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About the OECD

The Organisation for Economic Co-operation and Development (OECD) is an intergovernmental organisation in which representatives of 38 countries in North and South America, Europe and the Asia and Pacific region, as well as the European Union, meet to co-ordinate and harmonise policies, discuss issues of mutual concern, and work together to respond to international problems. Most of the OECD's work is carried out by more than 200 specialised committees and working groups composed of member country delegates. Observers from several Partner countries and from interested international organisations attend many of the OECD's workshops and other meetings. Committees and working groups are served by the OECD Secretariat, located in Paris, France, which is organised into directorates and divisions.

The Environment, Health and Safety Division publishes free-of-charge documents in twelve different series: **Testing and Assessment**; **Good Laboratory Practice and Compliance Monitoring**; **Pesticides**; **Biocides**; **Risk Management**; **Harmonisation of Regulatory Oversight in Biotechnology**; **Safety of Novel Foods and Feeds; Chemical Accidents; Pollutant Release and Transfer Registers; Emission Scenario Documents; Safety of Manufactured Nanomaterials;** and **Adverse Outcome Pathways.** More information about the Environment, Health and Safety Programme and EHS publications is available on the OECD's World Wide Web site (https://www.oecd.org/en/topics/chemical-safety-and-biosafety.html).

This publication was developed in the IOMC context. The contents do not necessarily reflect the views or stated policies of individual IOMC Participating Organizations.

The Inter-Organisation Programme for the Sound Management of Chemicals (IOMC) was established in 1995 following recommendations made by the 1992 UN Conference on Environment and Development to strengthen co-operation and increase international co-ordination in the field of chemical safety. The Participating Organisations are FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank, Basel, Rotterdam and Stockholm Conventions and OECD. The purpose of the IOMC is to promote co-ordination of the policies and activities pursued by the Participating Organisations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

Foreword

OECD Member countries are increasingly interested in enhancing the use of omics technologies for supporting chemical risk assessment using chemical grouping and read-across approaches. Following a 2021 workshop, regulators noted the need for demonstrations of how omics could be standardised and applied to regulatory assessments. To meet this need, the OECD has developed the Chemical Grouping - Application Reporting Module (CG-ARM), which represents the first Application Reporting Module appended to Guidance Document No. 390, OECD Omics Reporting Framework (OORF): Guidance on reporting elements for the regulatory use of omics data from laboratory-based toxicology studies.

The CG-ARM provides a clear and structured framework for stakeholders to report the application of omics data to form groups of chemicals to identify candidate source analogues, to substantiate the similarity of chemicals for read-across, and/or to provide mechanistic information related to the endpoint predicted from similar substances. The reporting module, which is designed specifically for omics data, complements existing guidance on how to report grouping and read-across approaches. It is appended to OECD Guidance Document No. 418, Guidance on Grouping of Chemicals.

The application reporting module is structured around a five-step workflow for chemical grouping using omics data, accommodating a range of approaches, including bioactivity profile-based grouping and bioactivity signature-based grouping. It includes reporting of the experimental design, bioactivity similarity assessment and, where relevant, a plausible toxicological interpretation. Reporting uncertainties associated with the grouping hypothesis is also included. The CG-ARM supports both single-omics and multi-omics studies, providing sufficient flexibility to accommodate a variety of grouping approaches.

Ultimately, the CG-ARM is intended to increase the transparency of both the methods and results from a bioactivity similarity assessment and promote the reproducibility of omics-based chemical grouping approaches for regulatory toxicology applications. It also seeks to help broaden the adoption of omics technologies across chemical sectors and jurisdictions, benefiting all OECD Member countries and supporting implementation of new approach methods.

The CG-ARM was developed by an ad hoc drafting group, led by Mark R. Viant (University of Birmingham, UK), with Reza Farmahin and Anthony Reardon (Health Canada), Hennicke Kamp (BASF Metabolome Solutions GmbH), Aniko Kende (Syngenta Crop Protection), Julia M. Malinowska (European Commission, Joint Research Centre) and Grace Patlewicz (United States Environmental Protection Agency). It was supported by the Alternative Methods Team at the European Chemicals Agency. The document was reviewed by the OECD Expert Group on Omics in July-September 2025, the Working Party on Hazard Assessment (WPHA) in October-November 2025, and is published under the responsibility of the OECD Chemicals and Biotechnology Committee.

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List of Acronyms

ADME	Absorption, Distribution, Metabolism and Excretion
AOP	Adverse Outcome Pathway
ARF	Analogue Reporting Format
ARM	Application Reporting Module
CG-ARM	Chemical Grouping - Application Reporting Module
CRF	Category Reporting Format
DAPRM	Data Acquisition and Processing Reporting Module
DARM	Data Analysis Reporting Module
GD	Guidance Document
IATA	Integrated Approaches to Testing and Assessment
MoA	Mode of Action
NAM	New Approach Methodology
OORF	OECD Omics Reporting Framework
SOP	Standard Operating Procedure
UVCBs	Substances of Unknown or Variable Composition, Complex Reaction Products and Biological Materials

Glossary of Terms

Terms are ordered according to the flow of information presented in this document.

Features – genes, proteins and/or endogenous metabolites that can be annotated or unannotated, and which together form input data for a bioactivity similarity assessment.

Omics profile – comprises the set of all measured features or a subset of statistically pre-filtered features, i.e., this is a *data-driven profile that does not use any external toxicological knowledge*. These features may be annotated/identified molecules (genes, proteins and/or endogenous metabolites), unannotated features, or a combination of both.

Omics signature – comprises a pre-specified, reduced (i.e., targeted) set of measured features that are associated with one (or more) molecular pathway, mode of action (MoA), adverse outcome pathway (AOP), effect, or endpoint(s), i.e., this is a *knowledge-driven signature that does use external toxicological (and/or biological) knowledge*. These features are typically annotated/identified molecules (genes, proteins and/or endogenous metabolites), but may also include unannotated features.

Metadata – defined as data that describes and gives information about other data. Examples of metadata that are important for data analysis and interpretation include sample type (e.g. control or treatment group), sex, dose level, exposure duration, etc.

Bioactivity thresholding – the process of defining and applying a threshold magnitude of molecular responses above which substance treatment groups qualify as input data for chemical grouping. It is a discretionary step that serves to remove non- and low-responding treatment groups prior to calculating bioactivity similarity.

Bioactivity similarity – describes for example the similarity(ies) in omics feature abundances (for those features in either an omics profile or signature) between biological samples, where those feature abundances are measured in a defined test system following exposure to two or more test substances, often as part of a bridging study.

Effect anchor chemical – a chemical that causes a relatively well-defined and characteristic molecular effect, for example acting via a known MoA. The (dis)similarity of omics responses between an effect anchor chemical and a test chemical can potentially contribute towards a plausible toxicological interpretation. For the specific case that the induced effect is characteristic of a MoA, the effect anchor can be referred to as a MoA anchor chemical. It can also be referred to as a positive control chemical for a particular effect. Effect anchors can be “in-group” or “out-group”, dependent upon the effects they induce compared to the effects of the source and target substances.

