigants have become more assertive about seeking compensation for personal injuries or property damage allegedly caused by exposure to harmful substances. While toxicology has long played a role in criminal cases, its use in civil litigation has emerged more recently and its importance to proving causation is now recognized by federal and state courts across the nation. Examples of cases where toxicology can play a determinative role include lawsuits over the use or misuse of pharmaceuticals, litigation about workplace exposure to toxins and claims arising out of environmental exposure to chemicals in the ground, water or air.

Toxicology melds chemistry, biology and statistics. It is focused on determining the dose at which a chemical will produce a harmful effect. A fundamental concept that should be communicated to the finder of fact is that any chemical can be harmful at a sufficient dose: even water is harmful if too much is consumed. The challenges for attorneys in tort litigation are *first*, to understand whether and how the toxicological evidence supports their position and *second*, to make the science of toxicology both comprehensible and compelling to judges and jurors who decide the issues.

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The great majority of toxicology studies involve research on laboratory animals, cells or tissues.<sup>4</sup> Such studies are used to reach conclusions about human responses to toxins although, in the litigation context, there are often disputes about the extent to which animal or cell studies are predictive of effects in people. It is, of course, unethical to expose healthy humans to doses of chemical agents anticipated to cause harmful effects outweighing any therapeutic purpose. In some instances, however, where humans have been exposed to toxic substances in the environment or in the workplace, researchers may observe the effects of exposure although they lack the ability to measure the extent of exposure or to control for confounding variables, leading to disputes about the reliability and validity of conclusions drawn from such studies.

Toxicology evidence is typically adduced through the testimony and opinions of qualified experts under the relevant *Daubert* or *Frye* standards. The questions addressed by toxicologists include:

- Is the substance to which the plaintiff was exposed capable of causing the alleged injury?
- How does the dose or level of exposure affect the chance of injury?
- How does the route and frequency of exposure affect injury?
- What is the expected time lag between exposure to the toxic substance and observed injuries?
- How long will the substance stay in the body?
- Are the alleged injuries reversible?
- To what extent are animal studies showing toxic effects useful for making conclusions about toxic effects in humans?
- How much risk of harm exists from the presence of a substance in the environment to those who live or work in that area?

Identifying the proper questions for a given case and presenting supporting evidence depends, in part, on some understanding of the science of toxicology. Although we do not attempt to provide a detailed scientific education, we offer the following sections as an introduction to the concepts of toxicology and their use in tort litigation,

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<sup>4</sup> Bernard D. Goldstein & Mary Sue Henifin, *Reference Guide on Toxicology*, in Reference Manual On Scientific Evidence 401, 405 (Federal Judicial Center, 2nd ed. 2000).

which should provide a platform for review of the individual chapters and cases that follow.

## I. Toxicology and Toxicologists

In a nutshell, toxicology is the study of poisons.<sup>5</sup> According to its largest professional organization, the Society of Toxicology, “Toxicology is the science that studies the effects of exposure to drugs, environmental contaminants, and naturally occurring substances found in food, water, air, and soil.”<sup>6</sup> Toxicology deals with chemical substances and how they affect living organisms, including substances generally harmless that prove toxic under certain conditions.<sup>7</sup> Toxicology studies are routinely performed to assess the safety of medicines, household and garden chemicals, and industrial and natural compounds to which humans and other animals may be exposed.<sup>8</sup>

“Poisons” can take many forms. A toxicant can be any solid, liquid, or gas substance that when introduced into or applied to the body of an organism can interfere with the life processes of cells of the organism by its own inherent qualities without acting mechanically and irrespective of temperature. A “poison” can be beneficial at one dose and toxic at another.<sup>9</sup> It can be toxic to one person and harmless to another person under the same conditions. It may be a naturally occurring chemical such as lead, of biologic origin such as the toxin causing botulism, or it may be manufactured such as a pesticide. Although chemicals having similar structures usually cause similar effects, a chemical having a certain structure may be highly toxic at a low dose while a chemical having a very similar structure may cause no adverse effect at even a high dose.

Toxicologists are trained in biochemistry, pharmacology, industrial hygiene, or a related scientific discipline and typically have advanced degrees. Some toxicologists are medical doctors, although not all physicians have advanced training in toxicological research.<sup>10</sup> Toxicologists are trained to examine the cellular, biochemical, and molecular mechanisms of action of adverse effects of chemicals on living organisms and to assess

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<sup>5</sup> *Id.* at 403.

