Provisional Peer Reviewed Toxicity Values for

Dinoseb
(CASRN 88-85-7)

Derivation of an Oral Slope Factor

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### Acronyms and Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>bw</td>
<td>body weight</td>
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<tr>
<td>cc</td>
<td>cubic centimeters</td>
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<tr>
<td>CD</td>
<td>Caesarean Delivered</td>
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<tr>
<td>CERCLA</td>
<td>Comprehensive Environmental Response, Compensation and Liability Act of 1980</td>
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<tr>
<td>CNS</td>
<td>central nervous system</td>
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<tr>
<td>cu.m</td>
<td>cubic meter</td>
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<tr>
<td>DWEL</td>
<td>Drinking Water Equivalent Level</td>
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<td>FEL</td>
<td>frank-effect level</td>
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<tr>
<td>FIFRA</td>
<td>Federal Insecticide, Fungicide, and Rodenticide Act</td>
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<tr>
<td>g</td>
<td>grams</td>
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<tr>
<td>GI</td>
<td>gastrointestinal</td>
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<tr>
<td>HEC</td>
<td>human equivalent concentration</td>
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<td>Hgb</td>
<td>hemoglobin</td>
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<tr>
<td>i.m.</td>
<td>intramuscular</td>
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<tr>
<td>i.p.</td>
<td>intraperitoneal</td>
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<tr>
<td>IRIS</td>
<td>Integrated Risk Information System</td>
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<tr>
<td>IUR</td>
<td>inhalation unit risk</td>
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<tr>
<td>i.v.</td>
<td>intravenous</td>
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<tr>
<td>kg</td>
<td>kilogram</td>
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<td>L</td>
<td>liter</td>
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<tr>
<td>LEL</td>
<td>lowest-effect level</td>
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<tr>
<td>LOAEL</td>
<td>lowest-observed-adverse-effect level</td>
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<tr>
<td>LOAEL(ADJ)</td>
<td>LOAEL adjusted to continuous exposure duration</td>
</tr>
<tr>
<td>LOAEL(HEC)</td>
<td>LOAEL adjusted for dosimetric differences across species to a human</td>
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<tr>
<td>MCL</td>
<td>maximum contaminant level</td>
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<tr>
<td>MCLG</td>
<td>maximum contaminant level goal</td>
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<tr>
<td>MF</td>
<td>modifying factor</td>
</tr>
<tr>
<td>mg</td>
<td>milligram</td>
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<tr>
<td>mg/kg</td>
<td>milligrams per kilogram</td>
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<td>mg/L</td>
<td>milligrams per liter</td>
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<td>MRL</td>
<td>minimal risk level</td>
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<td>MTD</td>
<td>maximum tolerated dose</td>
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<tr>
<td>MTL</td>
<td>median threshold limit</td>
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</table>
NAAQS  National Ambient Air Quality Standards
NOAEL  no-observed-adverse-effect level
NOAEL(ADJ)  NOAEL adjusted to continuous exposure duration
NOAEL(HEC)  NOAEL adjusted for dosimetric differences across species to a human
NOEL  no-observed-effect level
OSF  oral slope factor
p-IUR  provisional inhalation unit risk
p-OSF  provisional oral slope factor
p-RfC  provisional inhalation reference concentration
p-RfD  provisional oral reference dose
PBPK  physiologically based pharmacokinetic
ppb  parts per billion
ppm  parts per million
PPRTV  Provisional Peer Reviewed Toxicity Value
RBC  red blood cell(s)
RCRA  Resource Conservation and Recovery Act
RDDR  Regional deposited dose ratio (for the indicated lung region)
REL  relative exposure level
RfC  inhalation reference concentration
RfD  oral reference dose
RGDR  Regional gas dose ratio (for the indicated lung region)
s.c.  subcutaneous
SCE  sister chromatid exchange
SDWA  Safe Drinking Water Act
sq.cm.  square centimeters
TSCA  Toxic Substances Control Act
UF  uncertainty factor
μg  microgram
μmol  micromoles
VOC  volatile organic compound
PROVISIONAL PEER REVIEWED TOXICITY VALUES FOR
DINOSEB (CASRN 88-85-7)
Derivation of an Oral Slope Factor

Background

On December 5, 2003, the U.S. Environmental Protection Agency's (EPA's) Office of Superfund Remediation and Technology Innovation (OSRTI) revised its hierarchy of human health toxicity values for Superfund risk assessments, establishing the following three tiers as the new hierarchy:

1. EPA's Integrated Risk Information System (IRIS).
2. Provisional Peer-Reviewed Toxicity Values (PPRTV) used in EPA's Superfund Program.
3. Other (peer-reviewed) toxicity values, including:
   - Minimal Risk Levels produced by the Agency for Toxic Substances and Disease Registry (ATSDR),
   - California Environmental Protection Agency (CalEPA) values, and
   - EPA Health Effects Assessment Summary Table (HEAST) values.

