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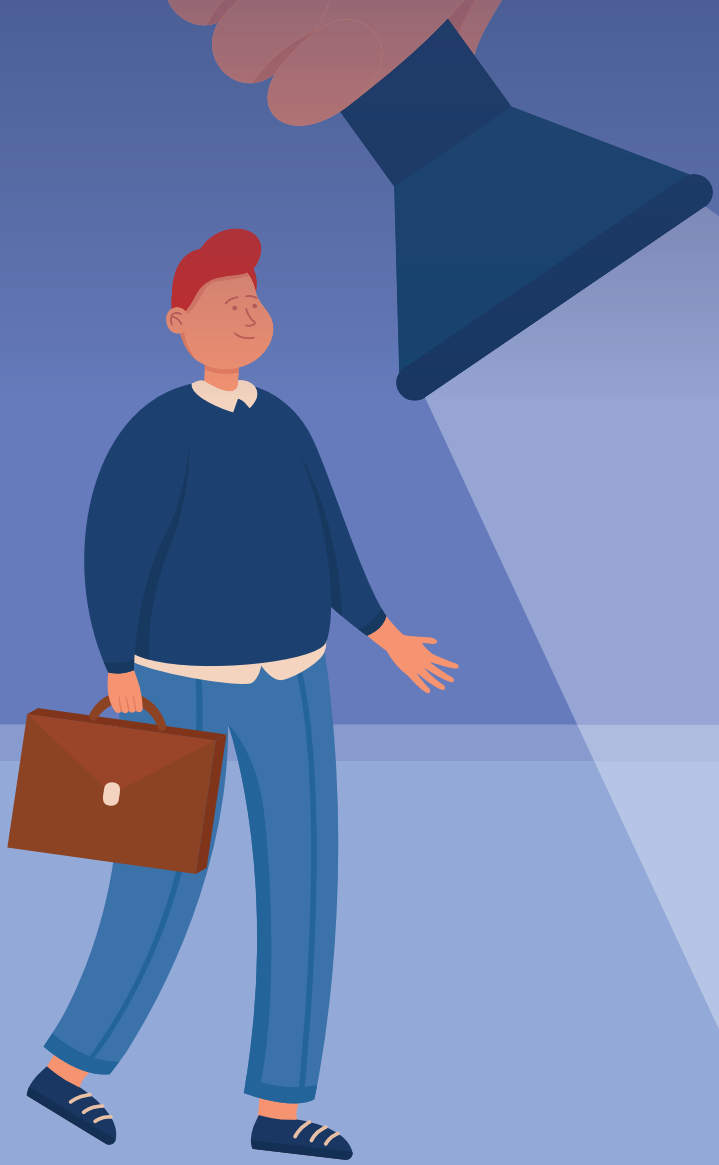

Toxic Torts and Environmental Law

Including . . .

What's Old May be New Again: Addressing Radioactive Toxic Tort Claims and Planning for the Next Frontier

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Modern Challenges of Social Media Discovery: Social Media Is Key in Litigation Involving Personal Injury

The Fifth Dimension: TPLF and Its Effect on the Judiciary

And More!

Litigation and Compliance Impacts of Proposed Ethylene Oxide Regulations Based on Flawed Science

By Robert E. Johnston, David Fusco, Heather Lynch and Aleksandra Rybicki

...plaintiffs have not been deterred from bringing new toxic tort lawsuits against sterilization companies...

The Carcinogenicity of Ethylene Oxide

The scientific literature demonstrates that ethylene oxide may cause cancer, but likely only under very specific exposure conditions. Experimental studies have reported increased cancer in rodents exposed to ethylene oxide at very high dose concentrations, well above those expected in humans, including occupationally exposed workers. Mechanistic studies (including those conducted in cells) indicate that ethylene oxide may cause cancer by directly interacting with and damaging DNA. However, the body has many mechanisms to repair damage and protect against cancer formation. Even direct-acting DNA reactive agents, including ethylene oxide, may exhibit threshold exposure-response relationships for genotoxicity. Jenkins, G. J., Doak, S. H., Johnson, G. E., Quick, E., Waters, E. M., & Parry, J. M. (2005). *Do dose response thresholds exist for genotoxic alkylating agents?. Mutagenesis*, 20(6), 389–398. In other words, DNA mutations and other permanent damage occur only at exposures sufficient to overwhelm the body's protective mechanisms. Ethylene oxide forms primarily a specific type of DNA adduct that is highly repairable, and these adducts may be cleared effectively at low exposures. Lynch, H. N., Kozal, J. S., Russell, A. J., Thompson, W. J., Divis, H. R., Freid, R. D., Calabrese, E. J., & Mundt, K. A. (2022). *Systematic review of the scientific evidence on ethylene oxide as a human carcinogen*. Chemico-biological interactions, 364, 110031.