<sup>6</sup> <http://www.toxicology.org>.

<sup>7</sup> David L. Eaton & Curtis D. Klaassen, *Principles of Toxicology*, in Casarett And Doull’s *Toxicology: The Basic Science Of Poisons* 13, 13 (5th ed. 1996).

<sup>8</sup> <http://www.toxicology.org>.

<sup>9</sup> David L. Eaton, *Scientific Judgment and Toxic Torts – A Primer in Toxicology for Judges and Lawyers*, 12 J.L. & Pol’y 5, 11 (2003) (“Indeed, the basic dictum of toxicology was stated by the Sixteenth Century Physician/Philosopher, Paracelsus, considered the ‘father of toxicology’: ‘All substances are poisonous – there is none which is not; the dose differentiates a poison from a remedy.’”).

<sup>10</sup> Goldstein & Henifin, *supra* note 4, at 416.

the probability of the occurrence of those adverse effects.<sup>11</sup> Toxicology experts thus should have a solid background in both statistics and disease pathogenesis.<sup>12</sup>

Toxicological evidence consists of data and analysis from controlled scientific studies. It is much more than just qualitative assessments, risk calculations, or opinions. The principles, techniques, and limitations of toxicology should be understood by anyone offering or evaluating toxicological evidence in the courtroom.

## II. Basic Principles of Toxicology

Virtually any substance is capable of inducing some form of toxic effect. The type and severity of effect of a substance depends on the dose (the amount of the substance that enters the body), the route of exposure (*e.g.*, ingestion, inhalation, injection, skin contact), the duration of exposure (*e.g.*, seconds to years), and the frequency of exposure (how many times and the intervals between exposures).<sup>13</sup>

The basic underlying principle of toxicology is that the toxicity of a substance to a living organism such as a human being depends on the dose of the substance the organism receives.<sup>14</sup> Most chemicals are not inherently “toxic” or “non-toxic.” For nearly every substance, there is some dose that will be fatal to recipients and some dose that is almost always safe, and between these levels will be observed a continuum of pathological conditions in recipients ranging from mild to severe in direct relationship to the dose of the substance received. Toxicologists plot this dose-response relationship as a curve. Much of toxicology is devoted to identifying dose-response curves.<sup>15</sup> Although individuals within a population may respond differently to the same relative dose of a substance, a key premise in toxicology is that the reactions of the population as a whole follow a general dose-response relationship.<sup>16</sup>

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<sup>11</sup> See *id.* at 403.

<sup>12</sup> *Id.* at 416.

<sup>13</sup> Eaton & Klaassen, *supra* note 7, at 15-16; Eaton, *supra* note 9, at 10.

<sup>14</sup> Eaton & Klaassen, *supra* note 7, at 14. The “dose” is the amount of the chemical that enters the body, is generally calculated by considering the quantity of the chemical and the body weight of the organism, and is expressed as mg/kg or the like. *Id.* at 11. Dose is the single most important factor to consider in evaluating whether an alleged exposure caused a specific adverse effect. *Id.*

<sup>15</sup> *Id.* at 18-25 (The dose-response relationship “is the most fundamental and pervasive concept in toxicology. . . . Whatever response is selected for measurement, the relationship between the degree of response of the biological system and the amount of toxicant administered assumes a form that occurs so consistently as to be considered classic and fundamental.”); Eaton, *supra* note 9, at 15.

<sup>16</sup> Eaton, *supra* note 9, at 15.

The dose-response relationship depends on many factors, including characteristics of the substance and characteristics of the recipient.<sup>17</sup> Toxicologists strive to determine the mechanism by which a substance causes adverse effects. They try to understand how a toxicant enters an organism, how it exerts its deleterious effects, how it interacts with the biological processes within the organism, and how the organism reacts to the insult. Key concepts in toxicology include exposure, absorption, distribution, metabolism, excretion, storage, frequency, and time.<sup>18</sup>

The route of exposure is critical. For example, the dose of a substance that can cause toxicity when inhaled may be lower than the dose of the same substance required to cause toxicity when swallowed. Many substances are minimally, if at all, absorbed through the skin.<sup>19</sup> The absorption of a chemical is related to the concentration of the chemical at the absorbing surface, the area of the exposed site, and the chemical properties of the toxicant.<sup>20</sup> Hours of exposure to a poorly-ventilated room saturated with a gaseous toxicant will cause a different amount of absorption, potentially through both the lungs and the skin, than will simply walking by an open container outdoors of the same toxicant in liquid or solid form.<sup>21</sup> Smaller particles of a toxicant have more surface area than the equivalent dose of the substance in larger particles and thus will be dissolved and absorbed more readily.<sup>22</sup> Other substances in the environment along with the substance at issue may enhance or prevent absorption. For example, an ingested chemical might not be absorbed if it binds with other materials present in the gastrointestinal tract.

