

Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed

Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed

Introduction

In this guide

[In this guide](#)

1. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Introduction](#)
2. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Background](#)
3. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Stepwise read-across guidance](#)
4. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Applicability domain of read-across](#)
5. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Conclusions](#)
6. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Questions for the Committee](#)
7. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Abbreviations](#)
8. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - References](#)

This is a paper for discussion. It does not reflect the views of the Committee and should not be cited.

Introduction

1. The European Food Safety Authority (EFSA) Scientific Committee (SC) have recently published a [Scientific Opinion](#) on the guidance on the use of read-across for chemical safety assessment in food and feed (EFSA SC, 2025). The document briefly reviews existing frameworks on read-across from organisations such as the European Chemicals Agency (ECHA) and the Organisation for Economic Cooperation and Development (OECD). The guidance goes on to describe a structured workflow to standardise and justify the read-across approach as a non-animal testing method for filling data gaps in chemical safety assessments, along with a discussion on the applicability domain and characterisation of the boundaries for read-across. The opinion also includes a series of appendices on read-across processes (Appendix A), information on available *in vitro* methods for toxicological characterisation of chemical substances (Appendix B), an uncertainty assessment template (Appendix C), case study examples (Appendix D) and a glossary of relevant terms and definitions (Appendix E).

2. This paper provides a brief overview of the EFSA Scientific Opinion. Its purpose is to support discussion around the guidance developed by EFSA. Members are invited to review the Scientific Opinion and share any comments or feedback they may have, with a view to determining whether they would be content to use the guidance.

Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed

Background

In this guide

[In this guide](#)

1. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Introduction](#)

2. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Background](#)
3. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Stepwise read-across guidance](#)
4. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Applicability domain of read-across](#)
5. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Conclusions](#)
6. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Questions for the Committee](#)
7. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Abbreviations](#)
8. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - References](#)

This is a paper for discussion. It does not reflect the views of the Committee and should not be cited.

3. Read-across is a method used in chemical risk assessment for screening, classification, prioritisation and hazard assessment of data-poor target substances based on toxicological data from one or more data-rich source substances that are structurally and mechanistically similar. It is one of the most common alternatives to animal testing.

4. The read-across prediction can be applied through two ways of chemical groupings, known as the analogue and category approaches. An analogue approach compares the properties of a target substance with a limited number of closely related source substances, whereas a category approach is based on the premise that structural similarity among several source substances can predict the target substance's properties.

5. Read-across involves a number of steps (i.e. problem formulation, data gap analysis, source substance identification and evaluation, data gap filling and uncertainty assessment), each of which may carry a certain level of uncertainty. Therefore, it needs to be carried out in as transparent, standardised and unbiased a manner as possible to make the overall conclusions scientifically

justified and reliable.

6. A number of read-across frameworks have been proposed, such as the OECD's Guidance on Grouping of Chemicals (OECD, 2014), and ECHA's Read-Across Assessment Framework (ECHA, 2017). Moreover, EFSA has previously considered the use of read-across in specific risk assessments, including those for smoke flavourings, feed additives, and pesticide active substances, and has drawn on related guidance documents that refer to its application (EFSA FAF Panel, 2021; EFSA SC, 2019 and ECHA/EFSA, 2023). However, these documents mention read-across only as a supporting line of evidence, without offering detailed guidance on its implementation. Therefore, EFSA argues that a generic and flexible framework, together with a standardised workflow that provide a scientific basis for the use of read-across for applicants and risk assessors is needed.

7. The present EFSA guidance outlines a stepwise approach for applying read-across to fill data gaps in the chemical safety assessments of individual substances in food and feed. The guidance also explains how to integrate different types of New Approach Methodologies (NAMs) data at relevant steps to support the read-across. In addition, it provides guidance on performing a thorough analysis of the uncertainties pertaining to each step of the read-across and assessing the overall uncertainty, along with a discussion on the applicability domain of read-across.

Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed

Stepwise read-across guidance

In this guide

[In this guide](#)

1. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Introduction](#)
2. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Background](#)
3. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Stepwise read-across guidance](#)

4. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Applicability domain of read-across](#)
5. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Conclusions](#)
6. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Questions for the Committee](#)
7. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Abbreviations](#)
8. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - References](#)

This is a paper for discussion. It does not reflect the views of the Committee and should not be cited.