Moreover, epidemiological studies reported statistically significant associations between ethylene oxide exposure and cancer only in highly exposed workers and only for breast and some types of lympho-




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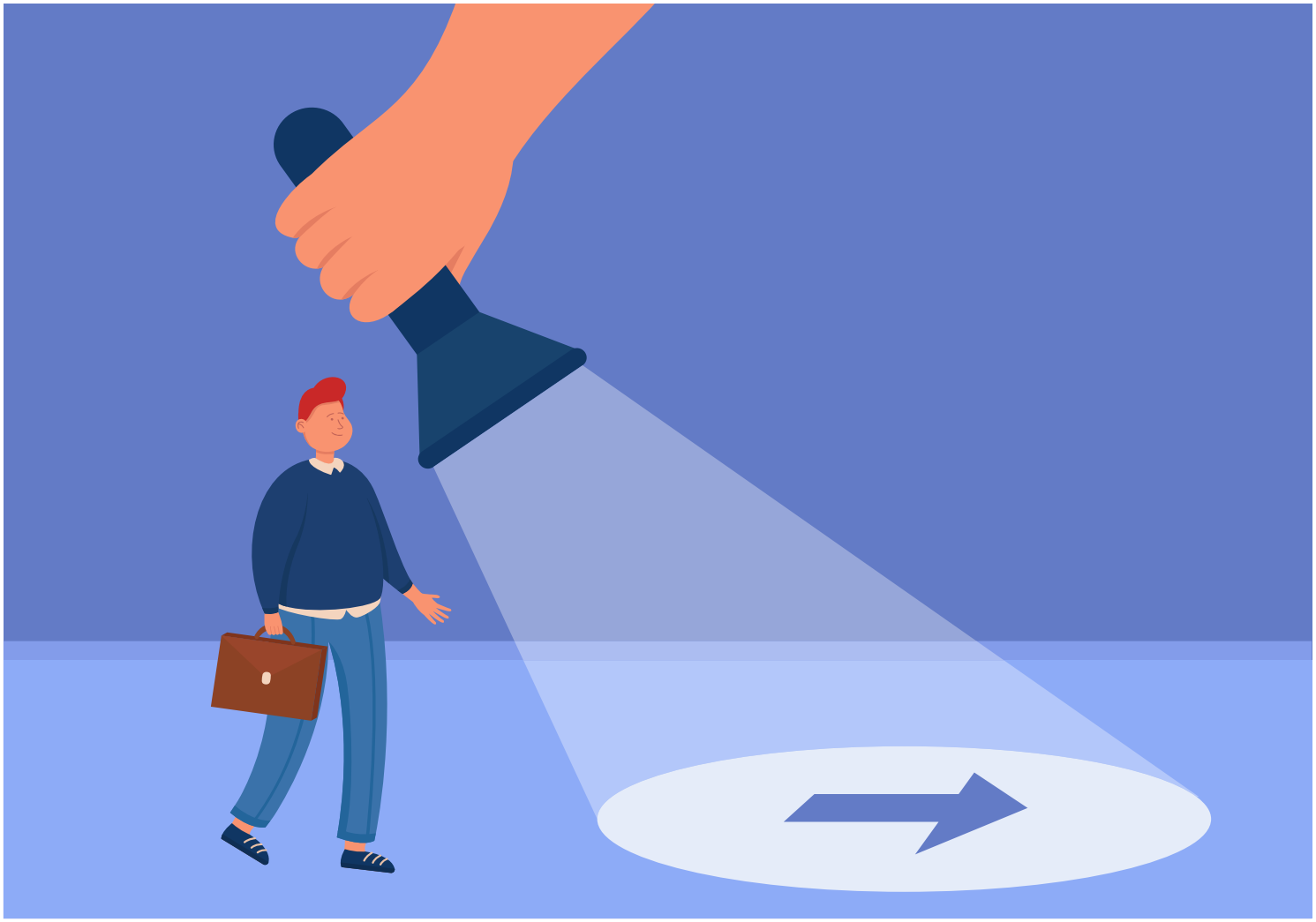