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<sup>17</sup> Although dose is generally expressed in relation to the body weight of the recipient because body weight is easily measured, toxicity analysis may be more appropriately based on the recipient's body surface area, particularly when extrapolating from one species of recipient to another with a significantly different body shape. See Eaton & Klaassen, *supra* note 7, at 27 ("On the basis of dose per unit of body surface, toxic effects in humans are usually in the same range as those in experimental animals. On a body weight basis, humans are generally more vulnerable than are experimental animals, probably by a factor of about 10."). See also Shayne Cox Gad, *Model Selection and Scaling, in Animal Models In Toxicology* 813, 824-25 (Shayne Cox Gad & Christopher P. Chengelis eds., 1992).

<sup>18</sup> Eaton & Klaassen, *supra* note 7, at 15.

<sup>19</sup> *Id.* ("Toxic agents generally produce the greatest effect and the most rapid response when given directly into the bloodstream (the intravenous route). An approximate descending order of effectiveness for the other routes would be inhalation, intraperitoneal, subcutaneous, intramuscular, intradermal, oral, and dermal.").

<sup>20</sup> Zoltan Gregus & Curtis D. Klaassen, *Mechanisms of Toxicity, in Casarett And Doull's Toxicology: The Basic Science Of Poisons* 35, 36 (5th ed. 1996).

<sup>21</sup> See Karl K. Rozman & Curtis K. Klaassen, *Absorption, Distribution, and Excretion of Toxicants, in Casarett And Doull's Toxicology: The Basic Science Of Poisons* 91, 97-100 (5th ed. 1996).

<sup>22</sup> *Id.* at 94-97.

Toxicologists also look at how a substance is distributed in the body.<sup>23</sup> A substance may act locally at the point of entry or it may be carried through the bloodstream to act on a target organ elsewhere or systemically on many different tissues throughout the body. Some chemicals are capable of passing through the blood-brain barrier or across the placenta, while many are not.<sup>24</sup>

How the body handles the substance is important to understand. Transformation of the substance within the body may make it more or less harmful. Some substances are not harmful themselves, but cause injury when metabolized by the body through the production of a toxic metabolite or free radicals.<sup>25</sup> A substance may be detoxified by the body at low doses, but cause adverse effects when detoxifying pathways within the body are overwhelmed by a higher dose. A substance may cause its harmful effects by interfering with processes within the body causing natural body substances to reach harmful levels.

Toxicants can be eliminated from the body by various routes, including urine, feces, exhalation, sweat, and lactation.<sup>26</sup> Routes of elimination must be understood because, for example, a person with kidney problems will be unable to eliminate a toxin through the urine as readily as a person with normal kidney function. Also, excretion into breast milk exposes a nursing infant to the substance.

Metabolism and excretion are especially important considerations when more than one toxicant is involved. Exposure to multiple toxicants at “safe” doses may cause toxic effects if the toxicants are all metabolized or eliminated through the same biologic pathways or can interact with each other for a synergistic effect.<sup>27</sup> Certain chemicals are not immediately eliminated from the body but may get stored and accumulate in body fat, lungs, bone, or other tissues and persist for decades.<sup>28</sup> Stored toxicants may cause a toxic episode long after the time of exposure.<sup>29</sup>

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<sup>23</sup> Gregus & Klaassen, *supra* note 21, at 38; Rozman & Klaassen, *supra* note 22, at 101.

<sup>24</sup> Gregus & Klaassen, *supra* note 21, at 38; Rozman & Klaassen, *supra* note 22, at 104-05. The placental barrier consists of cell layers interposed between the maternal and fetal circulations. The number of layers varies between species.

<sup>25</sup> Gregus & Klaassen, *supra* note 21, at 39-41.

<sup>26</sup> *E.g.*, Rozman & Klaassen, *supra* note 22, at 105-09.

<sup>27</sup> *See* Gregus & Klaassen, *supra* note 21, at 42-43.