Plausible toxicological interpretation – describes how the changes in omics feature abundances are associated with existing and well-established toxicological knowledge, for example from a MoA or AOP. The plausible toxicological interpretation may only be possible for a subset of features due to current lack of knowledge, for example in the identities of measurable omics features and their functional importance in molecular pathways.

Bridging study – Comparable studies on the source and target chemicals that allow a direct side-by-side comparison of the chemicals for a particular toxicological property, which could form the justification for predicting other toxicological effects of the target by reading across from the source (OECD, 2025).

1 Introduction to chemical grouping, omics data and the CG-ARM

a. Background

Read-across is frequently used in chemical risk assessment as a technique to fill data gaps for human health and environmental endpoints within analogue and category approaches (OECD, 2025). This involves using empirical data from one or more source chemicals to predict the same endpoint for the target chemical. Chemicals whose physicochemical, toxicological and ecotoxicological properties are similar, usually as a result of structural similarity, may be considered as a group or category of chemicals. Herein, data gap filling can be performed in several ways, including by read-across from one or more category members. Such read-across may be one-to-one, many-to-many, one-to-many or many-to-one. Typically, an analogue approach comprises a source analogue and target, whereas a category consists of three or more members. While source analogues/category members are often first identified on the basis of structural similarity, justifying their relevance for read-across relies on evaluating them with respect to other contexts of similarity such as physicochemical properties, chemical reactivity, similarity in ADME as well as similarity in toxicological profile. Each of these similarity contexts serve to build scientific confidence in the overall analogue/category approach.

Relevant biologically-driven evidence can also play a key role in demonstrating similarity with the source analogue or between category members. One type of biological evidence can be derived from omics technologies, which are a type of New Approach Methodology (NAM) that can comprehensively measure the profiles of expressed genes (transcriptomics), proteins (proteomics), and small molecule endogenous metabolites (metabolomics) within cells or tissues (Westmoreland *et al.*, 2022; Meier *et al.*, 2025; OECD, no date). These measurements reveal the bioactivity induced by chemical exposure, and an assessment of the similarity of bioactivity can serve as the basis for grouping chemicals using this type of biological evidence (Viant, Barnett, *et al.*, 2024), i.e., to identify candidate source analogues and/or substantiate similarity for read-across.

If a chemical group was initially defined based on structural similarity considerations, with the objective of reading across a defined endpoint, the omics data would serve as a secondary source of information to substantiate the hypothesis underpinning the group. Such data would address one of the uncertainty components described in GD 418 for the similarity rationale. For example, if a category was being developed on the basis of one of the six scenarios outlined within the ECHA Read-Across Assessment Framework (European Chemicals Agency, 2017), omics data could provide supporting evidence to address specific assessment elements. Alternatively, the omics data may serve as a primary source of data to identify candidate analogues to address one or more endpoint data gaps. Although this approach can be applied to substances with defined structures, it may be the most practical means of finding relevant candidate analogues (i.e. potential source substances) for organic substances of Unknown or Variable Composition, Complex Reaction Products and Biological Materials (UVCBs), for example.

Other documents on the topic of read-across, such as the guidance document from the European Food Safety Authority on the use of read-across in food and feed risk assessment (applicable to individual substances) (EFSA Scientific Committee *et al.*, 2025), also provide considerations for the integration of NAM-based data (including omics data) to support the read-across, where appropriate.

Different types of omics data can be used in the bioactivity similarity assessment, primarily 'omics profiles' and 'omics signatures' (see Glossary of terms), with the corresponding grouping approaches referred to as 'bioactivity profile-based grouping' and 'bioactivity signature-based grouping', respectively (Table 1; van Ravenzwaay et al., 2016; House et al., 2022; Viant, Amstalden, et al., 2024). Both profiles and signatures refer to the composition of the features (genes, proteins, and/or endogenous metabolites) that are being used to group the biological samples, with profiles not including any external toxicological knowledge and signatures including such knowledge.

Table 1. Description of the two principal omics data types and corresponding grouping approaches. See *Glossary of terms* for extended definitions. For both cases, the type of similarity being assessed is referred to as 'bioactivity similarity'.

Name of grouping approach	Type of omics data being grouped
Bioactivity profile-based grouping	Omics *profile*, comprising the set of all measured features or a subset of statistically pre-filtered features[1], i.e., this is a *data-driven* profile that does not use any external toxicological knowledge.
Bioactivity signature-based grouping	Omics *signature*, comprising a pre-specified, reduced (i.e., targeted) set of measured features that are associated with one (or more) molecular pathway, MoA, AOP or endpoint(s), i.e., this is a *knowledge-driven* signature that does use external toxicological knowledge.

[1] 'Statistically pre-filtered features' refers to features that have been assessed for significant changes between treated versus control groups, and only those that change significantly are retained in the omics profile.

b. Purpose and scope

The purpose of the Chemical Grouping - Application Reporting Module (CG-ARM) is to describe how to report the application of omics data to form a group of chemicals, i.e., for identifying candidate source analogues or substantiating similarity for read-across. This includes describing approaches for quantifying the similarity between test substances and, where possible, providing a plausible toxicological interpretation of the molecular data. As such, the CG-ARM is not intended to describe all the steps involved in forming analogue and categories to facilitate read-across, instead it complements existing guidance and reporting of read-across. Specifically, the CG-ARM forms part of two other OECD documents (Figure 1):

1. OECD Guidance Document (GD) *Guidance on Grouping of Chemicals*, Series on Testing & Assessment No. 418 (GD 418) (OECD, 2025). The CG-ARM forms Appendix 10.4 in this GD, and is interoperable with the existing Analogue Reporting Format (ARF) and Category Reporting Format (CRF);

2. *OECD Omics Reporting Framework (OORF): Guidance on reporting elements for the regulatory use of omics data from laboratory-based toxicology studies*, Series on Testing & Assessment No. 390 (OECD, 2023). The CG-ARM is the first Application Reporting Module (ARM) of the OORF, focused specifically on describing approaches for quantifying bioactivity similarity for grouping using omics data.

The CG-ARM is intended to describe a well-structured human-readable narrative for grouping chemicals using omics data, cross-referencing to other OORF reporting modules that contain technical descriptions of omics data acquisition, processing and data analysis, as illustrated in Figure 1. For further information on the modular structure of the OORF, the reader is referred to GD No. 390 (OECD, 2023).

It should be noted that the scope of the CG-ARM has been defined based upon current practices. It is recognised that the application of omics data to chemical grouping will evolve over time, such that version-controlled revisions of this reporting module are anticipated. Furthermore, the scope is focused on reporting the use of omics data in chemical grouping and associated read-across, not describing best practice. For example, while quantitative measures of similarity should be reported, this document does not prescribe the thresholds to determine whether two substances induce sufficiently similar bioactivity to be considered as belonging to the same group since this will depend on the decision context and regulatory purpose. Finally, the CG-ARM is intended to be sufficiently flexible to support different ways that omics data can be used within grouping approaches, and to allow the reporting of single- and multi-omics grouping studies.

