Memorandum

Date: July 2024

To: J.R. Giska, Apollonia Goeckner, and Susan MacMillan, Oregon Department of Environmental Quality; David Farrer and Holly Dixon, Oregon Health Authority

From: Eastern Research Group, Inc. (ERG)

Subject: QC of Toxicity Reference Values

1. Background

The Oregon Department of Environmental Quality (DEQ) Cleaner Air Oregon program within DEQ's Air Quality Division regulates emissions of Toxic Air Contaminants (TACs) from facilities operating in Oregon based on estimation of related public health risks. As part of the Cleaner Air Oregon program, DEQ and Oregon Health Authority (OHA) periodically review and update the inhalation Toxicity Reference Values (TRVs) used to assess the potential health impacts of facility emissions. DEQ's TRVs are based primarily on reference values published by one or more of four "Authoritative Sources" identified in Oregon Administrative Rule (OAR) 340–247-0030(1). Specifically, DEQ and OHA review TRVs published by U.S. EPA (including both the IRIS and PPRTV programs), California EPA's Office of Environmental Health Hazard Assessment (OEHHA), and U.S. Agency for Toxic Substances and Disease Registry (ATSDR). In addition, DEQ may derive its own TRV in consultation with an Air Toxics Science Advisory Committee (ATSAC).

The Cleaner Air Oregon rules require a triennial review of DEQ's TRVs. In early 2024, DEQ completed its initial review and contracted with Eastern Research Group (ERG) to conduct a Quality Control (QC) review of DEQ's TRV database. Specifically, ERG QC'd data on 327 Toxic Air Contaminants (TACs) housed within the database. The purpose of this QC was to help the Agency reduce the potential for error in the TRV review. ERG conducted this QC from February through May 2024. This memorandum describes the overall approach for the QC and major themes related to the identified errors. A detailed matrix of QC comments and findings for each TAC are attached as an Appendix.

2. Approach

On February 8, 2024, DEQ and OHA presented to ERG on the overall TRV rulemaking process and the approach taken by OHA toxicologists to develop the TRV database. As a part of this presentation, OHA demonstrated the TRV tool that ERG would QC and described a workflow document that the toxicologists followed when compiling data for the database. These materials were used by ERG to develop a QC workflow approach.

To ensure consistency and thoroughness when searching reference files and QC'ing the output of the TRV database, ERG internally trained its analysts on a standardized QC protocol. DEQ/OHA provided ERG with a sample batch of TACs to QC. Each batch of TACs was provided as an Excel file with two worksheets per TAC. The primary worksheet was titled "Review of Authoritative Sources". The second worksheet was titled "Target Organ Analysis" (TOA). All ERG analysts QC'd this same sample batch of TACs and resolved

any discrepancies on the QC approach with each other and with DEQ/OHA. For the remaining TACs, ERG would QC the TRVs in batches of approximately 30 TACs and iteratively discuss its findings with DEQ/OHA during weekly meetings.

For each TAC assigned to ERG, the QC review team searched all authoritative sources for inhalation TRVs. In addition, other data elements were cross-checked including units, applicable exposure durations, critical effects, and pertinent derivation information (e.g., time adjustments, uncertainty factors). All QC findings were recorded in an Excel workbook, which included page numbers and direct links to the relevant sources for ease of reference and verification. This Excel compilation is attached as an appendix. If an error was identified that would impact the TRV derivation or was otherwise substantial, a second senior QC reviewer would confirm the finding.

General steps for each phase in the QC review are described below.

Authoritative Source Search. ERG reviewers searched each of the three authoritative sources (EPA PPRTV, EPA IRIS, ATSDR, and OEHHA) by CASRN and name for the TAC. Reviewers confirmed accurate retrieval of all inhalation TRVs and that values were converted to the appropriate units, as necessary. The date the TRV was derived and any related comments documented in DEQ's TRV database were also verified for accuracy. This information corresponded to up to 52 information points to check in the Excel file.

Target Organ Verification. For every non-cancer TRV from an authoritative source, reviewers verified the number and type of critical effect target organ(s) using the supporting documentation. Each non-cancer TRV had up to 6 information points to check in the primary TRV worksheet, "Review of Authoritative Sources". In addition, reviewers checked the TOA worksheet to confirm the correct endpoints were listed, and that the target organs were consistent with the endpoints.