<sup>28</sup> Rozman & Klaassen, *supra* note 22, at 102-04.

<sup>29</sup> *Id.* at 103. For example, highly lipophilic toxicants may be stored in body fat. This can result in less severe toxicity in an obese person than in a lean individual, and a sudden episode of toxicity when rapid mobilization of fat occurs at a time of starvation.

The toxic dose also depends on the duration and frequency of administration.<sup>30</sup> The body may be able to more readily recover from a brief high dose exposure than a continual exposure at a lower dose. A dose may cause severe effects if given all at once, but no effect when divided into several smaller doses totaling the same amount. Exposure to a substance day after day for a lifetime may be more likely to cause adverse effects than a single exposure to the same dose of the same substance, although some metabolic pathways are enhanced by frequent encounters with certain types of substances and detoxify such substances progressively more rapidly, leading to decreased toxicity. Repeated exposures at intervals shorter than the time required to eliminate previous doses will cause levels of a substance to rise and increase the chance of a toxic effect, whereas repeated exposures after complete elimination of previous doses may have no cumulative effect.<sup>31</sup>

Toxic effects may appear immediately or may take hours or days to become noticeable.<sup>32</sup> Some effects may appear only after a latency period of many years, such as cancers. Certain toxicants may only cause adverse effects in the exposed victim's offspring. Understanding when effects are typically expressed after exposure can support or refute a plaintiff's claim that a particular exposure caused a particular injury.

Some toxic effects are reversible, while others are irreversible.<sup>33</sup> The tissue targeted by the toxicant or its by-products is a major determinant of this characteristic. Liver tissue, for example, is known to have a high ability to regenerate after injury while nervous tissue is thought to lack any appreciable ability to repair or regenerate itself.

Occasionally, an individual's response may not correlate with the dose of a substance, as when the individual's immune system has been "sensitized."<sup>34</sup> In such cases, even a minimal amount of the substance can trigger an "allergic" reaction that may be severe. Such a reaction is usually qualitatively different than the response exhibited at toxic doses by the majority of the population, reflecting immune system pathogenesis. This phenomenon is thought to be the basis for the most controversial claims in toxicology litigation, including "Multiple Chemical Sensitivity" and "Sick Building Syndrome."<sup>35</sup>

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<sup>30</sup> Eaton & Klaassen, *supra* note 7, at 15-16.

<sup>31</sup> *Id.*

<sup>32</sup> *Id.* at 17.

<sup>33</sup> *Id.*

<sup>34</sup> *Id.* at 16; Eaton, *supra* note 9, at 20-21.

<sup>35</sup> Eaton, *supra* note 9, at 20-21.

### III. The Methodology Underlying Toxicology

The living organism exposed to the substance at issue introduces many variables that affect the dose-response relationship.<sup>36</sup> The species, genetics, gender, age, health status, metabolic rate, amount of body fat, reproductive status, and other factors of the substance recipient can all affect the toxicity of the substance at a given dose, as can concurrent exposure to other substances.<sup>37</sup> Environmental and lifestyle factors such as smoking, drug use, alcohol consumption, diet, infectious agents (viruses and bacteria), stress, and physical activity can also modify the dose-response relationship.<sup>38</sup> Toxicology studies are performed by controlling as many of these variables as possible so that the effects of the substance being studied can be isolated.<sup>39</sup>

Toxicology studies are performed on bacteria or fungi, human or animal cell cultures or tissues *in vitro* in the laboratory, or *in vivo* on laboratory animals, although toxicology research may also be conducted on people under certain circumstances. Deliberately exposing people to potential toxins at doses intended to discover or demonstrate adverse effects including death is considered unethical.<sup>40</sup> But researchers frequently study the effects of environmental contaminants or workplace hazards by collecting ongoing data about exposures and their effects. For example, employers may conduct medical surveillance studies of employees who are exposed to industrial chemicals.<sup>41</sup> A government entity may sponsor studies of the effect of groundwater contamination on residents of a community. In those instances, exposure to the toxicant of interest is not under the researcher's control and confounding variables are controlled for by statistical analysis rather than experimental design.

Toxicity tests in laboratory animals or *in vitro* are designed to characterize the toxic effects of a chemical, not demonstrate that the chemical is safe.<sup>42</sup> Each toxicology study is designed to look for a particular characteristic of a substance, such as acute (short-term) or chronic (long-term) toxicity, mutagenicity (genetic alteration), teratogenicity (causing birth defects), carcinogenicity (cancer-causing), or eye or skin irritation.<sup>43</sup> Depending on the purpose of the study, a single dose may be used, doses may be given daily for a period of time such as three months, doses may be given during

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<sup>36</sup> See Eaton & Klaassen, *supra* note 7, at 25-27.