A PPRTV is defined as a toxicity value derived for use in the Superfund Program when such a value is not available in EPA's Integrated Risk Information System (IRIS). PPRTVs are developed according to a Standard Operating Procedure (SOP) and are derived after a review of the relevant scientific literature using the same methods, sources of data, and Agency guidance for value derivation generally used by the EPA IRIS Program. All provisional toxicity values receive internal review by two EPA scientists and external peer review by three independently selected scientific experts. PPRTVs differ from IRIS values in that PPRTVs do not receive the multi-program consensus review provided for IRIS values. This is because IRIS values are generally intended to be used in all EPA programs, while PPRTVs are developed specifically for the Superfund Program.

Because new information becomes available and scientific methods improve over time, PPRTVs are reviewed on a five-year basis and updated into the active database. Once an IRIS value for a specific chemical becomes available for Agency review, the analogous PPRTV for that same chemical is retired. It should also be noted that some PPRTV manuscripts conclude that a PPRTV cannot be derived based on inadequate data.
Disclaimers

Users of this document should first check to see if any IRIS values exist for the chemical of concern before proceeding to use a PPRTV. If no IRIS value is available, staff in the regional Superfund and RCRA program offices are advised to carefully review the information provided in this document to ensure that the PPRTVs used are appropriate for the types of exposures and circumstances at the Superfund site or RCRA facility in question. PPRTVs are periodically updated; therefore, users should ensure that the values contained in the PPRTV are current at the time of use.

It is important to remember that a provisional value alone tells very little about the adverse effects of a chemical or the quality of evidence on which the value is based. Therefore, users are strongly encouraged to read the entire PPRTV manuscript and understand the strengths and limitations of the derived provisional values. PPRTVs are developed by the EPA Office of Research and Development’s National Center for Environmental Assessment, Superfund Health Risk Technical Support Center for OSRTI. Other EPA programs or external parties who may choose of their own initiative to use these PPRTVs are advised that Superfund resources will not generally be used to respond to challenges of PPRTVs used in a context outside of the Superfund Program.

Questions Regarding PPRTVs

Questions regarding the contents of the PPRTVs and their appropriate use (e.g., on chemicals not covered, or whether chemicals have pending IRIS toxicity values) may be directed to the EPA Office of Research and Development’s National Center for Environmental Assessment, Superfund Health Risk Technical Support Center (513-569-7300), or OSRTI.

INTRODUCTION

were: TOXLINE, MEDLINE, CANCERLIT, CCRIS, TSCATS, HSDB, RTECS, GENETOX, DART/ETICBACK, and EMIC/EMICBACK.

**REVIEW OF THE PERTINENT LITERATURE**

**Human Studies**

Case-control studies in Swedish cancer patients, described in U.S. EPA (1984), found no evidence of increased risk of malignant lymphomas or malignant mesenchymal soft tissue tumors associated with dinoseb exposure (Eriksson et al., 1979; Hardell et al., 1981).

**Animal Studies**

Long-term studies of dinoseb exposure in mice (Innes et al., 1969; Dow Chemical Co., 1981) and rats (Dow Chemical Co., 1977) did not show an increase in tumors and/or were inadequate studies of carcinogenicity (U.S. EPA, 1984, 2001). No additional studies subsequent to the 1989 IRIS review were located.

**Other Studies**

Genotoxicity assays of dinoseb have generally shown no mutagenic activity, but have demonstrated an ability to interact with DNA and RNA (U.S. EPA, 1984, 2001). In bacteria, dinoseb was not mutagenic in multiple assays in *Salmonella typhimurium* and *Escherichia coli*, but produced positive results in differential toxicity tests comparing growth of repair-/recombination-deficient and proficient strains of *S. typhimurium*, *E. coli* and *Bacillus subtilis*. Assays for mitotic gene conversion in the yeast *Saccharomyces cerevisiae* produced mixed results. A sex-linked recessive lethality assay in *Drosophila* was negative. Results were also negative for unscheduled DNA synthesis in cultured human lung fibroblasts. Sperm morphology studies showed an increase in the occurrence of abnormal sperm in treated rats, but no effect in mice.

**FEASIBILITY OF DERIVING A PROVISIONAL ORAL SLOPE FACTOR FOR DINOSEB**

A provisional oral slope factor for dinoseb cannot be derived due to lack of human and inadequate animal cancer data.
REFERENCES

http://www.atsdr.cdc.gov/gsql/toxprof.script


http://193.51.164.11/cgi/iHound/Chem/iH_Chem_Frames.html


http://ntp-server.niehs.nih.gov/cgi/iH_Indexes/ALL_SRCH/iH_ALL_SRCH_Frames.html