hematopoietic malignancies. *Id.* In fact, the largest worker cohort studies reported no increased cancer risk in sterilization or production workers compared to the general population, and reported elevated incidence or mortality of cancer only when the most highly exposed workers were compared to the least-exposed workers. Steenland, K., Whelan, E., Deddens, J., Stayner, L., & Ward, E. (2003). *Ethylene oxide and breast cancer incidence in a cohort study of 7576 women (United States).* Cancer causes & control: CCC, 14(6), 531–539; Steenland, K., Stayner, L., & Deddens, J. (2004). *Mortality analyses in a cohort of 18 235 ethylene oxide exposed workers: follow up extended from 1987 to 1998.* Occupational and environmental medicine, 61(1), 2–7. However, the apparent excess cancers may be an artifact of the selected referent groups—the lowest-exposed workers—who had profoundly decreased rates of cancer incidence (or mortality) relative to the general population. Compared to the referent groups with very low cancer rates, all other exposure groups spuriously appeared to have increased relative risks of cancer. This apparently spurious excess has profound implications on the perception of ethylene oxide's carcinogenic potency because these studies serve as the basis for EPA's inhalation unit risk (IUR) for ethylene oxide.

The Ethylene Oxide Regulatory Framework

Although ethylene oxide's most recognized application is the sterilization of medical devices and equipment, ethylene oxide is a highly versatile compound with a wide variety of applications, including the fumigation of spices and the production of ethylene glycol, polyurethanes, and household cleaners. It is found in materials used by the building and construction, transportation, manufacturing, and health and safety industries, as well as countless downstream products. Ethylene Oxide - An

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Essential Raw Material for Many Important Products (***https://www.americanchemistry.com/industry-groups/ethylene-oxide/resources/ethylene-oxide-an-essential-raw-material-for-many-important-products***). Many unsuspecting companies in these industries will likely face significant regulatory hurdles and litigation risks concerning ethylene oxide emissions in the years ahead.

EPA's Flawed 2016 IRIS Assessment

Although ethylene oxide was first recognized as a hazardous air pollutant under the Clean Air Act (CAA) in 1990, *see* 42 U.S.C. § 7412(b)(1), the regulatory landscape began to change significantly in August 2018 when EPA released the 2014 National Air Toxics Assessment (NATA) that classified ethylene oxide as a "regional cancer risk driver" and identified numerous census tracts as having potentially increased risk as a result of ethylene oxide emissions. US ENV'T PROT. AGENCY, 2014 National Air Toxic Assessment: 2014 NATA Summary of Results. This was a significant change from previous NATA assessments because it incorporated the inhalation unit risk (IUR) factor from EPA's 2016 Integrated Risk Information System (IRIS) Assessment for ethylene oxide, which concluded that ethylene oxide was carcinogenic and 60 times more toxic than previously thought. US ENV'T PROT. AGENCY, EPA/635/R-16/350FA, Evaluation of the Inhalation Carcinogenicity of Ethylene Oxide (2016).

The IUR represents the upper-bound excess lifetime cancer risk associated with continuous exposure to 1 µg/m3 of any given substance. EPA's IUR for ethylene oxide is higher than those derived by any other agency, resulting in a much lower air concentration of ethylene oxide that is deemed to be "safe" by EPA. This exceedingly low number is driven partially by overestimations of risk in the peer-reviewed literature but also by the overly conservative exposure model that EPA employed to extrapolate exposure levels below those evaluated in the highly exposed cohorts. Vincent, M. J., Kozal, J. S., Thompson, W. J., Maier, A., Dotson, G. S., Best, E. A., & Mundt, K. A. (2019). *Ethylene Oxide: Cancer Evidence Integration and Dose-Response Implications. Dose-response: a publication of International Hormesis Society*, 17(4). The ethylene oxide IUR, like other EPA cancer potency estimates, is intended to be highly conservative and reflects EPA's policy to err on the side of overestimating rather than underestimating risk to protect against cancer in the entire population. However, EPA's IUR suggests that ethylene oxide is much more potent (perhaps up to several hundred times more potent) than other potent carcinogens like vinyl chloride. *Id.* The underlying science simply does not support that ethylene oxide is one of the most potent human carcinogens.