8. Figure 2 in EFSA's opinion illustrates the read-across workflow, while Table 2 summarises each step.
9. EFSA recommends organising the data collected for both the target and the source substances in a matrix. This data matrix should be structured in a tabular format and information should be arranged in a suitable order to facilitate the integration of the supporting evidence into the read-across process (examples are given in Appendix A).

Step 1: Problem formulation

10. A read-across assessment generally begins when the target substance lacks data—or has unreliable data—for the endpoint of interest. According to EFSA's guidance, the problem formulation step sets the purpose and expectations of the assessment and outlines the available approaches to achieve the objective. These considerations must be framed within the relevant regulatory context and the specific endpoints being addressed.
11. The problem formulation also involves defining the level of uncertainty that can be tolerated for the read-across to be considered acceptable, in light of its contribution to the overall weight of evidence (WoE). It includes identifying data gaps for the endpoint in question and evaluating whether there is sufficient justification for the read-across. This step will also inform potential

future strategies to reduce uncertainty (see *Step 6: uncertainty assessment*).

Step 2: Target substance characterisation

12. EFSA's opinion indicates that this step should unambiguously identify the target substance, as well as consider the hazard information and the data gaps that need to be addressed. The characterisation of the target substance forms the basis for the read-across hypothesis and informs the selection of an initial set of source substances.

13. At this stage, all available information should be collected, including physicochemical properties, metabolic transformation, toxicokinetic and toxicodynamic aspects, as well as *in vivo*, *in vitro* and *in silico* predictions, and any structural alerts for the target substance. While EFSA does not prescribe specific requirements or limitations for these data, the guidance emphasises that the information should be aligned with the needs identified during problem formulation.

14. EFSA also recommends consulting multiple data sources and, where appropriate, gather evidence through a systematic review. This process should adhere to general principles for the adequacy of data.

Step 3: Source substance identification

15. EFSA refers to this step as the process of searching for candidate source substances that are similar to the target substance. The overarching similarity rationale should be stated and justified within the read-across and will dictate how the search for a source substance will be conducted.

16. Structural and chemical similarity provides the starting point and is at the basis of all the other phenomena. It can be measured in various ways, offering different numerical results. However, the guidance states that additional relevant data must also be carefully considered, such as:

- Physicochemical characteristics, e.g. structural alerts, stability and chemical reactivity or conformation in space that might impact active-site binding.
- Endpoint under consideration and the mechanism of action (MoA) of the target substance, if known.
- Toxicokinetic profile.
- Metabolic profile, e.g. generation of common metabolites between target and source substance or when the target substance is a metabolite of the

source substance, and thus, similar biological properties may be expected.

- Breakdown products not associated with metabolism, e.g. generation of common breakdown products or when the source substance is a breakdown product of the target substance. The latter assumes that the toxicity data on the breakdown product would be expected to be representative of the toxicity expected from the parent substance.
- Manufacturing process.

17. The identification of a source substance can follow a supervised and or an unsupervised search method.

18. In a supervised approach, similar source substances with the same MoA as the target substance are filtered. EFSA's guidance recommends proposing a conceptual scheme that outlines the hierarchical sequence of events leading to the observed effect in the target substance. This scheme should then be compared to determine whether the same sequence applies to the source substance.

19. In the absence of information on the MoA underlying the adverse effect, an unsupervised approach should be applied. This involves using all similarity metrics described in paragraph 16. However, EFSA notes that this method carries greater uncertainty regarding the relevance of the specific features used to establish similarity. Therefore, multiple similarity metrics should be applied to strengthen the justification. The unsupervised approach may also be employed to predict non-specific toxicity or the absence of toxicity, though it typically requires extensive supporting evidence.

Step 4: Source substance evaluation

20. EFSA notes that Step 4 is the formal process to identify and justify those analogues that are most similar to the target substance in terms of the metrics described in paragraph 16. Data and other information relevant to the endpoint being read across should be prioritised.

21. This step can be performed manually by an expert or by using an *in silico* system (examples can be found in Appendix A, Table A.1). Expert evaluation should consider the reliability and relevance of the data associated with the selected source substances and whether the data were obtained by systematic techniques. *In silico* and *in vitro* methods can also be used in this step to generate new supporting information, confirm the suitability of selected source substances, further characterise potency trends across analogues, or to support the case for

excluding certain source substances.

