State of Oregon Department of Environmental Quality

Target Organ Spreadsheet Criteria

January 1, 2020

The Department of Environmental Quality and the Oregon Health Authority used the following criteria to populate the Target Organ Spreadsheet. These criteria, along with the Target Organ Spreadsheet, are technical tools that DEQ and OHA have used to guide Hazard Index rulemaking. DEQ and OHA developed these criteria with input from a Technical Advisory Committee. The last portion of this document describes the process that DEQ and OHA staff used to systematically apply the criteria in populating the Target Organ Spreadsheet.

The codes "a", "b", "c", and "o" in the following sections of this document refer to designations for types of information displayed in the Target Organ Spreadsheet. The footnotes to the Target Organ Spreadsheet include more details about these codes. This document describes the criteria DEQ and OHA applied in deciding whether or not to include information found in toxicological literature in the spreadsheet and how to code it.

DEQ and OHA designated toxic air contaminants with "a", "b", "c", or "o" codes in the "reproductive" or "developmental" columns in the Target Organ Spreadsheet as being expected to have reproductive or developmental health effects for purposes of the Hazard Index rulemaking. DEQ and OHA did not designate toxic air contaminants as having reproductive or developmental health effects if those columns contained "x" or were blank.

The term "authoritative source" in this document refers to a specific set of governmental agencies that routinely and systematically review published literature from the toxicological and epidemiological sciences and evaluate the overall weight of scientific evidence related to the health effects of exposure to toxic air contaminants. The list of authoritative sources that DEQ and OHA used can be found in the Cleaner Air Oregon rule 340-245-0300.

Inclusion criteria for *reproductive and developmentally* toxic air contaminants

"a" = A reproductive or developmental effect is the basis for the toxicity reference value or TRV,
OR
"b" = A reproductive or developmental effect is identified by the authoritative source for the TRV, but is not the basis of the TRV,
OR
"c" = A reproductive or developmental effect is identified by another authoritative source.

In the cases where reproduction or developmental effects are flagged as "b" or "c", the criteria below were used:

- At least one inhalation studies in animals or humans that show significant effects on reproductive or developmental endpoints that could be the basis for a lowest observable adverse effect level or LOAEL.
    - Consistent with U.S. Environmental Protection Agency 3guidance, developmental effects should be considered regardless of maternal toxicity.

- Occupational studies that are confounded by the presence of other simultaneous co-exposures are not sufficient as the sole evidence for reproductive and developmental effects. Results from occupational studies should be considered if such confounders are adequately controlled for.
- Do not include studies for which authoritative sources note a lack of statistical significance (i.e. a significant pairwise test or trend test)
- If other chemicals in the chemical class have reproductive or developmental effects that haven't been evaluated in the chemical in question (unless an authoritative source makes a clear statement that the chemical with more data is unlikely to be predictive, e.g. due to differences in metabolism).

OR
"o" = reproductive or developmental effects are documented through other routes of exposure. In the absence of sufficient inhalation studies for reproductive and developmental endpoints, studies using other routes of exposure (oral or injection) can be used to demonstrate significant reproductive and/or developmental toxicity, as detailed below:

- Oral reproductive and developmental studies should be evaluated using the same criteria described above for inhalation studies.
- Oral effects should not be considered if the authoritative source specifically states that it is inappropriate to extrapolate across routes of exposure for that chemical.

"x" = data gaps

- An authoritative source specifically notes that there is no data or insufficient data or "database deficiencies" for potential reproductive and developmental effects following inhalation exposure and there is either no information or another stated gap in data for the same endpoints following oral exposure. (Often found in documentation for derivation of the TRV in the description of uncertainties; try searching for key terms "reproductive" "developmental" "database" "insufficient data")

AND/OR

- If the limited studies that are available are excluded because results are suggestive but not statistically significant

Inclusion criteria for *all other target organs*

"a" = An effect on that target organ is the basis for the TRV
"b" = The TRV source cites at least one study with a LOAEL for that target organ
"c" = Another authoritative source cites at least one study with a LOAEL for that target organ

Categorization Rules

- Developmental and reproductive effects should be categorized separately
- If a toxic air contaminant has developmental effects, do not also mark the target organ within the fetus/embryo (e.g. if developmental effect is delayed ossification, do not also include musculoskeletal system as a target organ)
- Effects on the olfactory epithelium should be considered respiratory. For the purposes of this spreadsheet, they will not be considered neurological effects.

Review Protocol and Quality Assurance Plan

1. Reviewers will be assigned groups of chemicals that are different from the set of chemicals they reviewed in the first draft of the table.
2. Reviewers will first consider each chemical "blind", without looking at previous conclusions.
    a. Scan alternate authoritative sources for which documentation is available, starting with the TRV source, then scanning other authoritative source for endpoints that are not mentioned by the TRV source. Searches should focus on:
        i. IRIS summary (or PPRTV documentation if there is no IRIS assessment)
        ii. ATSDR toxicological profile (starting with dose array tables and MRL documentation; review narrative sections on reproductive and developmental effects for both inhalation and oral exposures)
        iii. OEHHA documentation (starting with REL documentation and any discussion of evidence of developmental effects)
    b. evaluate reproductive and developmental evidence and determine whether inclusion criteria for a, b, c, o, or x are met
    c. Identify other target organs and determine whether inclusion criteria for a, b, or c are met.
    d. Record all conclusions in a new table.
3. Reviewers will then compare new conclusions with previous conclusions in existing table.
    a. If conclusions are the same as before, the review for that chemical is done.
    b. If conclusions in the new table are different, flag these conclusions for second review by highlighting all edited cells yellow.
4. The reviewer will also review and clean up the "description" columns and make sure that specific effects on all target organs are described, using language taken directly from authoritative sources where possible; if an "x" is in "reproductive and developmental" columns, these description should describe conclusions from authoritative sources and cite the specific source (e.g.: "IRIS notes database deficiencies in reproductive and developmental effects"). The reviewer should compare new description with description in the original spreadsheet to make sure all major health outcomes of interest are captured.
    a. Example format for description columns: "respiratory effects include nasal lesions in rodents and decreased lung function in workers; liver effects include increased liver weight in rats; developmental effects include decreased pup weight in rats"
5. For any chemicals that need a second review, a new reviewer will go through the same process.
6. If the second reviewer does not arrive at the same conclusions as the first reviewer, a third review will try to resolve the discrepancy and/or the group as a whole will review and discuss together.
7. Points that are unresolved after this review process may be topics for further discussion with a technical advisory committee.