<sup>37</sup> Gad, *supra* note 18, at 826-32.

<sup>38</sup> *Id.*

<sup>39</sup> Goldstein & Henifin, *supra* note 4, at 406.

<sup>40</sup> *Id.* at 405.

<sup>41</sup> See, e.g., Robert R. Lauwerys, *Occupational Toxicology*, in Casarett And Doull's *Toxicology: The Basic Science Of Poisons* 987, 987-1007 (5th ed. 1996).

<sup>42</sup> Eaton & Klaassen, *supra* note 7, at 27.

<sup>43</sup> *Id.* at 27-32; Goldstein & Henifin, *supra* note 4, at 405-06.

certain or all phases of the gestation period, or animals may be continually exposed to the substance for their entire lives.<sup>44</sup> The largest tolerated doses are generally included in toxicology studies to enhance the chances of observing effects at rates demonstrating statistical significance over unexposed controls subject to the same conditions.<sup>45</sup>

During and after a toxicology study, cells are examined for abnormalities, laboratory tests are run on samples from exposed animals, clinical signs are observed, and postmortem examinations are conducted at gross and microscopic levels. Pharmacokinetic studies may be performed to reveal information on absorption, distribution, metabolism, and elimination of the substance and its by-products. Results are compared to results from matched control groups not exposed but similar in all other relevant characteristics and treated in the same way.<sup>46</sup> Toxicologists particularly look for the highest level of exposure at which no effects are detectable and the maximum dose that can be tolerated without significant overt toxicity.<sup>47</sup>

The animals most commonly used in toxicology studies are mice and rats, for many reasons.<sup>48</sup> They are small, so less of the substance being studied is needed to achieve any specified dose, and they are easy to house and handle. They are unable to vomit, so any substance given orally will be reliably presented to the gastrointestinal tract. They have relatively short lifespans, so lifetime exposure data can be evaluated in a reasonable period of time. They are readily available at reasonable cost from reliable vendors who can provide large numbers of healthy subjects closely matched in age, weight, genetics, and other factors. Moreover, they have been used widely in research for many years, so a large database has developed about their biology and diseases.<sup>49</sup> Mice and rats are also useful models because they are mammals, and thus similar anatomically and physiologically to humans in many (though not all) respects.<sup>50</sup>

#### **IV. Strengths and Limitations of Toxicology**

As a general rule, properly conducted toxicology studies produce reliable data of considerable value to understanding the effects of human exposures. In fact, the

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<sup>44</sup> Eaton & Klaassen, *supra* note 7, at 27-32.

<sup>45</sup> *Id.* at 27; Goldstein & Henifin, *supra* note 4, at 409.

<sup>46</sup> Goldstein & Henifin, *supra* note 4, at 406.

<sup>47</sup> *Id.* at 407-09.

<sup>48</sup> James M. Andress, *The Mouse: Toxicology*, in *Animal Models In Toxicology* 165, 166 (Shayne Cox Gad & Christopher P. Chengelis eds., 1992); Shayne Cox Gad, *Susceptibility Factors*, in *Animal Models In Toxicology* 841, 851 (Shayne Cox Gad & Christopher P. Chengelis eds., 1992).

<sup>49</sup> David E. Semler, *The Rat: Toxicology*, in *Animal Models In Toxicology* 21, 22 (Shayne Cox Gad & Christopher P. Chengelis eds., 1992).

<sup>50</sup> *Id.*

scientific community is nearly unanimous in believing that animal studies can be reliable indicators and useful predictors of human disease.<sup>51</sup> But this is not to say that every animal study is a reliable indicator or predictor of human disease. The study data must be evaluated with a critical eye and the testing conditions must be carefully considered because toxicology studies have limitations. In particular, comparative information on factors affecting the absorption, distribution, metabolism and excretion of chemical substances between the species tested and the plaintiff's species must be considered.<sup>52</sup> Key to valid toxicology studies is the selection of an appropriate test animal species, given the substance being studied and the mechanisms of the toxic effects suspected.<sup>53</sup>