DEQ TRVs. When QC'ing TRVs derived by DEQ, reviewers referred to DEQ's derivation notes to understand the reasoning and any adjustments. Reviewers confirmed the correct dose-response or toxicity values and study information (e.g., exposure continuity, uncertainty factors) were pulled from the alternate source. All DEQ TRVs were recalculated to ensure that the up to 7 information points in the Excel file were accurate.

TRV Selection and Hierarchy. After confirming all inhalation TRVs were correctly extracted from every authoritative source, reviewers verified that the TRV selection was consistent with DEQ's stated algorithm for selecting a TRV. Cancer and chronic non-cancer TRVs should align with the most recent source, unless otherwise specified by Agency staff. For acute TRVs, preference is given in the following order: ATSDR acute MRLs, OEHHA acute RELs, or ATSDR intermediate MRLs, unless otherwise specified by Agency staff. A list of preferred TRV attributes that staff considered for TRV selection is described in the DEQ document: *Updates to the TRV Update and Selection Process after the ATSAC Meeting on January 20, 2023*.

Confirmation of Hazard Index (HI) Designation. Reviewers searched the U.S. Department of Transportation's (DOT) inhalation hazards list (49 CFR §172.101) by CASRN and name to confirm every TAC's DOT status. If a TAC appeared on the DOT list, reviewers checked whether it had a 6.1 designation with a special provision code between 1 and 6 or a 2.3 designation, ensuring TACs with either of these designations were identified as on the DOT list.

If a TAC was not on the DOT list but reproductive or developmental effects were identified, reviewers verified the endpoints using the documentation from the authoritative source. If a TAC had non-cancer TRVs but no developmental or reproductive effects were identified, reviewers searched across every authoritative source's documentation to ensure no such effects were missed. If a TAC had reproductive or developmental effects, multiple target organs, or was on the DOT list, ERG confirmed the TAC was categorized as HI3. Otherwise, ERG confirmed the TAC was categorized as HI5.

TOA Worksheet. Reviewers confirmed there was an entry in the TOA worksheet for every cancer TRV, non-cancer TRV target organ, and any instances where reproductive or developmental effects were pulled from authoritative sources. For each entry, reviewers used the authoritative source's documentation to confirm the following study and derivation information was correctly documented: species, target organ, TRV endpoint, study author and year, uncertainty factors, Point of Departure (POD) method, Human Equivalent Concentration (HEC) adjustments, exposure duration, and time adjustments. If the HEC adjustment factor (e.g., RGDR, DAF) was equal to one, reviewers ensured the HEC status was marked as 'no'. Additionally, reviewers ensured any reproductive or developmental effects following oral exposure were noted as such, and that intermediate exposures were classified as acute. The TOA table for each TAC contained up to 17 information points per TRV, for anywhere from 1 to 8 different TRVs.

3. Findings

Out of the 327 TACs reviewed, approximately 111 had a potential error and 106 were updated by DEQ as a result. ERG also classified each error into a 'substantial error' or not by whether it could have impacted the final TRV or HI3/HI5 status. Most of these errors were not substantial (e.g., the date of the authoritative source was not precise). A description of the errors identified within these broader categories is detailed below. A complete summary of QC errors and observations is attached separately as an Excel spreadsheet.

3.1.Substantial errors that potentially impacted final TRVs or HI3/HI5 designation

Below are examples of identified errors that ERG considered to be 'substantial' as they did or could have impacted the final regulatory TRV and HI3/HI5 designation.

Reproductive and developmental effects: ERG reviewers identified two TACs, p-nitroaniline and dicyclopentadiene, were misclassified as not having evidence of reproductive or developmental effects. As a result of correcting these errors, the HI designation for these TACs changed from HI5 to HI3.

Status on the DOT list: One TAC, sulfuric acid, had an inaccurate DOT list status. However, the HI3/HI5 comment indicated its presence on the DOT list, so this error did not affect its HI3/HI5 designation.

Number of target organs: Two TACs, bis(2-chloroethyl) ether and methyl amyl ketone, were incorrectly listed as having more than one target organ for their critical effects. Both of their HI designations changed from HI3 to HI5.