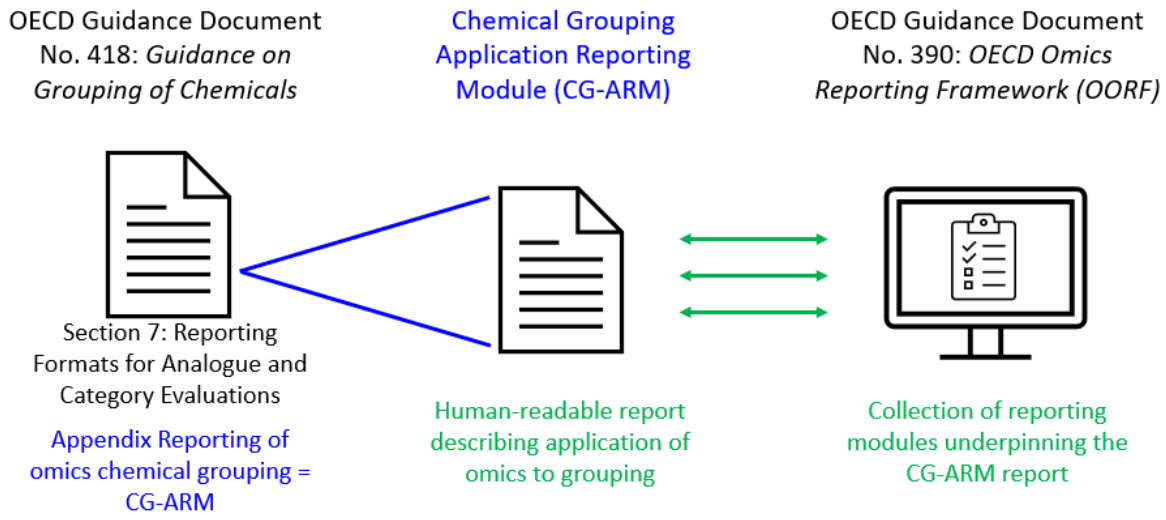

Figure 1. Relationship between OECD Guidance Document No. 418: Guidance on Grouping of Chemicals, the Chemical Grouping Application Reporting Module (CG-ARM), and OECD Guidance Document No. 390: OECD Omics Reporting Framework (OORF): Guidance on reporting elements for the regulatory use of omics data from laboratory-based toxicology studies.

c. Structure of reporting module

The development of the CG-ARM took into consideration the five-step workflow for chemical grouping using omics data (Figure 2). This includes providing a rationale for the experimental design and use of omics data for grouping chemicals; description of the omics data and input data for grouping; description

of the **bioactivity similarity** assessment; description of any **plausible toxicological interpretation** of the grouping (discretionary); and the analogue or category justification with uncertainties associated with the experimental design, data and results; see *Glossary of terms* for further information on these components of an omics-based grouping study.

The development of the CG-ARM also considered the structure of the OECD template for IATA Case Studies using read-across, which attempts to be compatible with national (or wider regional) reporting of analogue/category approaches to enable read-across. Additionally, the CG-ARM has been designed to use other reporting modules in the OORF, as indicated in Figures 1 and 2. In particular, it is highly recommended to report omics data acquisition and processing in Data Acquisition and Processing Reporting Modules (DAPRM), while statistical analyses of the omics data should be reported in Data Analysis Reporting Modules (DARM), and cross referenced to the reporting in the CG-ARM.

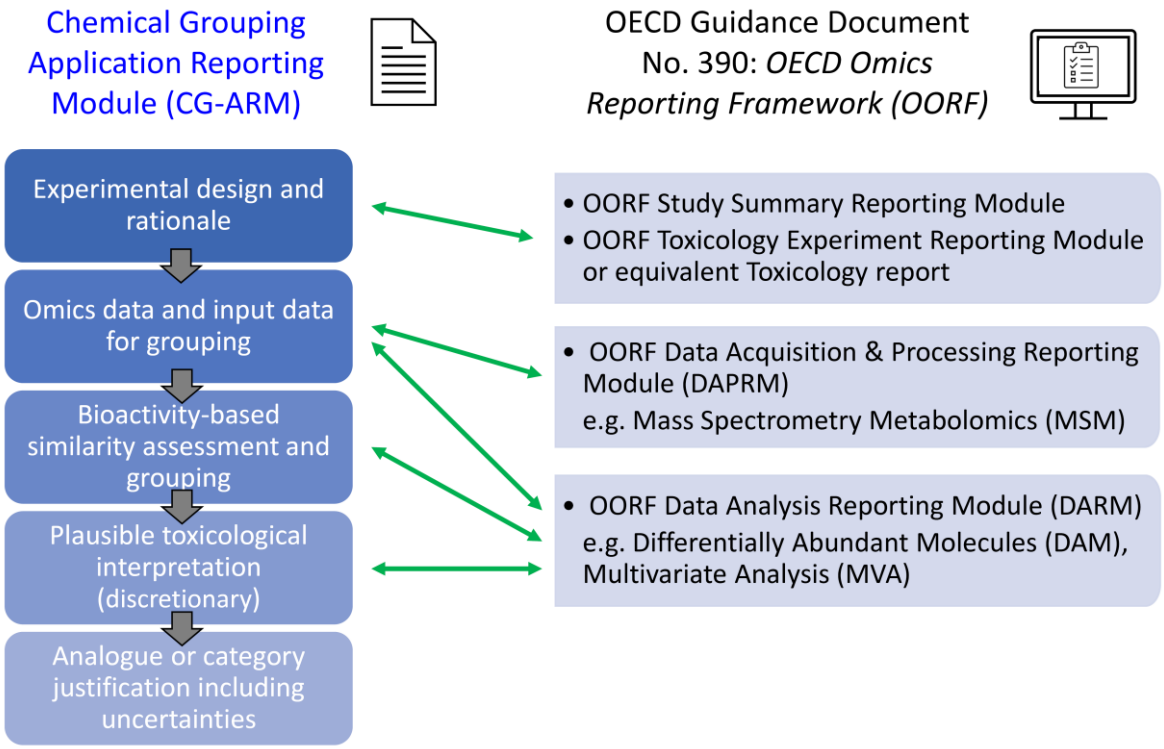

Figure 2. Chemical Grouping Application Reporting Module (CG-ARM) is designed to enable the reporting of a five-step workflow for utilising omics data towards forming an analogue or category justification. Step 1: design of the grouping study, including a rationale for selecting the biological test system and omics technology(ies), according to the purpose of the chemical grouping. Step 2: acquire, or derive from existing sources, the omics data and input data for grouping. Step 3: group the chemicals based on a statistical assessment of the bioactivity similarity of the omics responses to chemical exposure. Step 4 (discretionary, dependent on the intended purpose of the grouping study): provide a plausible toxicological interpretation of the molecular responses induced by the group of similar chemicals to increase confidence in that grouping. Step 5: summarise and integrate these findings into the analogue or category justification, documenting the uncertainties in the omics grouping study. The CG-ARM cross-references to other OORF

reporting modules that contain technical descriptions of, for example, omics data acquisition, processing and data analysis.

