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Introduction

The focus of the chapters presented in this background paper are screening and test strategies for reviewing the Toxic Substances Control Act (TSCA) inventory of existing chemicals in commerce.[1] The screening problem poses a challenge, not only in terms of the numbers of chemicals that have undergone little testing or review, but also in terms of the many exposure routes and ecological and health endpoints of potential concern. The foremost goal of a review strategy must be to identify the chemicals that pose the greatest potential ecological and health risks, and allocate limited testing resources to better characterize these risks.

BACKGROUND

In 1994, the Senate Environment and Public Works, Subcommittee on Toxic Substances, Research and Development asked the Congressional Office of Technology Assessment to carry out a study of Existing Chemicals Program under the Toxic Substances Control Act (TSCA, PL 94-469).

Congress originally enacted TSCA in 1976. Administered by the U.S. Environmental Protection Agency (EPA), the law gives EPA authority to screen and require further testing of both new and existing chemicals in commerce as necessary to protect public health and the environment. TSCA states, "It is the policy of the United States that . . . adequate data should be developed with respect to the effect of chemical substances and mixtures on health and the environment and that the development of such data be the responsibility of those who manufacture and those who process such chemicals and mixtures. "

The task of addressing the large number of existing chemicals has proven to be daunting. A 1984 study by the National Research Council (2) concluded that no toxicity data was available for almost 80 percent of the chemicals in general commerce and only 10 percent of substances had test data that were adequate for conducting a health-hazard assessment. In 1994, the Government Accounting Office reported that the EPA has fully reviewed only about 2 percent of the existing chemicals in commerce (1).

The current estimates are that approximately 70,000 chemicals have been used in U.S. commerce since 1976. Of these, roughly 30,000 are polymers that present little health risk. Another 25,000 are produced in low volume (less than 10,000 lbs/year), with some no longer in production. Thus, it is certainly debatable whether all 70,000 chemicals in commerce present equal concerns. Still, there remain some 15,000 chemicals that are produced in significant volumes. with approximately 3 - 4,000 produced in excess of 1,000,000 lbs/year. For perhaps thousands of these chemicals of potential concern, toxicity and exposure data remain inadequate for risk assessment.

The complete toxicological evaluation of thousands of chemicals would be both time consuming and extraordinarily expensive. Full toxicological evaluations for a single chemical can cost

[1]**The phrase "chemical in commerce" is used to mean all chemical substances that are potentially regulated under TSCA. TSCA covers most chemicals except drugs, pesticides, tobacco, food products, food additives, and radioactive materials. The inventory of existing chemicals includes some 60,000 substances registered as being in commerce when TSCA was passed, plus others that have subsequently been reviewed by EPA as new chemicals.**

Table 1-1: Workshop Topics

Carcinogenicity	**Environmental toxicity** (ecological endpoints)
Dermal and ocular toxicity	Multiple endpoints (integrated test strategies)
Immunological toxicity	Exposure assessment (biomarkers)
Neurological toxicity	Structure-activity methods
Reproductive and developmental toxicity	

up to $2,500,000, involve several thousand test animals, and take five years to complete. An effective screening strategy must cheaply identify those chemicals that pose the greatest potential risk, before committing limited resources.

THE WORKSHOP

On April 24-25, 1995, OTA held a workshop to address the question of whether there were technologies that could be used to rapidly screen existing chemicals in commerce for effects on human health and the environment. The purpose of the workshop was to compile and review current and developing systems that may be relevant to the needs of TSCA.

We invited panels of experts to cover various specific testing endpoints and general screening approaches (listed in table l-l). Each panel was chosen to include individuals from a mix of academic, government, and industry backgrounds. The individual chapters of this background paper were written by the panels that participated in the workshop. Each panel was asked to address the following questions in their chapters:

- What are the best currently used methods to identify chemicals of concern and their health effects?
- Cost and time are critical considerations for an evaluative strategy. What faster and cheaper screening technologies are available that can inform the review process or set priorities for further testing? Address the issue of using these assays to evaluate various number of chemicals (100, 1,000, 10,000, etc.).
- What are the tradeoffs in using the cheaper and faster screens? Consider confidence as well as ambiguities of results and reproducibility between different laboratories?
- For the specific endpoints (e.g. carcinogenicity), what is the contribution from receptor-based assays, SAR approaches, and mechanism-based assays?
- For the specific endpoints, how efficiently can the screening tests be integrated into an overall screening and test strategy for a comprehensive evaluation of a chemical?
- Finally, test technology is a discipline in constant development, and test strategies should be designed to adopt technological innovations. What new developments might we expect for test technologies in the next decade?

The efforts to answers to these questions are contained in this background paper and are worthy of an audience among legislators, regulators, and the informed public, as well as toxicologists. Although several of the papers are quite technical, all offer considerable insight as to current regulatory practices and scientific capabilities.

REFERENCES

1. Guerrero, P. F., U.S. General Accounting Office, “Toxic Substances Control Act: EPA’s Limited Progress in Regulating Toxic Chemicals,” testimony at hearings before the Senate Subcommittee on Toxic Substances, Research and Development, GAO/T-RCED-94-212, May 17, 1994.
2. National Research Council, Commission on Life Sciences, *Toxicology Testing: Strategies to Determine Needs and Priorities*, (Washington, DC: National Academy Press, 1984).