Although data from laboratory animals are sometimes helpful in predicting effects in humans, it must be recognized that each species is unique in potentially significant ways. Humans and other animals have anatomic, physiologic, and metabolic differences. Rats, for example, have no gallbladder, so will never demonstrate toxic effects on this organ. Only primates experience menstrual cycles; other mammals go through estrous cycles, which are fundamentally different.<sup>54</sup> The most common conjugation pathway for metabolizing and detoxifying chemicals used by mammals is glucuronidation, but cats lack the enzyme necessary for this process.<sup>55</sup> Some animals practice coprophagy, which exposes them a second time to substances excreted in the feces.<sup>56</sup> Nocturnal animals, like rats and mice, metabolize chemicals received during the day more slowly than those received at night, and will consume more of a test compound mixed with feed during the night.<sup>57</sup> Rats singly housed experience more stress than those housed in compatible groups, so can be more sensitive to chemicals' toxic effects. Skin structure varies between species in ways that affect dermal absorption.<sup>58</sup> Subjective symptoms expressed

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51 Erica Beecher-Monas, *A Ray of Light for Judges Blinded by Science: Triers of Science and Intellectual Due Process*, 33 Ga. L. Rev. 1047, 1063-64 (1999); Goldstein & Henifin, *supra* note 4, at 414.

52 Goldstein & Henifin, *supra* note 4, at 419. For example, the cardiac output of a mouse is such that it essentially recirculates its entire blood volume every minute, which is about twenty times faster than a human. Gad, *supra* note 18, at 823.

53 Goldstein & Henifin, *supra* note 4, at 419-20.

54 See generally *Laboratory Animal Medicine* (James G. Fox et al. eds., 1984).

55 E.g., Nicholas H. Booth, *Nonnarcotic Analgesics*, in *Veterinary Pharmacology And Therapeutics* 351, 353 (L. Meyer Jones et al. eds., 4th ed. 1977).

56 Address, *supra* note 49, at 177.

57 Semler, *supra* note 50, at 41-42.

58 Christopher P. Chengelis & Shayne Cox Gad, *Introduction*, in *Animal Models In Toxicology* 1, 9 (Shayne Cox Gad & Christopher P. Chengelis eds., 1992).

by humans, such as headache or fatigue, are difficult if not impossible to assess in animals.<sup>59</sup>

On the other hand, the similarities of biochemical and metabolic processing in any particular organ may be similar across species. The target organ of a chemical substance in one species is likely to be the same in another species.<sup>60</sup> Nearly all chemicals causing cancer in humans also cause cancer in some other species.<sup>61</sup> There are obvious differences between species and extrapolating across species involves complex issues.<sup>62</sup>

Toxicology studies should describe in detail the conditions under which they were conducted, because significant differences in the dose-response curve can be created by varying the testing conditions.<sup>63</sup> Toxicity can be affected by, for example, room temperature, humidity, lighting, noise, bedding type, cage design, and subclinical viral infections.<sup>64</sup> A basic consideration in this regard is conformance to the requirements of the federal Good Laboratory Practice regulations,<sup>65</sup> which require written standard operating procedures and meticulous recordkeeping.<sup>66</sup> *In vitro* tests should preferably have been validated by replication in many different laboratories or by comparison with outcomes in animal studies to support their ability to predict human toxicity.<sup>67</sup> Because of these limitations to toxicological studies, epidemiological studies in humans or another species of interest may be viewed as important supplemental information.

Dose-response relationships established by toxicology studies may be reliable predictors for populations and circumstances similar to those of the studies on which they are based, but they cannot provide a “bright line” above which exposure proves causation

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<sup>59</sup> Goldstein & Henifin, *supra* note 4, at 420.

<sup>60</sup> *Id.* at 410.

<sup>61</sup> Eaton & Klaassen, *supra* note 7, at 27 (“All known chemical carcinogens in humans, with the possible exception of arsenic, are carcinogenic in some species but not in all laboratory animals. Whether the converse is true – that all chemicals carcinogenic in animals are also carcinogenic in humans – is not known with certainty, but this assumption serves as the basis for carcinogenicity testing in animals.”).

<sup>62</sup> Gad, *supra* note 18, at 820-26.

<sup>63</sup> Semler, *supra* note 50, at 24-38; Gad, *supra* note 18, at 826-32; Gad, *supra* note 49, at 847-48, 852-55.

<sup>64</sup> Semler, *supra* note 50, at 24-38.