The CG-ARM reporting module is described in the following section, comprising of narrative text to explain the reporting requirements and a series of reporting fields (labelled REPORT). While based around the five-step grouping workflow, the actual structure of the CG-ARM has been designed to facilitate its use both by a data submitter and reviewer, and tested in a series of trials. It contains the following eight sections:

(1) Executive summary

(2) Background, objective and rationale for omics-based grouping study

(3) Omics data and existing toxicological knowledge used in the grouping

(4) Generation of input data for grouping

(5) Methods for bioactivity similarity assessment and plausible toxicological interpretation

(6) Results of bioactivity similarity assessment

(7) Plausible toxicological interpretation of the grouping

(8) Analogue or category justification including uncertainties in the grouping.

Please note, some reporting elements may not be relevant to every type of omics-based grouping study (denoted as 'if relevant' in the text below). These reporting elements are discretionary, and their reporting is deferred to those completing the CG-ARM. If a reporting element is omitted, please provide a short explanation as to why this is the case.

2 Description of the CG-ARM reporting module

1. EXECUTIVE SUMMARY

The Executive Summary should provide a concise yet thorough summary of the omics-based grouping study. The minimum information required is defined in the reporting field, below. As a guide, it is anticipated that the summary will be ca. 1-2 pages.

REPORT: 1.1 Summarise the grouping study with the following minimum information: background; objectives; approach taken including the biological test system, exposure design (i.e., treatment groups, sampling time points), omics technology and grouping approach(es) used; results of chemical grouping with associated uncertainties; conclusion; and a statement on data availability including the use of the OORF.

2. BACKGROUND, OBJECTIVE AND RATIONALE FOR OMICS-BASED GROUPING STUDY

Given the rationale for the overall grouping study, describe the background, objective and justify why this omics grouping study, including the choice of biological test system and omics assay(s), will enable the omics data to contribute towards strengthening an analogue or category justification. Cross-reference to the OORF's Study Summary Reporting Module(s) and the Toxicology Experiment Reporting Module(s) or to a relevant toxicology report(s). Multiple omics studies may underpin a single CG-ARM report.

REPORT: 2.1 Background of omics-based grouping study.

- Describe the background to the study.

REPORT: 2.2 Objective of omics-based grouping study.

- Describe the objective(s) of the study.

REPORT: 2.3 Rationale for biological test system and sample type.

- Describe and justify how the test system and sample type are relevant to the purpose of the grouping study, for example that they are capable of exhibiting changes at the molecular level that are (1) directly associated with the endpoint to be read across, or (2) associated with a MoA that is known to manifest in that endpoint.

REPORT: 2.4 Rationale for the design of the toxicology study.

- Describe and justify the experimental design, in particular dose/concentration selection, time point selection and number of biological replicates (particularly within the control group), indicating how

these are appropriate for a grouping study using omics data. Also, describe and justify the selection of any effect anchor chemicals that are used in the study.

REPORT: 2.5 Rationale for the approach used to acquire omics data.

- Describe and justify how the omics approach(es) applied is relevant to the purpose of the grouping study, for example it is capable of measuring (at least some of the) changes at the molecular level that are (1) directly associated with the relevant endpoint, or (2) associated with a MoA that is known to manifest in the endpoint.

REPORT: 2.6 Indicate whether the omics data and metadata have been reported according to (inter)national standards and are accessible to the relevant stakeholders for review.

- For example, reported using the OECD Omics Reporting Framework.

3. OMICS DATA AND EXISTING TOXICOLOGICAL KNOWLEDGE USED IN THE GROUPING

This section reports the data and knowledge that exists at the start of an omics-based grouping study, prior to any further data analyses. Specifically, this includes the omics data (and metadata) and existing toxicological knowledge that will be used for the bioactivity similarity assessment and (if relevant) plausible toxicological interpretation. Omics data may be derived from one or more sources, for example: newly generated omics data from a laboratory; re-using existing omics data, either from the same laboratory or a different laboratory; or obtained from an external library. The source(s) must be clearly documented, as described below.

Note that section 3 reports the underlying omics data, while section 4 describes the input data that is calculated from the omics data. Here, input data refers to the actual data used in the bioactivity similarity calculation and in any statistical analyses used to support a plausible toxicological interpretation.

Several types of omics data might be used for chemical grouping. Possible omics measurement strategies include: untargeted assays to measure the levels of gene expression (transcriptomics), proteins (proteomics) and/or metabolites (metabolomics); targeted assays that measure toxicologically relevant molecular signatures covering one or more pathway(s), MoA(s), AOP(s) or endpoint(s); or 'hybrid' assays that incorporate both targeted and untargeted measurement modalities.

Do not provide a detailed report of omics data acquisition and processing in this section, as those components of the study should be reported in a Data Acquisition and Processing Reporting Module (DAPRM) of the OORF. Instead, provide a summary description only, and refer to the relevant DAPRM modules (Figure 2).

REPORT: 3.1 Description of the omics data that were used either directly or indirectly, in full or in part, in the grouping study.

- For each omics dataset, name the data source (e.g., newly generated by a laboratory, existing data from the same or different laboratory, or from an external library, etc.), including the version number, DOI, or other forms of citation, as appropriate.
- For each dataset, include the type of omics assay(s) used, a summary of the exposure design (e.g. test substances, controls, sampling time points, number of replicates), and corresponding number and type of samples analysed.
- Report the omics data quality and how it was assessed.
- Where two or more datasets are being combined, indicate whether the datasets were acquired and processed using the same SOPs.

- When using multi-omics data, indicate how they will be combined (e.g., multiple data sets prepared from the same sample, or following a sequential integration where different omics layers are processed one after the other).
- Refer (where possible) to the relevant DAPRMs, including identifiers of the omics data matrix or matrices that have been described in the DAPRMs.

Existing toxicological knowledge may take many forms, for example in the form of an existing omics signature for a defined MoA or effect that is used for bioactivity signature-based grouping.

REPORT (if relevant): 3.2 Description of any existing toxicological knowledge (e.g., an omics signature) used in the bioactivity signature-based grouping or for the plausible toxicological interpretation of the grouping.

- Include the source(s) of this toxicological knowledge, including version number (if relevant), DOI, or other forms of citation, as appropriate.

4. GENERATION OF INPUT DATA FOR GROUPING

This section reports any processing steps to convert the omics data to the actual input data used in the bioactivity similarity calculation and to support the plausible toxicological interpretation of the chemical grouping.

