

EXPOSURE INFORMATION IN THE IARC INTERNATIONAL REGISTER
OF PERSONS EXPOSED TO PHENOXY HERBICIDES AND CONTAMINANTS

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INTRODUCTION

An International Register of Persons Exposed to Phenoxy Acid Herbicides and Contaminants (referred to as the Register hereafter) has been established at the International Agency for Research on Cancer in collaboration with the National Institute of Environmental Health Sciences (USA). The purpose of this Register is 1) to investigate through epidemiologic studies the adverse health effects associated with exposure to phenoxy herbicides, chlorophenols, and their contaminants; and, 2) to serve as a system of scientific information exchange and collaboration at the international level.

This Register was begun after publication in the early 1980's of reports of increased cancer risk among exposed workers, particularly soft-tissue sarcomas and malignant lymphomas. Many research questions with regard to human health effects of phenoxy herbicides remain unanswered. The evidence for the carcinogenicity of occupational exposure to chlorophenols and chlorophenoxy herbicides in humans has been evaluated by IARC as limited (IARC, 1986), and for 2,3,7,8-tetrachlorodibenzo-para-dioxin (TCDD) as inadequate (IARC, 1982).

The purpose of this paper is to describe a large occupational cohort resource, the IARC International Register of Persons Exposed to Phenoxy Herbicides and Contaminants, and to illustrate the use of various kinds of exposure data in the analysis of the potential health effects of herbicides.

REGISTER DEFINITION

The Register includes persons exposed occupationally either in the manufacture of any of these substances or during occupational use of herbicides (sprayer cohorts). Investigators were also encouraged to enroll workers in manufacture who were not exposed to these substances, but who worked in the same factories.

Criteria to be met for cohorts to be eligible for enrollment in the Register are the availability and completeness of individual information necessary for the conduct of epidemiologic studies and the existence of facilities for ascertainment of vital status, cause of death, and a follow-up completeness of greater than 90%. To preserve confidentiality, names of individuals and companies are not included in the data base.

DATA COLLECTION

The first step in establishing the Register was the development of a directory of world's major producers of phenoxy acid herbicides and chlorophenols. Out of 26 producer countries identified, investigators from 10 countries are participating (Australia, Austria, Canada, Denmark, Finland, Italy, Netherlands, New Zealand, Sweden, United Kingdom). Inclusion of manufacturer cohorts from the Federal Republic of Germany has recently been confirmed.

A standard protocol was developed for data collection which included individual information on cohort members, company exposure history questionnaires, company reports on production or consumption (use) figures and, copies of individual study protocols.

REGISTER POPULATION

Presently, 18,972 workers are enrolled in this Register. Sixteen cohorts are from companies which have manufactured and formulated phenoxy acids (n=5241), chlorophenols (n=532) or both (n=7007); 4 cohorts are sprayers of phenoxy herbicides (n=6192). A potential control group of workers in the manufacturing industry not exposed to these chemicals is also enrolled (n=4028).

Vital status of the Register members is updated periodically and most cohorts have mortality follow-up through 1986. Cancer incidence data are available for 4 out of 10 countries already enrolled in the Register. An analysis of mortality and cancer incidence is presently under way.

EXPOSURE DATA

For each individual in the Register, a detailed occupational history is the basis for determining a worker's exposure status. Information includes periods of employment

in different departments and jobs from date of first to last employment, as well as history of chloracne, and exposure during accidents. According to departments and job titles, an individual's exposure status is determined as exposed, unexposed, or unknown.

For companies manufacturing or formulating herbicides, exposure information includes dates of manufacture of several specific compounds, number of workers in each department by calendar period, amounts and types of raw materials used, other chemicals produced, chemical methods employed, production figures, process changes and occasionally industrial hygiene measurements of dioxin/furan concentrations in the working environment. Information concerning concentrations of dioxin and furan in air and wipe samples, process streams and waste products was also requested, but has generally not been available. Likewise, responses from company exposure questionnaires completed to date indicate that rabbit ear tests have not been conducted, process reaction temperatures and pressures are generally not specified, companies are reluctant to commit themselves to ranking workers according to dioxins and furan exposure, and biological monitoring of workers has been rare.

For the sprayer cohorts, information from exposure questionnaires includes the number and percentage of workers engaged in spraying or applying different types of phenoxy herbicides, the average amounts and proportions of various herbicides sprayed according to different methods and calendar period, use of protective equipment and spraying of other pesticides.

USE OF EXPOSURE INFORMATION

The quality of exposure information in epidemiological studies, depends on its availability and completeness and on the accuracy with which it estimates the dose to individual workers. The following types of exposure information will be used in the epidemiological analysis.

The broadest level of exposure information, ever employed in the industry, is by definition an inclusion criterion in the Register and will be used as a basis for comparisons with national populations. Although data on workers not exposed to the herbicides in question have also been included in the register, these will not be used for the main analyses basically because non-exposed workers were not selected under defined criteria and are actually exposed to a variety of other chemicals.

The next level of exposure information is duration of employment in the industry. Instead of using total duration of employment in the industry, as is often done, duration in departments or jobs where the individual's status is classified as exposed

will be used. This will make duration, as a surrogate of exposure, more specific in reflecting actual exposed time.

For the majority of subjects classified as exposed in the Register, information on employment in various departments or job titles with dates of start and stop for each is available. Only a few companies have been able to provide information on exposure levels, and lack of hygiene measurements has proven to be one of the major difficulties in reconstructing historical exposures. Workers in the manufacturing cohorts have been classified into four groups of departments (production, maintenance/cleaning, other, unclassified), but it has been proven very difficult to produce a joint ordinal ranking scheme for level of exposure based on available information on job titles or departments.

A further issue to be considered when attempting to rank workers in this industry by exposure levels is the definition of the exposure of interest, since both manufacturers and sprayers are exposed to a variety of chemicals with different concentrations of their individual components. The majority of workers have been exposed either in manufacture or in spraying to 2,4-D and MCPA. A distinction, however, can be made between cohorts where in addition exposure to 2,4,5-TCP or 2,4,5-T (and consequently TCDD) was likely to have occurred, and those where it was not. Frequently the issue of interest has been limited to exposure to TCDD. Exposure to TCDD does not, however, necessarily correlate with levels of exposure to other chemical compounds, to which workers in these cohorts are exposed.

CONCLUSION

This Register of Persons Exposed to Phenoxy Herbicides and their Contaminants serves as an important data base for epidemiologic studies of potential health effects. The availability of exposure data on individuals, the variability of both the level of exposure and type of compounds to which persons are exposed, and the large size of the Register are assets that will contribute to knowledge of the health hazards of these compounds and will facilitate the detection of moderate increases in rare tumours.

REFERENCES

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