EPA's conclusions have faced significant challenges from scientists and industry, including a 2020 Texas Commission on Environmental Quality (TCEQ) assessment which concluded that available epidemiologic data did not support EPA's findings, that EPA wrongfully concluded that ethylene oxide was 2400 times more dangerous than the science supports, and that even background levels of ethylene oxide in certain environments would present a hazard using EPA's IUR. *See* TEX. COMM'N ENV'T QUALITY, Ethylene Oxide Carcinogenic Dose-Response Assessment (May 15, 2020). The TCEQ also included data not considered by EPA in its analysis, including an additional human cohort and post-2016 data. Despite additional consideration of criticisms from the TCEQ and others, however, EPA concluded in December 2022 that the 2016 IRIS IUR would be used in future regulations. US ENV'T PROT. AGENCY, Reconsideration of the 2020 National Emission Standards for Hazardous Air Pollutants: Miscellaneous Organic Chemical Manufacturing Residual Risk and Technology Review, FED'L REG. (21 December 2022).

Moreover, although EPA has consistently recognized that the NATA results are a screening tool and do not represent actual risk, those results present a simple method for identifying potential emitters of ethylene oxide that have subsequently been targeted in litigation. The attention on these emitters also significantly increased after the EPA Office of Inspector General called for action in 2020 "to inform residents who live near facilities with significant ethylene oxide emissions about their elevated estimated cancer risk so they can manage their health risks." US ENV'T PROT. AGENCY, OFF. OF INSPECTOR GEN., 20-N-0128, *At a Glance Management Alert: Prompt Action Needed to Inform Residents Living Near Ethylene Oxide-Emitting Facilities About Health Concerns and Actions to Address Those Concerns* (2020). The Inspector General's alert ultimately led to federal and state public outreach efforts throughout various EPA regions to educate communities, particularly those surrounding commercial sterilizers and industrial facilities with ethylene oxide emissions.

At the same time, claims by states and private citizens were filed against ethylene oxide emitters. The most notable examples are commercial sterilizers, but industrial manufacturers have also found themselves being named in personal injury and class action suits around the country as public attention to issues surrounding ethylene oxide has increased. The majority of these claims involve the alleged development of an actual injury, like breast cancer or lymphatic cancer. They have also taken the form of class actions seeking medical monitoring for large numbers of individuals allegedly exposed to low-level environmental emissions over extended periods of time. Significantly, many of these claims are being pursued against companies despite their compliance with state and federal emissions regulations.

Recent EPA Proposals

Meanwhile, as ethylene oxide litigation has gained steam, EPA has moved forward to revisit and amend numerous regulations regarding ethylene oxide emissions. *See* EPA, Hazardous Air Pollutants: Ethylene Oxide (***https://www.epa.gov/hazardous-air-pollutants-ethylene-oxide***). This includes the National Emission Standards for Hazardous Air Pollutants (NESHAPs) for various industries. The EPA recently issued new Commercial Sterilizer and Synthetic Organic Chem. Mfg. Ind. (SOCMI)/(HON) NESHAPs and has maintained that it will propose updated NESHAPs for the Polyether Polyol Production and Chemical Manufacturing Area Sources sectors in 2024. These rules will have wide-reaching impacts on industries throughout the United States. For example, the Commercial Sterilizer NESHAP includes much stricter requirements for emissions

reductions in connection with existing and newly regulated sources, reductions which may difficult to attain with existing technologies. Similarly, the HON NESHAP goes as far as to address heat exchange systems, process vents, storage vessels, transfer racks, wastewater, and increased equipment leak monitoring at chemical facilities subject to CAA classifications for organic chemicals, and it is likely similar requirements will be extended to other NESHAPs as they are completed. *EPA Accepting Public Comments on Amended Ethylene Oxide Regulations*, Washington Legal Foundation, Vol, 31 No. 2 (June 9, 2023). It is clear that more stringent regulations can be expected for virtually every company that uses ethylene oxide in its operations. Inherently, entrepreneurial plaintiffs' attorneys will follow similar toxic exposure litigation models and pursue claims against companies responsible for even the lowest levels of environmental emissions.

