

Screening-Level Review of the Recent Health Effects Literature for IRIS Chemicals

OVERVIEW

The Integrated Risk Information System (IRIS) is a U.S. Environmental Protection Agency (EPA) database containing summaries of potential adverse health effects that may result from chronic (or lifetime) exposure to chemical substances found in the environment. This database is maintained by EPA's National Center for Environmental Assessment (NCEA). IRIS summaries contain qualitative and quantitative health effects information, including reference doses (RfDs) for noncancer health effects resulting from oral exposure, reference concentrations (RfCs) for noncancer health effects resulting from inhalation exposure, cancer weight-of-evidence (WOE) designations, and cancer slope factors (CSFs) and inhalation unit risks (IURs) for the carcinogenic effects of chemicals resulting from ingestion and inhalation, respectively.

In 2000, EPA initiated an on-going screening-level review of the scientific literature for chemicals in the IRIS database. The purpose of this project was to reach a preliminary determination regarding the likelihood that a toxicological reassessment based on an evaluation of more current health effects literature could potentially result in a significant change to the existing toxicity values or WOE designations currently on IRIS. In addition, the results of the screening-level review provided information for the annual IRIS Program priority-setting process for identifying chemicals for reassessment.

A screening-level methodology was adopted because an in-depth evaluation of recent health effects literature is a time- and resource-intensive process that represents the majority of the effort required in an IRIS assessment of a chemical. The screening-level methodology was designed to provide a preliminary identification and characterization of new health effects literature for chemicals listed in the IRIS database. The methodology was not intended to provide a comprehensive or critical evaluation of this literature. This report summarizes the methodology used to conduct the on-going screening-level review.

METHODS

The screening-level review of toxicity values in the IRIS database was conducted in four steps: 1) identifying recent toxicological secondary source documents prepared by EPA and other authoritative scientific organizations, 2) conducting literature searches to identify relevant health effects literature published since the IRIS assessment for a given chemical was completed and posted on IRIS, 3) sorting the literature (based primarily on a review of titles and abstracts) identified during the literature searches, and 4) evaluating the new health effects information and determining if this information could potentially produce a significant change in the existing IRIS toxicity values.

Identification of Existing Authoritative Reviews of the Scientific Literature

EPA programs and other authoritative scientific organizations periodically review and summarize the toxicology literature for chemicals that are included in the IRIS database. Where available, these authoritative secondary sources were used to identify the more recent health effects literature for an IRIS chemical (see Table 1).

Table 1. Authoritative Secondary Sources Considered the Screening-Level Review

Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profiles
Health Canada assessments
International Agency for Research on Cancer (IARC) Monographs
World Health Organization/International Programme on Chemical Safety (WHO/IPCS) Environmental Health Criteria
National Toxicology Program (NTP) Cancer Bioassay
NTP Report on Carcinogens
Office of Pesticide Programs (OPP) Reregistration Eligibility Decision (RED) documents
NCEA Provisional Peer-reviewed Toxicology Values
Documents submitted to the IRIS Submission Desk
World Health Organization/International Programme on Chemical Safety (WHO/IPCS) Concise International Chemical Assessment Documents (CICADS)

Literature Searches

Literature searches were conducted where no authoritative secondary sources were available and to supplement available secondary sources. The following Web-based databases were searched: TOXLINE Special, MEDLINE, CCRIS, TSCATS, and EPA's Office of Pesticide Programs (OPP).

A consistent set of search terms was used in searching these on-line databases (see Table 2).

Table 2. Literature Search Terms

CAS number	oncogen	reproduct, toxic
chemical name & synonyms	neoplasm	development, toxic
toxic	mutat	neurotox
adverse effect	genotox	immunotox
cancer	fetotox	pharmacokinetic
carcinog	embryotox	metabolism
tumor	teratolog	epidemiol
	teratogen	human stud

A reference managing software program was used to manage and organize results obtained from the literature search.

When the literature search retrieved a very large number of references (i.e., greater than 300), additional key words were used to refine the literature search in order to screen out records not relevant to a given chemical's toxicity.

Screen of Literature Search Results

Study records for the references retrieved in the literature search were screened and sorted with respect to the study's possible relevance to the development of an IRIS toxicity value. This screen was limited to the information contained in the literature search record (study title and abstract). Reviewing full-text articles and conducting in-depth data reviews were outside the scope of this screen. Individual references were sorted into the following nine categories:

1. Potential to produce a significant change in an existing noncancer toxicity value
2. Potential to produce a significant change in an existing cancer toxicity value
3. Potential to produce a significant change in an existing cancer WOE designation
4. Physiologically-based pharmacokinetic (PBPK) modeling studies
5. Other toxicity studies not directly useful for establishing IRIS toxicity values
6. Studies with information on health effects in young populations
7. Compilations of health effects studies
8. Not useful
9. Unknown relevance

In general, those references considered potentially relevant to the development of an IRIS toxicity value were those assigned a code of 1, 2, 3 or 4.

Evaluation of Health Effects Information

Summary information contained in available secondary source documents and in the screened literature searches was evaluated to determine (1) if major new health effects studies have become available since existing IRIS toxicity values were derived, and (2) if these studies could potentially produce a significant change in existing IRIS toxicity values or WOE designations. The findings of the screening-level review were summarized in brief narratives.

Given the application of a screening-level methodology to evaluate current IRIS assessments, certain limitations and uncertainties were inherent in the results.

- This strategy is not comprehensive.
 - Literature was identified from study summaries in secondary sources and from literature search records (based on review of titles and abstracts only).
- The literature screen did not include an in-depth assessment or critical evaluation of identified literature.
- The literature search may not have captured all relevant information, especially unpublished studies.
- Literature search records did not always present enough information to make a determination of relevancy to toxicity value development.
- Consideration of how the application of new risk assessment methodologies might affect existing IRIS values was beyond the scope of this screening-level review.
- A determination of whether the available toxicity information might support the derivation of a toxicity value not currently available in IRIS was beyond the scope of this review.