The input data may take several forms, for example whole omics profiles comprising all measured features, or selectively reduced sets of features. Also, the input data may either derive from a single omics study or a multi-omics study. To illustrate this more clearly, several examples of input data for the bioactivity similarity assessment are listed here:

- **Whole omics profile**, comprising the set of all measured gene, protein and/or metabolites, or a combination of more than one data type, with their corresponding abundances measured in a series of treated and control biological samples.
- **Omics profile**, comprising a qualifying subset of statistically pre-filtered gene, protein and/or metabolite abundances that are differentially abundant between treated versus control biological samples, or a combination of more than one data type. For example, only features that respond significantly (p<0.05 or false discovery rate corrected q<0.05) to chemical exposure are included in the bioactivity similarity calculation.
- A qualifying subset of the omics features – termed an **omics signature** – comprising a pre-specified, reduced (i.e., targeted) set of measured genes, proteins and/or metabolites that are associated with one (or more) molecular pathway, MoA, AOP or endpoint(s). For example, ‘anchor metabolites’ might be selected, which are features with a known high toxicological relevance as their perturbations are essential to a specific MoA (e.g., increased plasma tyrosine and 4-hydroxyphenylpyruvic acid concentrations when 4-hydroxyphenylpyruvate dioxygenase inhibitors are administered (van Ravenzwaay *et al.*, 2007, 2014; Lewis and Botham, 2013).
- A qualifying subset of the omics data, specifically only those *treatment groups* passing criteria – termed the **bioactivity threshold** – that confirm a significant molecular response was measured in the group of biological samples in response to chemical exposure. For example, if the lowest exposure dose/concentration of a substance did not induce sufficient molecular responses to exceed the bioactivity threshold, that treatment group can be removed prior to calculating the bioactivity similarities between the remaining treatment groups.
- Statistical parameters derived from the analysis of the omics data, such as fold-changes or t-statistics derived from the differential abundance of molecules. The fold changes or t-statistics

could be derived from feature abundances for whole omics profiles, or for a qualifying subset of features (i.e., a signature).

Do not provide a detailed report of any statistical analysis applied to convert the omics data to input data in this section as those components of the study should be reported in the Data Analysis Reporting Modules (DARM). Instead, this section of the report should provide a summary description only, and refer to the relevant DARM modules (Figure 2).

REPORT: 4.1 Description of the input data used to calculate bioactivity similarities and to support the derivation of a plausible toxicological interpretation, including the methods used to generate the input data from the omics data, and the rationale for selecting this input data.

- Dependent upon what analyses are being reported, it may be appropriate to report this section as (i) input data for bioactivity profile-based grouping (type of input data, methods to generate, rationale for use), (ii) input data for bioactivity signature-based grouping (type of input data, methods to generate, rationale for use), and/or (iii) input data for further statistical analyses to support the derivation of a plausible toxicological interpretation (type of input data, methods to generate, rationale for use).
- Refer to relevant DARMs. Where possible, include identifiers of the input data matrix or matrices that have been described in the DARMs, and an overview of the input data structure (e.g., number of features, treatment groups).
- When describing the rationale for the selection of input data, explain, for example, why only a qualifying subset of the omics data is being used, and why statistical parameters derived from an analysis of the omics data are used.

5. METHODS FOR BIOACTIVITY SIMILARITY ASSESSMENT AND PLAUSIBLE TOXICOLOGICAL INTERPRETATION

This section reports the methods used to calculate the bioactivity similarity between test substances and, if relevant, the methods used to derive a plausible toxicological interpretation.

Several statistical approaches can be used to calculate bioactivity similarities, including pairwise analyses, which first calculate the bioactivity similarity (or distance) between each pair of substances, or network-based approaches that calculate distance metrics describing the similarities between all substances. The choice of distance measure will depend on the nature of the input data (i.e., category, binary, continuous), and examples might include Jaccard distance, Rogers-Tanimoto, Hamming distance, etc. If many omics responses are being compared (e.g., responses to multiple test substances), then a pairwise distance square matrix can be constructed and clustering can be applied to reveal the pattern of similarities of the responses to the test substances. Decision criteria can be applied to partition different responses into separate groups or categories.

Do not provide a detailed report of the statistical approaches applied to the omics data here as that should be reported in a DARM. Instead, provide a summary of the methods and refer to the relevant DARM modules.

REPORT: 5.1 Description of the methods to calculate the bioactivity similarity between omics responses, and to cluster and visualise these similarities if relevant.

- Include the software used, any important parameters (if relevant), and refer to the relevant DARM(s).

REPORT: 5.2 Description of the approach to set decision criteria for group membership, and the threshold(s) selected.

- If relevant, include the software used, any important parameters, and refer to the relevant DARM(s).

Various approaches may be used to derive a plausible toxicological interpretation of the chemical grouping. For example, following the derivation of group membership based upon an assessment of bioactivity similarities, supervised statistical analyses might be applied to discover which genes, proteins and/or metabolites are perturbed by exposure to test chemicals within one specific chemical group. Existing toxicological knowledge, such as from the AOP-Wiki, may also be used to facilitate the interpretation of the molecular responses. Pathway enrichment analyses may also be conducted, again focused on molecular perturbations observed within a specific group.

Furthermore, “in-group” and “out-group” **effect anchor chemicals** may also be used to increase confidence in a plausible toxicological interpretation (described below and in Figure 3). For example, in bioactivity profile-based grouping, if the source and target substances exhibit high bioactivity similarity with an in-group effect anchor, then the source and target can be hypothesised to exhibit the same toxicological effect as that anchor. Conversely, if available, an out-group anchor that does not cluster with the source or target can help to rule out off-target effects, and additionally can serve as a confirmation point for the grouping approach. For the case of bioactivity signature-based grouping, where the signature is known to describe a particular MoA, the high bioactivity similarity between the source, target and in-group effect anchor can directly provide a plausible toxicological interpretation (i.e., acting via that MoA).

REPORT (if relevant): 5.3 Description of the approach for deriving a plausible toxicological interpretation.

- Describe the overall strategy and methods used for the plausible toxicological interpretation, including whether in-group or out-group effect anchor chemicals have been used.
- If relevant, include the software used, any important parameters, and refer to the relevant DARM(s).

6. RESULTS OF BIOACTIVITY SIMILARITY ASSESSMENT

This section reports the results of the bioactivity similarity assessment between test substances and is used predominantly to define whether test substances form groups based upon the omics responses to chemical exposure. The reporting should include comparing the results to the pre-defined decision criteria used to define a group.

Do not provide a detailed report of the results of the statistical analysis applied to calculate the bioactivity similarity in this section, that information should be reported in the corresponding DARM(s) of the OORF.