<sup>65</sup> *E.g.*, 21 C.F.R. Part 58; 40 C.F.R. Part 792.

<sup>66</sup> *See* Goldstein & Henifin, *supra* note 4, at 411-12.

<sup>67</sup> *Id.* at 410.

for a particular plaintiff and below which causation is refuted for that plaintiff.<sup>68</sup> Indeed, the jump from a dose-response relationship to conclusions in an individual plaintiff's case is one of the principal areas of dispute in tort litigation.

## V. Toxicological Evidence in the Courtroom

In the courtroom, toxicological evidence can be used either to support or refute claims that a disease or injury was caused by chemical exposure. The basic issues are whether, based on reliable and valid research, exposure can or is not known to cause such diseases or injuries at the dose, by the route of exposure, and in the time frame claimed, which is information toxicological research can provide. However, toxicology research such as cell toxicity studies or animal research does not necessarily provide valid bases for conclusions about injury in the circumstances of a given plaintiff. An extreme but not uncommon example shows the dilemma: should an expert be allowed to offer the opinion that an elderly diabetic plaintiff was harmed by a chemical by extrapolating the results of a dose-response curve obtained from exposures of young, healthy laboratory rats to the same chemical? Expert evidence can be both powerful and misleading. The proof will be useful to the extent that the individual's situation resembles the testing conditions, but loses weight as factors are added that differentiate the plaintiff's exposure from the test conditions.

The United States Supreme Court recognized many toxicological principles in evaluating the evidence in *General Electric Company v. Joiner*, 522 U.S. 136 (1997). In *Joiner*, the Court went more deeply than simply considering the question of whether toxicology studies had analyzed the effects of the chemical at issue (PCB). Rather, the Court also considered the relevance and reliability of the evidence in the context of the claimed dose, the exposure pathway, the specific type of cancer developed by the laboratory mice in the studies, and the consistency of the study results. The case illustrates that lawyers representing parties in tort litigation need not only to develop a sophisticated understanding of the toxicological issues of relevance but present them to the non-scientist so that the conclusions and their bases are both understandable and persuasive.

Finally, no matter how well founded toxicological studies may be, they can almost never show individual or specific causation. Other evidence must be used to prove that the plaintiff was exposed, that the exposure was of a type that can result in absorption into the body, and that the dose was sufficient to cause the effects described. Substances or factors present in the environment, or the plaintiff, which could have enhanced or interfered with absorption, distribution, metabolism, or excretion of the toxicant should

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<sup>68</sup> For a discussion of the various ways experts, courts, and regulatory agencies use the dose-response relationship created by toxicology studies in risk assessment, *see generally* Wayne Roth-Nelson & Kathy Verdeal, *Risk Evidence in Toxic Torts*, 2 *Env'tl. Law.* 405 (1996).

be taken into account. Other factors present in or around the plaintiff which could alternatively explain the injury also should be considered. The temporal relationship between the exposure and the onset of adverse effects should be evaluated to see if a relationship is biologically plausible and whether it supports or refutes causation.

## **VI. Issues Addressed in the Chapters**

Jurisdictions vary in their approach to toxicological evidence, but most courts treat toxicology as a generally accepted science adhering to well-recognized principles and methodology and permit the presentation of relevant toxicological evidence. Judges and juries have the formidable task of assessing the expertise and qualifications of the toxicologist offering the evidence and the reliability of the data offered and probing the relevance of the laboratory evidence to the plaintiff's alleged exposure and injury, as well as determining whether the circumstances alleged could have resulted in the plaintiff's exposure at a sufficient dose.

The chapters that follow review the use and treatment of toxicological evidence in each federal circuit and the courts of all fifty states, jurisdiction by jurisdiction. Authors were asked to describe the state of the law in each jurisdiction with respect to at least these issues:

- a. Definition and scope of toxicological evidence;
- b. Use of toxicological evidence in product liability, mass tort, and environmental litigation;
- c. Posture of plaintiffs and defendants, types of claims, types of products or exposures, and types of injuries;
- d. Use of toxicological evidence to support or refute causation;
- e. Key cases, including fact patterns, rulings, and reasoning for admitting or barring toxicological evidence; and
- f. Notable differences, if any, between state and federal court approaches to use of toxicological evidence, including the impact of *Frye* versus *Daubert* approaches, and other factors of interest to practitioners.

While the authors and editors have tried to ensure the accuracy of these materials, case law should be verified and research updated prior to any court submission.