Overcoming Challenges in Ethylene Oxide Litigation: A Trial Perspective

The IRIS Assessment is a regulatory document, and the EPA has conceded that "IRIS values cannot be validly used to accurately predict the incidence of human disease or the type of effects that chemical exposures have on humans." US EPA, Nat'l Ctr. For Env't. Assessment, Integrated Risk Information System, at ***https://cfpub.epa.gov/ncea/risk/recordisplay.cfm?deid=2776*** (under "History" tab); Integrated Risk Information System (IRIS); Health Risk Assessment; Guidelines, etc., 53 Fed. Reg. 20,162, 20,163 (June 2, 1988). Still, toxic tort plaintiffs rely on the 2016 IRIS Assessment to attempt to establish general causation, bolster their corporate conduct themes, and confuse the jury about the mechanisms of cancer.

Risk Assessments Should Not Be Used to Prove Causation at Trial

General causation requires a showing that ethylene oxide is capable of causing cancer—that is, it is a carcinogen—while specific causation requires a tailored showing that ethylene oxide, in the specific amount inhaled by plaintiff, caused plaintiff's specific cancer. Thus, to determine causation, the focus must be on the plaintiff's actual exposure—by conducting a plaintiff-specific exposure assessment and dose characterization—and not a hypothetical risk. While plaintiffs do produce a calculated assessment of plaintiff's alleged specific exposure, it is based on the unreliable IRIS risk assessment.

To demonstrate general causation, plaintiffs focus on the IRIS Assessment's colorful language that ethylene oxide is a mutagen in living organisms, that it has been shown to be carcinogenic in mice and rat studies, that it can be inhaled by residents living near facilities that produce or use ethylene oxide or near sterilization facilities, and, notably, that there is strong evidence of an increased risk of cancer of the lymphohematopoietic system and of breast cancer in females. In some jurisdictions, a plaintiff may only need to show that defendant's emission of ethylene oxide was a contributing factor to the plaintiff's development of cancer, and not a substantial factor. Thus, by using the IRIS Assessment as a crutch for general causation, plaintiffs argue that ethylene oxide emitted by sterilization facilities contributed to plaintiffs' cancers.

Unfortunately, many courts, particularly state courts, are not troubled by the fact that other courts have routinely rejected plaintiffs' efforts to rely exclusively on environmental regulatory action to establish causation. *See Parker v. Mobil Oil Corp.*, 857 N.E.2d 1114, 1121–22 (N.Y. 2006); *Rider v. Sandoz Pharms. Corp.*, 295 F.3d 1194, 1201 (11th Cir. 2002; *Hollander v. Sandoz Pharms. Corp.*, 289 F.3d 1193, 1215 (10th Cir. 2002); *Glastetter v. Novartis Pharms. Corp.*, 252 F.3d 986, 991 (8th Cir. 2001); *Allen v. Pa. Eng'g Corp.*, 102 F.3d 194, 196 (5th Cir. 1996). In extreme instances, these courts go so far as to preclude the defense from showing or even describing to the jury the conclusions of the scientific papers that the defense contended demonstrated that there is no risk of cancer arising from environmental exposure to ethylene oxide in response to the presentation of regulatory conclusions. Courts have also barred the defense from telling the jury that ethylene oxide exists naturally in the environment and that the human body independently produces ethylene oxide, facts that help put ambient ethylene oxide levels into perspective.

Defendants should be laser-focused on case law supporting not only the unreliability of regulatory science as competent evidence of general causation but also on persuading courts that they are entitled to present the true scientific facts to the jury and explain how the IRIS has incorrectly, or at least speculatively, used those facts to reach its regulatory conclusions. In the case of ethylene oxide, these conclusions are based on *sui generis* theoretical analysis without any data showing an actual case of cancer at the levels deemed unsafe by EPA.