While the formation of a robust chemical category for reading across a discernible toxic effect (e.g., of an apical endpoint) requires evidence of high bioactivity similarity, in some situations there is a need to provide evidence that two substances have *dissimilar* MoAs and produce distinct omics responses (Langsch *et al.*, 2018). The same methods can be applied for both cases, as bioactivity dissimilarity is the conceptual inverse of bioactivity similarity. Demonstrating dissimilar MoAs using omics data is important when attempting to read across low or no toxicity for a particular endpoint, where a test substance should be shown to *not* act via some MoAs (that are known to manifest in a particular apical endpoint) but instead act via different MoAs. Demonstrating either similarity or dissimilarity can be conducted by comparing the omics responses for the test substances to the omics responses for ‘effect anchor chemicals’ (sometimes referred to as ‘MoA anchor chemicals’). Figure 3 provides a hypothetical grouping to further explain this concept, showing how the optional inclusion of four effect anchor chemicals can be used to better define the groups. Such an observation would provide supporting evidence towards proving the absence of an apical endpoint in a target substance.

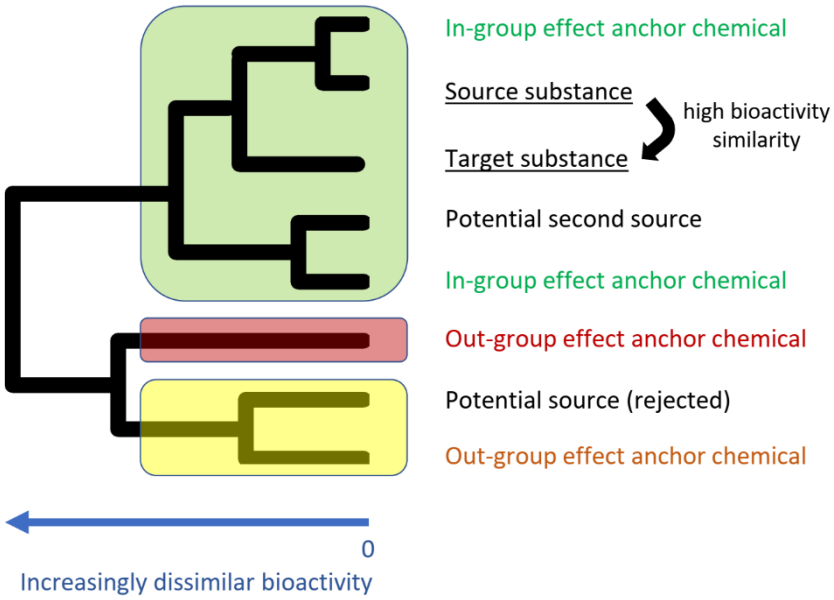

Figure 3. Hypothetical grouping visualised using a dendrogram, to illustrate the concept of using 'effect anchor chemicals' to demonstrate the bioactivity similarity or dissimilarity of source and target chemicals relative to several established MoAs. These results depict an omics grouping study with 8 chemicals, comprising one target, three potential source substances, two "in-group" effect anchor chemicals that were included as it was hypothesised that the source and target chemicals act via this MoA (or effect), and two "out-group" effect anchor chemicals that were hypothesised to have different MoAs (or effects) to the source and target chemicals. Based on the dissimilarity of the omics responses, the clustering of the out-group effect anchors (red and yellow boxes) away from the target provides supporting evidence that the target does *not* act via those MoAs. Furthermore, the relatively high bioactivity similarity depicted by the green box provides supporting evidence for the target and selected source substances acting via the MoA of the "in-group" anchor chemicals. It is important to note that the inclusion of effect anchor chemicals in a grouping study is optional.

REPORT: 6.1 Description of results from the bioactivity similarity assessment.

- Describe the results as appropriate for the methods listed in REPORT 5.1 and decision criteria in REPORT 5.2. For example, report dendrograms if applying hierarchical cluster analysis, showing the analogue or category members, evidenced against the pre-defined decision criteria for group membership.
- Dependent upon what analyses have been conducted, it may be appropriate to report this section as (i) results for bioactivity profile-based grouping, and (ii) results for bioactivity signature-based grouping.
- Provide a supporting narrative for the results of the bioactivity similarity assessment and refer to the relevant DARM(s) for further details.

7. PLAUSIBLE TOXICOLOGICAL INTERPRETATION OF THE GROUPING

This section reports (if conducted) the plausible toxicological interpretation of the molecular perturbations that are associated with exposure to a defined group of chemicals, i.e., it serves to describe and justify the molecular basis for the analogue or category approaches derived from the bioactivity-based grouping.

Refer to section 5 for an introduction to various approaches that may be used to derive a plausible toxicological interpretation of the chemical grouping. For example, the interpretation may be based on a high similarity of the test substance omics bioactivity to one or more effect anchor chemicals. Or the interpretation may be based on an over-representation or enrichment analysis of the molecular responses to chemical exposure.

REPORT (if relevant): 7.1 Plausible toxicological interpretation of one or more groups of chemicals that have been shown to exhibit (dis)similar bioactivities.

- Provide a supporting narrative for the results, which may be based on how in-group or out-group effect anchor chemicals have been used to derive a plausible toxicological interpretation, or how an over-representation or enrichment analysis has supported the interpretation.

8. ANALOGUE OR CATEGORY JUSTIFICATION INCLUDING UNCERTAINTIES IN THE GROUPING

This section reports the uncertainties in the omics data, bioactivity similarity and plausible toxicological interpretation, and the perceived impact (low, moderate or high) associated with each of these uncertainties on the analogue or category justification. It also reports the analogue or category justification from the omics-based grouping study.

The uncertainties described below have been developed according to the following scope:

- These uncertainties arise specifically from the use of omics data; see OECD GD 418 for uncertainties in the grouping justification associated with other types of data.
- Some uncertainties relate to the methodological quality and the omics data quality, in particular the reliability of the data used to assess the bioactivity similarity.
- Other types of uncertainties relate to the methodological rationales (including the relevance of the omics data to the endpoint in question) and the plausible toxicological interpretation of the omics data (including the toxicological knowledge used in that interpretation).

The uncertainties are structured according to the multi-step grouping workflow (Figure 2), considering experimental design (including generation or re-use of omics data), reliability of omics data, the statistical assessment of bioactivity similarity and, discretionarily, the plausible toxicological interpretation of the molecular responses. Note that different regulatory jurisdictions may have differing requirements for the inclusion of a plausible toxicological interpretation. For the case of including such an interpretation, the perceived impacts of these uncertainties on the grouping justification may be described as:

- Low uncertainty: Compelling evidence that the substances within a group induce similar bioactivities, e.g., high similarity metrics from relevant experimental omics data, supported by a plausible toxicological interpretation.
- Moderate uncertainty: Partial evidence that the substances induce similar bioactivities, e.g., moderate similarity metrics from omics data, supported by a plausible toxicological interpretation.
- High uncertainty: Only limited evidence that the substances induce similar bioactivities, e.g., moderate similarity metrics from omics data, but lacking a plausible toxicological interpretation.

For the case where no toxicological interpretation is required, the perceived impacts of uncertainties on the grouping justification may be described as low, moderate or high depending on the value(s) of the bioactivity similarity metrics derived from the omics data, with low uncertainty requiring a high similarity score. It is for those writing the CG-ARM report to provide the rationale for their selected uncertainty level.

