**Data extraction template**

Primary aim of the data extraction template is the collection of key data from articles that passed the full-text literature search on bases of the selection and filter criteria set up in the CADIMA system. The data extraction should be performed by the evaluators without any judgement or assessment, i.e. data are collected as presented in the original article. In addition, outcomes of the Risk-of-Bias assessment are transferred from the Risk-of-Bias (RoB) Excel tool into the data extraction template, completed by a final judgement whether the data entry can be considered as appropriate for the quantitative comparative mixture assessment. If the latter is judged positive, it will be imported into the data bank system which serves as data repository for the meta-analysis.

The template is organised as table sheet in MS Excel, with each line referring as individual data entry to a unique “mixture experiment”. A “mixture experiment” is defined hereby as a chemical mixture that was tested in a well-defined experimental dose-response context. If in the same article a mixture was tested under identical testing conditions at different mixture ratios then it counts as one data entry, including mixtures that were tested at smaller number of compounds (e.g. a binary mixture as part of a multi-component mixture). If the data entry is accepted for the meta-analysis then that experimental mixture is used which showed the largest deviation to the expected mixture effect dose (concentration). If mixture responses are documented for more than one effect endpoint from the same mixture study, only those endpoints will be considered as separate data entries which were defined by the authors as the primary targets of the mixture study, and molecular endpoints will only be considered as data entry if no other apical/adverse endpoints were investigated in the same mixture study. However, if the same mixture was tested in various assays then each mixture experiment is counted as individual data entry. Consequently, an article can have more than one data entry and the data extraction template operates on two unique identifiers, one for the article and for the data entry of the mixture experiment.

The table sheet is structured along variables which are divided into nine blocks: (1) article ID and Evaluator, (2) meta data of the article, (3) mixture ID, (4) information about the experimental test system, (5) information about the chemicals of the mixture, (6) key characteristics about the mixture, (7) information about the mixture study, (8) Risk-of-Bias (RoB) summary, and (9) the final judgement about inclusion for data bank.

1. Article ID and Evaluator: the article ID is setup by CADIMA as numeric identifier and is used in the data extraction template and data bank system as universal ID reference of the article. Four persons are considered as potential evaluators, all are experts in the interpretation of experimental mixture studies and all have been trained on the use of this template and the BoR tool.
2. Meta data of the article: key information about the article such as authors, publication year, title, journal name and issue, journal pages, full abstract text, funding source and category (public, private/industry, private/other, undisclosed), doi. All data are available on CADIMA and can be downloaded as structured Excel file such that these data can be copied 1:1 into the data extraction file.
3. Mixture ID: a unique alphanumeric ID for the data entry which is defined as “article ID - X”, with X numeric starting from 1 per article data entry.
4. Test system: key information about the experimental test system such as in vivo/ex vivo/in vitro, receptor (human, Environment), organism(s) (species/strains) or cell line, bioassay, nature of effect (e.g. neurotoxicity, endocrine disruption, mortality etc.), exposure timing (e.g. prenatal) and duration (acute, chronic), exposure route, and exposure regimen. *More details can be found in the data extraction template*.
5. Chemical information: variables include chemical names, CAS, chemical class(es) or structure(s), chemical uses, and regulatory regime.
6. Mixture characteristics: variables include information about the similarity of sites (or Modes) of-Action (as reported) and stated sites (or modes) of-action, max number of chemicals, mixture composition, and application of substances for mixture testing.
7. Information about the mixture study: variables include testing aim (e.g. proof-of-principle, sample characterisation, low-dose, env. exposure simulation, product design), dosing design (e.g. surface, fixed-ratio, A in presence of B, isobologram, single dose summing up), timing of substance and mixture testing (e.g. before or simultaneous to mixture experiment), mixture expectation (e.g. effect summation, dose addition, response addition, no addition, mixed dose and response addition, TEF/TEQ), how the mixture observation are reported, and the mixture assessment in relation to the mixture expectation (e.g. Dose addition, Independent action/Response addition, Mixed additivity, Super/Supra-additivity, Antagonism, Synergism, etc.
8. Risk-of-Bias summary: RoB summaries about the three key stages of the comparative mixture assessment (Mixture Expectation, Mixture Observation, Comparative Assessment), and the overall conclusion (with comments on high-risk bias judgements).
9. Acceptable for meta-analysis and thus included in data bank system: an data entry is considered as appropriate for inclusion into the data bank system (including a potential data (re-)analysis) only when sufficient data are provided such that at least for an effect level the corresponding expected and observed mixture dose are reported, or can be estimated from the data provided by the article. It should be noted that a high-risk bias judgement does not qualify automatically for exclusion.