Attacking Plaintiffs' Corporate Conduct Themes

Plaintiffs' corporate conduct story is simple: plaintiffs allege that the company emitting ethylene oxide knew or should have known that ethylene oxide is a carcinogen and routinely put the surrounding community at risk for fatal cancers. At trial, plaintiffs argue that the 2016 IRIS Assessment demonstrates retroactively that defendants' regulatorily compliant, pre-2016 emissions were unsafe and that communities in the vicinity of ethylene oxide sterilization facilities had actually been cancer "hot spots" for decades. Plaintiffs present evidence of the company's failure to control ethylene oxide emissions via available emission control devices, despite the fact that the controls were not required, were potentially considered unsafe by EPA during certain periods, and, even if installed, would have captured a *de minimis* number of emissions. Plaintiffs also attempt to characterize companies' collaboration with industry organizations like the Ethylene Oxide Sterilization Association (EOSA)—done only in an effort to educate EPA on IRIS flaws and shortcomings—as regulatory capture. One focus of any trial against sterilization facilities must be to persuade the jury that company employees acted reasonably by following current regulations and evaluating scientific studies and, in fact, maintained emissions at safe levels.

Demystifying Plaintiffs' One-Molecule Theory

To counter plaintiffs' causation case, it is critical to demystify plaintiffs' one-molecule theory. The one-molecule theory—unsupported by any empirical evidence—states that each and every molecule of ethylene oxide inhaled has the potential

to induce cancer because of its mutagenic and genotoxic properties. While plaintiffs use this to try to convince the jury that the "extra" molecules emitted from defendants' facilities are what caused plaintiffs' cancers, it is important to challenge this theory through experts.

Plaintiffs' experts will agree that ethylene oxide is present in the air we breathe, is emitted from everyday functions like using a lawn mower, and is produced by our bodies endogenously. At trial, plaintiffs conveniently shy away from the mathematical comparison of exposure levels between plaintiff's specific exposure and exposure levels in studies, as well as levels of ethylene oxide in the ambient air. The reality is that if ethylene oxide causes cancer, then endogenous and other environmental sources of ethylene oxide also cause cancer, and there should be a much larger number of cancers—particularly rare blood cancers that are frequently the basis for claims—in the general population. However, plaintiffs' experts are not able to quantify the exact amount of ethylene oxide exposure needed to actually cause cancer, notwithstanding that the scientific studies (not the theoretical extrapolations) find no excess cancer risk until very high levels of exposure. Helping the jury compare a plaintiff's ethylene oxide exposure to ethylene oxide levels in the ambient air as well as other sources of ethylene oxide will allow the jury to understand how low a plaintiff's dosage is and to question the reliability of plaintiffs' assertions.

Finally, depending on the cancer type at issue, plaintiffs cannot ignore the findings of scientific studies showing no association between ethylene oxide exposure and plaintiff's cancer, findings that defense experts can explain and with which plaintiffs' experts must be confronted.

Educating the Jury about Cancer and Genotoxicity

It is crucial to educate the jury about cancer—the various types of cancers, their methods of development, and potential causes. Simply stated, cancer is the uncontrolled replication of cells. The jury must be able to understand that ethylene oxide is not cancer-causing despite its genotoxicity and mutagenicity or its ability to cause DNA or chromosomal damage. As discussed, the DNA adducts related to ethylene oxide are not at locations that control the replication of genes. The jury must be educated about the body's natural DNA repair mechanism process to comprehend that, most of the time, cancer is caused by flaws in the natural replication process.

To put this in perspective, the literature states that all cancers are caused by either hereditary factors (~5%), environmental factors (~29%), or natural replication (~66%). Research shows that the higher the rate of cell replication, the higher is the chance of developing cancer. For example, ~89% of leukemias are attributable to mutations resulting from natural replication. Once jurors understand natural replication as a cause of cancer and the frequency in which it occurs, they are less likely to submit to plaintiffs' baseless theories.

Experience shows that when these facts are presented to a jury, plaintiffs cannot meet their causation burden and it results in a defense verdict. Still, plaintiffs have not been deterred from bringing new toxic tort lawsuits against sterilization companies and are not afraid to try cases in which plaintiffs experienced even smaller levels of ethylene oxide exposure.