

Towards a safer occupational environment: The U.S. approach The example of the glycol ethers

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ABSTRACT

This short review outlines the United States Federal Programs for conducting research and setting safety standards for occupational hazards to male reproductive function. The National Institute for Occupational Safety and Health, the National Institute of Environmental Health Sciences and the Environmental Protection Agency conduct research on the effects of toxicants on the male reproductive system. The Occupational Safety and Health Administration and the Environmental Protection Agency regulate exposures. These agencies work in harmony to limit reproductive toxicants in the workplace. The role each agency played in identifying and limiting exposure to the male reproductive toxicants 2-methoxyethanol and 2-ethoxyethanol is presented as a successful example of this approach.

In 1970, the Occupational Safety and Health Act was signed into law with the goal of providing a safe and healthy work environment for all United States workers. This act established two federal agencies to achieve this goal. The National Institute for Occupational Safety and Health (NIOSH) was established within the U.S. Department of Health and Human Services. The charge to NIOSH was to conduct research in occupational safety and health, to support educational programs, to provide an adequate supply of occupational safety and health professionals, and to make health and safety recommendations to the Occupational Safety and Health Administration (OSHA). OSHA, in the Department of Labor, was the second agency formed by the Occupational Safety and Health Act. OSHA establishes the occupational safety

standards and enforces them. The National Advisory Committee on Occupational Safety and Health (NACOSH), a committee that advises both OSHA and NIOSH on program activities and policies, was also established.

At approximately the same time the occupational agencies were formed, similar agencies were established for evaluating environmental health issues. The National Institute for Environmental Health Sciences (NIEHS) was founded within the National Institutes of Health in U.S. Department of Health and Human Services with the mission of conducting research in environmental health. The Environmental Protection Agency (EPA) was also founded in the Executive Branch to conduct research, and to set and enforce environmental health standards (among other environmental

issues). Many environmental contaminants are present (often to a larger degree) in the manufacture or occupational use of the toxicant, so studies of occupational hazards may provide the first warning of environmental hazards and coordination between all these agencies is essential.

The National Toxicology Program (NTP) was established in 1978 to coordinate the interactions of the various federal agencies within the Department of Health and Human Services conducting toxicological research in order to avoid duplication and strengthen research outcomes.

NIOSH conducts research on occupational health and safety hazards. Research is conducted in the laboratory using cellular and animal models and worker populations are directly evaluated for the impacts of workplace conditions. To make its recommendations to OSHA, NIOSH gathers information from intramural research from the NTP, scientific literature, and all other sources of scientific evidence.

NIOSH is leading the development of future research priorities in occupational health in United States through its National Occupational Research Agenda (NORA). Fertility and Pregnancy Abnormalities is one of the 21 research topics recognized as significant by NORA. A team of government and non-government scientists is currently developing an implementation plan to coordinate research in assessing the health effects of occupational exposure and reproductive health.

In assessing reproductive toxicants, NIEHS coordinates the NTP screening and testing of potential reproductive toxicants. NIEHS conducts research on environmental exposures (whereas, NIOSH investigates occupational exposures). The intramural program of NIEHS investigates both fundamental biological processes and selected toxicants by evaluating study methods and studying mechanisms of reproductive toxicant action. The NIEHS Division of Extramural Research and Training funds investigator initiated research and when specific needs arise can issue requests for applications (RFAs) in special topic areas.

The EPA also conducts reproductive research in intramural programs - this involves methods

development, testing or evaluating the toxicity of classes of compounds and investigating mechanisms of action. EPA gathers reproductive toxicology data from industry in two ways: First, the Toxic Substances Control Act (TSCA), enacted by Congress in 1976, gives EPA broad authority to identify and control substances that may pose a threat to human health or the environment. The New Chemicals Program within TSCA, identifies limitations (including prohibition of use) to be placed on the use of a new chemical before it is allowed into commerce. Actions are taken based on the estimation of the reasonableness of risk. This program requires all existing toxicologic data be supplied to the TSCA office. Reproductive testing is not initially required but may be requested as other toxicologic data are evaluated. Conversely, pesticides are required to have more extensive toxicological data due to the potential of widespread exposure. Second, pesticide manufacture, distribution, and use, which includes occupational scenarios, are regulated under the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). As part of the EPA's FIFRA requirements, every pesticide is evaluated for the ability to induce alterations in reproductive function over two generations in rodents, as well as developmental anomalies in the offspring of two species. Further, as part of the reproduction study protocol, FIFRA requires pesticides approved for use on food to be tested for male reproductive toxicity, including male fertility and histological changes of the testis and epididymis. These guidelines are currently under revision; the proposed changes have been published in the Federal Register, and finalization is expected to occur in early 1998.

OSHA must evaluate the toxicologic and epidemiologic data for a chemical and determine the occupational exposure standard (Permissible Exposure Limit, PEL). Based on available scientific and other data, OSHA drafts a proposed regulation and publishes it in the Federal Registry.

Based on public comment received from NIOSH and other interested parties, including the affected industries, worker representatives, and others, OSHA prepares a final regulation that is promulgated as a mandatory US standard.

The Glycol Ethers – 2-methoxyethanol (2ME) and 2-ethoxyethanol (2EE)

To illustrate how these programs work together, the example of the glycol ethers is provided.

The first reports of the toxic effects of glycol ethers on the male reproductive system date back to the late 1930s (1) and early 1940s (2). These animal studies reported testicular atrophy related to exposure. Little information exists in the literature on these solvents until the late 1970s when reports from Japan on the testicular toxicity stimulated several NIOSH research projects evaluating the chemical family of the glycol ethers (3). In 1983, NIOSH held an international symposium to summarize existing data and knowledge among scientists conducting glycol ether research and establish research needs (4). Two major needs were identified: 1) to understand how the glycol ethers were affecting the testis and 2) to determine if there were similar effects in humans. Following this meeting, in 1984, the EPA announced its intention to regulate 2-methoxyethanol (2ME) and 2-ethoxyethanol (2EE) (5). NIEHS and NIOSH conducted animal studies on a series of glycoethers to determine their reproductive toxicity and structure activity relationships. These studies included investigating testicular toxicity and the site of action for the acetic acid metabolite of the glycol ethers (6,7,8). NIOSH investigated glycol ether metabolism (9,10) and studied male fecundity in two populations of exposed workers using semen analysis (11). This multifaceted research approach has clearly defined a male reproductive toxicant, its site of action, and the susceptibility of male workers. In 1988, NIOSH developed a risk assessment model of human reproductive toxicity (12).

While EPA initially proposed to regulate 2-ME and 2-EE it was determined that the most significant human exposures were in the occupational setting and accordingly EPA deferred to OSHA to establish an exposure standard (5). Thus in 1987, OSHA announced its intent to regulate the use of 2-ME and 2-EE. NIOSH compiled all relevant data and in 1991, published a

Criteria document containing health-based recommendations for a comprehensive occupational standard including time-weighted exposure limits at 0.1 ppm for 2-ME and 0.5 ppm for 2-EE. In 1993, OSHA published a proposed rule for 2-ME and 2-EE in the Federal Register (13) that incorporated exposure limits and many other recommendations made by NIOSH. Public comments were received by OSHA, but the final standard has not yet been promulgated (14).

While almost two decades have passed from the initial intensified research investigations to final rulemaking, the open and interactive process involving industry, scientists, and regulators has provided the information necessary to produce and use these glycol ethers safely or to substitute safer (less toxic) alternatives to these solvents. Thus, even without a final mandatory standard worker safety and health has been improved.

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