Considering this uncertainty framework, applications of omics grouping studies become apparent. For example, one possible scenario is that grouping/read-across has been attempted using conventional *in vivo* toxicological data, and a grouping justification of moderate uncertainty has been developed. Subsequently, a bridging study using omics profiles could be conducted to attempt to strengthen the hypothesis that the overall bioactivity similarity is high between test substances (i.e., with low uncertainty), with the aim to lower the overall uncertainty in the grouping justification from moderate to low. A second scenario comprises a bridging study that uses omics signatures to attempt to strengthen evidence of similarity in the MoA or AOP for a specific endpoint that is being read-across.

8.1 Uncertainties associated with the relevance of the test system, experimental design, methodologies (including omics approaches applied), and omics data used in the grouping study

REPORT: 8.1.1 Whether the biological test system and sample type from which the omics data were generated are relevant to the purpose of the grouping study, e.g., relevant to the endpoint being read across.

- This uncertainty relates to the rationale already described in REPORT 2.3. Do not rewrite the rationale for the test system and samples type, instead state and explain the level of uncertainty.
- The uncertainty in the relevance could be lowered if the biological test system is well established (e.g., already part of a relevant OECD Test Guideline) or well supported by relevant scientific literature.

REPORT: 8.1.2 Whether other components of the experimental design, including dose/concentration selection, time point selection, number of biological replicates (particularly within the control group), and the selection of any effect anchor chemicals are relevant to the purpose of the grouping study.

- This uncertainty relates to the rationale already described in REPORT 2.4. Do not rewrite the rationale for the experimental design, instead state and explain the level of uncertainty.
- The uncertainty in the relevance could be lowered if dose levels/concentrations are either high enough to elicit an effect in the biological system or have reached levels that cannot be increased any further (e.g., limit dose in vivo; maximal solubility in vitro; kinetically modelled limit dose in vitro).
- Additionally, the uncertainty could be decreased if the sampling time points are chosen such that the test system is capable of producing the intended response at those time points.

REPORT: 8.1.3 Whether the omics approach(es) and resulting molecular data are relevant to the purpose of the grouping study.

- This uncertainty relates to the rationale already described in REPORT 2.5. Do not rewrite the rationale for the omics approach and data type, instead state and explain the level of uncertainty.
- The uncertainty in the relevance could be lowered if there is sufficient molecular coverage (with confident gene/protein/metabolite annotations) of the relevant molecular pathway(s), MoA(s), AOP(s) or endpoint(s).

Note that expert judgement is required for each of these assessments.

8.2 Uncertainties in the reliability of the omics data used in the grouping study

REPORT: 8.2.1 Whether the omics data quality (e.g., technical reproducibility) has been assessed according to community standards and whether the data have passed quality control.

- This applies to new omics data generated for a bridging study as well as the re-use of existing omics data. Provide a rationale for the level of uncertainty assigned.
- Uncertainty in the reliability of the omics data could be lowered by following community standards and providing evidence that the technical reproducibility of the data is high (e.g., through the use of intrastudy quality control samples).

REPORT (if relevant): 8.2.2 For the case of combining multiple omics datasets, whether those datasets were generated consistently.

- Specifically, whether data were generated in the same laboratory, using the same or similar methods, within one bridging study, or whether data were obtained from a range of different sources that may introduce uncertainty into the similarity assessments. This may consider whether the same omics approach(es) was used (e.g., transcriptomics, proteomics, metabolomics); the same technology(ies) was used for a given omics approach (e.g., RNA-seq); the same type of measurement was employed (e.g., targeted, untargeted or hybrid); and the same data format was investigated (e.g., profile or signature).
- The uncertainty could be lowered by providing evidence of the consistency of the datasets, for example by referring to OORFs that demonstrate a consistency of methods.
- Uncertainty in the reliability of the omics data could also be lowered by documenting evidence of interstudy (i.e. studies conducted within one laboratory) or interlaboratory quality control metrics (e.g., applied post omics data processing and prior to the calculation of bioactivity similarity).
- While a consideration of historical ranges of molecular data for controls may also help to reduce uncertainty in the reliability of the omics data, it is not currently possible for the majority of grouping studies and therefore is not considered here.

Provide a rationale for the level of uncertainty that you assign to each of these reporting elements. Note that while some expert judgement is required for these assessments, the rationales should as far as possible be based on quantitative and objective statements.

8.3 Uncertainties in the bioactivity similarity assessment of the omics data

REPORT: 8.3.1 Confidence that a discernible molecular response occurred following chemical exposure.

- This could be determined by considering what proportion of the features within the bioactivity profile or signature exhibited statistically significant changes between the control and treated samples.
- Uncertainty in the bioactivity similarity could be lowered by providing statistical evidence that significant molecular perturbations occurred to the profile or signature.

REPORT: 8.3.2 Confidence in the grouping pattern derived from the bioactivity profile- or signature-based similarity assessment.

- This could be determined by considering the bioactivity similarity score relative to a justifiable threshold for ‘how-similar-is-similar-enough’. Currently, no (inter)national standards exist for this threshold, leaving scope for the threshold to be defined by the user (Viant, Barnett, *et al.*, 2024).
- Additionally, statistical evidence for a robust grouping pattern can be provided (Viant, Amstalden, *et al.*, 2024).
- Uncertainty in the bioactivity similarity could be lowered by providing objective evidence of a high, statistically significant, similarity score.

Provide a rationale for the level of uncertainty that you assign to each reporting element related to bioactivity similarity assessment. While some expert judgement is required for these assessments, the rationales should as far as possible be based on quantitative and objective statements.

8.4 Uncertainties in the plausible toxicological interpretation

REPORT (if relevant): 8.4.1 Whether the level of confidence in identifying the genes/proteins/metabolites in the bioactivity profile (or signature) used in the plausible toxicological interpretation considers current community standards.

- Uncertainty in the interpretation could be lowered by providing objective evidence for the reliable identification of the molecular features (i.e., genes, proteins or metabolites).

REPORT (if relevant): 8.4.2 Confidence in the association of the genes/proteins/metabolites (i.e., that comprise an omics signature) to either the endpoint being read across or to a MoA that manifests in that endpoint, where those associations are used to provide the plausible toxicological interpretation.

- For the case of signature-based grouping, uncertainty in the interpretation could be lowered by referencing the information sources or knowledgebases that previously reported the association of molecular features to the effect.

REPORT (if relevant): 8.4.3 Whether the plausible toxicological interpretation is based on an appropriate level of similarity of the test substances' omics responses to each other or to that of an appropriate effect anchor chemical(s).

- Uncertainty in the interpretation could be lowered by demonstrating a high bioactivity similarity between the source, target and/or an in-group anchor chemical(s) of known effect, hence providing the toxicological interpretation.
- Evidence of low bioactivity similarity between the test substances (source and target) and out-group effect anchor chemical(s) could also lower the uncertainty in the plausible toxicological interpretation, specifically by ruling out the plausibility that the source and target induce the same toxicological effect(s) as the out-group anchor(s).

