Inclusion criteria for *developmental and reproductive* toxic air contaminants:

State of Oregon Department of Environmental Quality

"a" = A reproductive or developmental effect is the basis for the 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 LOAEL.
    - Consistent with EPA guidance, 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.

OR

"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

AND/OR

Inclusion criteria for *all other target organs* (less strict than reproductive and developmental criteria at this stage because we are trying to cast a wide net for effects that may be considered "other severe".)

"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 effects should be considered "reproductive and developmental". Do not also mark the target organ of developmental effects (e.g. if developmental effect is delayed ossification, do not also include musculoskeletal system and 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.