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Toxicological Issues in the Chemical Processing Industry

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ABSTRACT

The chemical processing industry has been a leader in addressing the toxicological effects of their chemical products and by-products. The science of toxicology, however, is advancing rapidly, and new issues are being raised that pose challenges and opportunities for the industry. This presentation will discuss the blurring of threshold and nonthreshold toxic effects, and its significance for 1) employee and community education, 2) strategic opportunities for toxic tort defense, and 3) siting, permitting, process operations and emergency response planning.

PAPER

Toxicologists define "hazard" as the ability to cause an adverse effect. "Risk" is the probability of an adverse effect occurring. For example, if you step out in front of an oncoming bus, that clearly presents the hazard of being injured or killed. If, however, the bus is five blocks away and you step out in front of it, the risk is small. The risk of chemical toxicity is much the same. If, for even the most toxic chemical,

there is no possibility of exposure, the risk of an adverse health effect occurring is zero.

The chemical industry has been an historical leader in defining the toxic properties of their chemicals and processes. Many of the earliest industrial toxicology laboratories in the United States were started by chemical companies, and the industry made available their proprietary toxicological studies to groups such as the American Conference of Governmental Industrial Hygienists (ACGIH) for development of early occupational exposure limits (TLVs) long before OSHA was created. Today, the chemical industry continues to sponsor state-of-the-art biomedical research programs through its in-house laboratories, at Universities worldwide, and through such organizations as the Chemical Manufacturers Association and the Chemical Industry Institute of Toxicology. I want to acknowledge that many of the issues discussed in this paper have developed in part from industry-sponsored research programs.

All of us are aware that there has been an explosion of new biomedical technologies during the past ten years – from the introduction of CAT scans, to methods allowing us to amplify and characterize small fragments of DNA, to methods that take a gene from one organism and put it into another. These and other technological advances have created in just a few years an increased understanding of the mechanisms of toxic injury. This paper focuses on a small piece of this emerging understanding (i.e., cancer causations), and its potential implications for industrial operations and liabilities.

In the 1970s, EPA began to implement a strategy of using mathematical risk models as the technical basis of regulatory decisions and policies. When they queried the scientific community at the time, they were told that cancer differs from other toxic effects in that cancer is a disease of a single cell. A high degree of correlation was seen in laboratory studies between the ability of a chemical to cause cancer and its ability to cause genetic mutations, suggesting that cancer might be triggered by chemical binding of a carcinogen to a critical "cancer" gene contained in the genetic blueprint of the cell. In theory, said the scientists, it was possible for a single molecule of a carcinogenic chemical to be absorbed into the body and find its way to attack a critical gene resulting in cancer

In the mutation paradigm, if one molecule has a finite risk of causing cancer, two molecules have twice that risk, etc. EPA therefore adopted a non-threshold linear model of cancer risk as their default for risk-based regulation. According to this model, no exposure to a carcinogen is considered safe. In contrast, noncarcinogenic toxicants generally produce toxic effects by poisoning thousands of cells such that total organ function is affected. The regulatory world, and the world of toxic tort litigation, was divided between toxicants with a dose-response threshold (noncarcinogens) and those without (carcinogens).

Much has been learned about the cancer process since the 1970s. Some of my favorite studies were carried out by Dr. Beatrice Mintz and her colleagues at the Fox Chase Cancer Center in Philadelphia. She took a normal cells from a mouse embryo and injected it into the testis of another mouse. This embryonic cell began to divide and produced a malignant tumor called a teratoma. Before the tumor could kill the recipient mouse, Mintz et al. took one of the malignant tumor cells and injected it into the testis of another mouse. This cell also divided to produce a malignant teratoma. Mintz and her colleagues repeated the process and passaged tumor cells for 100 generations. She then injected one of

the malignant teratoma cells back into an embryo from a mouse of a different fur color. The offspring of this embryo was born as a perfectly normal mouse, but because it had striped fur, we know that the transplanted tumor cell survived.

Why then did a normal embryonic cell become malignant when injected into the testis? There was no exposure to a chemical carcinogen, or evidence of genetic mutation. In fact, when injected back into its "normal" environment, the tumor cell acts like nothing has happened. The answer in simple terms is that scientists now understand that cancer is a much more complicated disease process that that assumed by the EPA in the 1970s.

Cancer is a disease caused by a single cell that fails to respond to the usual control signals from its environment. This may be 1) because the normal signal molecule is not present (as in Mintz's system), 2) because the receptor on the cell membrane is damaged or missing; or 3) because the biochemical processes triggered by the signal-receptor complex are not functioning properly. While genetic mutation by a chemical agent is one mechanism by which the above processes can be affected, other factors include viral infections, parasites, altered immune function, physical agents, repeated tissue injury, and others. Of interest, it has been suggested that the normal process of cell division (not chemical exposure) is the largest source of genetic mutations in man.

Most cancers require not one, but several genetic changes for the cell to become malignant. Because of the biological processes involved, data are accumulating for many types of cancer that there is a threshold of chemical exposure below which the risk of developing cancer is very low. Benzene, a known human carcinogen, is one of those chemicals for which an increased risk of developing Acute Myelogenous Leukemia (AML) is seen only at workplace vapor concentrations greater than 100 ppm.

New biomedical discoveries are obscuring the historical division between threshold and non-threshold toxicants, and the potential significance of these findings for the chemical processing industry are astounding. For example, the allowable levels of vapor exposure for a carcinogen like benzene may increase as regulatory officials evaluate the new data. Facility siting, permitting, operations, and workplace exposure control strategies may be reevaluated. Estimated impacts on surrounding communities may need to be revised, and education of both the community and employees of these changes should be initiated. Unmeritorious toxic tort litigation already appears to be more difficult to move forward successfully as a result of our better understanding of cancer causation and toxicity.

Cancer has been the toxicological endpoint that has driven the regulatory process in the United States since the 1970s. The chemical industry has invested many years and dollars in research programs designed to increase our understanding of the dangers posed by chemical agents. This investment in research is showing benefits, and the increase in biomedical knowledge is presenting new opportunities and new challenges for the chemical industry.

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