Authoritative source TRV transcription: Two TACs had discrepancies in the value of the TRV listed in the database when compared to the authoritative source. Specifically, the IRIS RfC for cerium oxide was not converted to the proper units, and the acute TRV for n-propylbenzene was missing a zero, which resulted in the value being off by an order of magnitude.

DEQ TRV derivation: Errors were found in the DEQ TRV derivation for seven TACs. Among these, three TACs (acetone, diethylene glycol monobutyl ether, and diethylene glycol monoethyl ether) had typos in the calculated TRV, although the formulas were correct. One TAC, parathion, was not converted to the proper units. Three of the PAH TACs (7,12-dimethylbenz[a]anthracene, 3-methylcholanthrene, and 5-nitroacenaphthene) had relative potency factors that were not used to calculate DEQ cancer TRVs. This changed the cancer TRV selection for these PAHs.

Recent updates to authoritative sources: Two TACs, chloroform and chloroethane, were recently updated by an authoritative source. ATSDR MRLs for chloroform and chloroethane were updated with their profiles in January 2024. As a result, the chronic non-cancer TRV selection for chloroform changed from OEHHA to ATSDR. The acute TRV for chloroethane was updated but the source of the selected TRV did not change.

TRV source attribution: One TAC, propylene oxide, attributed the cancer TRV to OEHHA, despite OEHHA adopting IRIS' IUR. The cancer TRV source was updated accordingly for this TAC.

3.2.Non-substantial errors that did not impact final TRVs or HI3/HI5 designation

Below are examples identified errors that ERG did not consider to be 'substantial.' These errors were still updated in the TRV database, but they did not have a potential to impact the regulatory TRV or HI3/HI5 designation.

Authoritative source date: Errors were identified in the TRV dates from authoritative sources for 64 TACs. This was the most common error. In many cases, these errors were attributed to defaulting to the first of the month as opposed to using the precise day. Overall, none of these errors altered the TRV selection for cancer or chronic non-cancer TRVs.

Acute or chronic status: Nine TACs inaccurately classified an endpoint as acute or chronic in the TOA worksheet. The primary reason for these errors was misclassifying reproductive or developmental effects from intermediate exposures as chronic rather than acute.

Target organs: Five TACs were found to have errors in their target organ tables, including discrepancies in the count or classification. These errors did not impact HI3/HI5 status. For example, for beryllium and compounds, the number of target organs for the IRIS chronic non-cancer TRV was updated to two from one and made to be consistent with the OEHHA chronic non-cancer TRV, which used the same critical study and effects.

HEC status: Three TACs were incorrectly marked 'yes' for having an HEC in the TRV despite the adjustment factor being one. According to DEQ/OHA's protocol this is incorrect. An additional three TACs had errors in the adjustment factor, such as a typo or missing adjustment factor.

Comment: Eight TACs had an error or were missing information in a comment field. For example, dichlorvos did not include a comment clarifying why the OEHHA IUR was not extracted. Other examples of comment errors included potency factor typos or missing adjustment factors.

Missing or outdated TOA entries: Four TACs were missing entries for critical effects or reproductive/developmental effects in the TOA table. Additionally, two TACs had outdated entries from previous TRV derivations or reproductive/developmental effects that were no longer available.

Authoritative source TRV transcription: One TAC had a transcription error from an authoritative source that was ultimately was not selected as the TRV.

Time adjustments: For three TACs, either the time adjustment factor was missing or incorrect.

Exposure duration: Incorrect exposure durations were identified in seven TACs.

Study author and year: Five TACs listed an incorrect study author or year.

Links to sources: Six TACs were missing links to supporting documentation from authoritative sources.

4. Conclusion

The QC review conducted by ERG for DEQ/OHA successfully identified and corrected several errors within the DEQ TRV database for TACs, many of which would have impacted the final regulatory TRVs. This QC process ensured that all TRVs were accurately derived, documented, and verified against authoritative sources, thereby improving the reliability and validity of DEQ's TRV database. The comprehensive review and subsequent updates enhance the Cleaner Air Oregon program's ability to regulate TAC emissions based on sound scientific data and protect public health effectively.

5. Appendix

Attached separately as an Excel file: ***ODEQ QA Task 1 Tracking Sheet - Final.xlsx***