REPORT (if relevant): 8.4.4 If the plausible toxicological interpretation is based on the use of approaches such as over-representation or enrichment analysis, whether the enriched gene/protein/metabolite sets are known to be associated with either the endpoint being read across or to a MoA that manifests in that endpoint.

- Uncertainty in the interpretation could be lowered by demonstrating that a relatively large proportion of the enriched molecular changes can be attributed to the toxicological interpretation, which would suggest that the interpretation covers the primary effect of the chemical.

Provide a rationale for the level of uncertainty that you assign to each of the reporting elements related to the plausible toxicological interpretation. Note that while some expert judgement is required for these assessments, the rationales should as far as possible be based on quantitative and objective statements.

8.5 Summary of uncertainties

REPORT: 8.5 Provide a summary table of the uncertainties using the template below.

Uncertainty class	Reporting element	Level of uncertainty
Uncertainties associated with the relevance of the methodologies and	Whether the biological test system and sample type from which the omics data were generated are relevant to the purpose of the grouping study	Low, Moderate or High
	Whether other components of the experimental design, including dose/concentration selection, time point selection and number of biological	

omics data used in the grouping study	replicates (particularly within the control group), are relevant to the purpose of the grouping study	
	Whether the omics approach(es) and resulting molecular data are relevant to the purpose of the grouping study	
Uncertainties in the reliability of the omics data used in the grouping study	Whether the omics data quality (e.g., technical reproducibility) has been assessed according to community standards and whether the data have passed quality control	
	For the case of combining multiple omics datasets, whether those datasets were generated consistently (if relevant)	
Uncertainties in the bioactivity similarity assessment of the omics data	Confidence that a discernible molecular response occurred following chemical exposure	
	Confidence in the grouping pattern derived from the bioactivity profile- or signature-based similarity assessment	
Uncertainties in the plausible toxicological interpretation (if relevant)	Whether the level of confidence in identifying the genes/proteins/metabolites in the bioactivity profile (or signature) used in the plausible toxicological interpretation considers current community standards	
	Confidence in the association of the genes/proteins/metabolites to either the endpoint being read across or to a MoA that manifests in that endpoint, where those associations are used to provide the plausible toxicological interpretation	
	Whether the plausible toxicological interpretation is based on an appropriate level of similarity of the test substances' omics responses to each other or to that of an appropriate effect anchor chemical(s)	
	If the plausible toxicological interpretation is based on the use of approaches such as over-representation or enrichment analysis, whether the enriched gene/protein/metabolite sets are known to be associated with either the endpoint being read across or to a MoA that manifests in that endpoint	

8.6 Summary of analogue or category justification and associated overall uncertainty from the omics-based grouping study

REPORT: 8.6 Provide the grouping justification derived from the omics data together with an overall estimate of uncertainty in this result.

3 References

EFSA Scientific Committee *et al.* (2025) "Guidance on the use of read-across for chemical safety assessment in food and feed," *EFSA Journal*, 23(7), p. e9586. Available at: https://doi.org/10.2903/j.efsa.2025.9586.

European Chemicals Agency (2017) *Read-Across Assessment Framework (RAAF)*. (ECHA-17-R-01-EN). Available at: https://echa.europa.eu/documents/10162/17221/raaf_en.pdf/614e5d61-891d-4154-8a47-87efebd1851a.

House, J.S. *et al.* (2022) "Grouping of UVCB substances with dose-response transcriptomics data from human cell-based assays," *ALTEX - Alternatives to animal experimentation*, 39(3), pp. 388–404. Available at: https://doi.org/10.14573/altex.2107051.

Langsch, A. *et al.* (2018) "Hexamoll® DINCH: Lack of in vivo evidence for obesogenic properties," *Toxicology Letters*, 288, pp. 99–110. Available at: https://doi.org/10.1016/j.toxlet.2018.02.008.

Lewis, R.W. and Botham, J.W. (2013) "A review of the mode of toxicity and relevance to humans of the triketone herbicide 2-(4-methylsulfonyl-2-nitrobenzoyl)-1,3-cyclohexanedione," *Critical Reviews in Toxicology*, 43(3), pp. 185–199. Available at: https://doi.org/10.3109/10408444.2013.764279.

Meier, M.J. *et al.* (2025) "Progress in toxicogenomics to protect human health.," *Nature reviews. Genetics*, 26(2), pp. 105–122. Available at: https://doi.org/10.1038/s41576-024-00767-1.

OECD (2025) *Guidance on Grouping of Chemicals, Third Edition, OECD Series on Testing and Assessment*. Paris: OECD Publishing (No. 418). Available at: https://one.oecd.org/document/ENV/CBC/MONO(2025)19/en/pdf

OECD (2023) *OECD Omics Reporting Framework (OORF): Guidance on reporting elements for the regulatory use of omics data from laboratory-based toxicology studies*. Paris: OECD Publishing (OECD Series on Testing and Assessment, No. 390). Available at: https://doi.org/10.1787/6bb2e6ce-en.

OECD (no date) *Omics technologies in chemical testing*. Available at: https://www.oecd.org/en/topics/sub-issues/testing-of-chemicals/omics-technologies-chemical-testing.html (Accessed: July 3, 2025).

van Ravenzwaay, B. *et al.* (2007) "The use of metabolomics for the discovery of new biomarkers of effect," *Toxicology Letters*, 172(1), pp. 21–28. Available at: https://doi.org/10.1016/j.toxlet.2007.05.021.

van Ravenzwaay, B. *et al.* (2014) "The sensitivity of metabolomics versus classical regulatory toxicology from a NOAEL perspective," *Toxicology Letters*, 227(1), pp. 20–28. Available at: https://doi.org/10.1016/j.toxlet.2014.03.004.

van Ravenzwaay, B. *et al.* (2016) "Metabolomics as read-across tool: A case study with phenoxy herbicides," *Regulatory Toxicology and Pharmacology*, 81, pp. 288–304. Available at: https://doi.org/10.1016/j.yrtph.2016.09.013.

Viant, M.R., Amstalden, E., *et al.* (2024) "Demonstrating the reliability of in vivo metabolomics based chemical grouping: towards best practice," *Archives of Toxicology*, 98(4), pp. 1111–1123. Available at: https://doi.org/10.1007/s00204-024-03680-y.

Viant, M.R., Barnett, R.E., *et al.* (2024) “Utilizing Omics Data for Chemical Grouping,” *Environmental Toxicology and Chemistry*, 43(10), pp. 2094–2104. Available at: https://doi.org/10.1002/etc.5959.

Westmoreland, C. *et al.* (2022) “Use of New Approach Methodologies (NAMs) in regulatory decisions for chemical safety: Report from an EPAA Deep Dive Workshop,” *Regulatory Toxicology and Pharmacology*, 135, p. 105261. Available at: https://doi.org/10.1016/j.yrtph.2022.105261.