22. Differences between the target and the source substances could result in changing the read-across hypothesis based on the assembled data. Thus, Step 4 might require several iterations, and/or refinement of the read-across strategy.

Step 5: Data gap filling

23. EFSA's guidance recommends implementing a strategy for filling data gaps in the data matrix to support read-across and enable prediction of the target substance's endpoint(s) of interest.

24. Different strategies can be applied, either data-driven (e.g. similarity weighted averages, closest neighbour based on similarity) or expert-driven, although EFSA considers that the preferable option is a data-driven approach with the least contribution of expert judgement, since the latter could introduce additional uncertainty factors.

25. Finalising the data matrix and deciding on a data gap filling strategy will indicate whether the data available on the analogues are sufficient to support a conclusion based on the read-across results, or whether at this point additional data need to be retrieved/generated before continuing.

Step 6: Uncertainty assessment

26. EFSA explains that the primary purpose of this step is to determine whether the read-across is scientifically robust and fit for purpose, or if further data or refinement are needed to reduce uncertainty to a tolerable level. The process consists in characterising the level of uncertainty at each step of the read-across process and assess whether it remains within tolerable limits, defined during problem formulation. The process for the assessment of uncertainty in a read-across is summarised in Figure 3 of the Scientific Opinion.

27. The uncertainty assessment can be conducted either qualitatively (i.e. through narrative descriptions) or quantitatively (i.e. using probabilistic or semi-quantitative methods). It is expected that the uncertainties will be documented in the read-across report using an appropriate template (an example is provided in Appendix C, based on the semi-quantitative method proposed by Pestana *et al.* (2021)).

28. Each step of the read-across workflow carries inherent uncertainties and these should be characterised. EFSA recommends that the assessor characterises the uncertainties at each step as they progress through the assessment. The primary sources of uncertainty associated with these steps are summarised in Table 4 of the guidance. Briefly, in Step 1, it is key to capture an acceptable level of uncertainty, whereas in Step 2 different levels of uncertainty are tolerated based on the specific regulatory context. In Step 3, the impact of the choice of structural representation used to conduct the searches should be considered, and whether this can be systematically evaluated. Three uncertainty sources should be considered in Step 4, i.e. the strength of the similarity rationale and the quality of supporting data, integration of multiple lines of evidence and inclusion of transparent and scientifically justified expert judgement. In Step 5, greater uncertainty in the overall assessment may arise when the data matrix is sparse, either due to few endpoints being filled or because the target substance lacks most endpoint data. In contrast, uncertainty is reduced when the relevant data gaps for both source and target substances have already been addressed.

29. The overall characterisation of uncertainty, which considers all aspects of uncertainty and requires expert judgement to reach a final evaluation, should be performed with reference to EFSA's Guidance on Uncertainty (EFSA SC, 2018). If all steps and criteria indicate low uncertainty, the overall impact may be considered low. In such a case, a narrative account of any residual uncertainties should be sufficient to justify the validity of the read-across. Conversely, if appropriate procedures have not been followed at one or more steps, the overall uncertainty may range from moderate to high.

30. When uncertainty is too high for a read-across to be deemed fit for purpose, it should be further evaluated—either through more detailed uncertainty analysis (e.g. semi-quantitative evaluation, quantitative statistical analysis) or by incorporating additional lines of evidence (NAMs). If uncertainty remains high despite these improvements the read-across approach may not be feasible, and experimental testing of the target substance may be necessary.

31. It is worth noting that the uncertainty discussed in EFSA's guidance pertains to hazard assessment. In contrast, risk assessment may tolerate moderate or high levels of uncertainty, depending on other lines of evidence and/or the application of additional uncertainty factors.

32. EFSA highlights the importance of applying standardised procedures throughout the read-across workflow to minimise uncertainty and improve regulatory acceptance. When each step is conducted using recognised

methods—such as OECD testing guidelines or studies performed under Good Laboratory Practice (GLP)—the overall uncertainty is considered low. In contrast, reliance on non-guideline studies, non-GLP data, or NAMs without sufficient documentation can increase uncertainty.

33. Overall, ensuring unambiguous identification and detailed characterisation of both target and source substances is critical. Using transparent, reproducible, and scientifically justified procedures throughout the read-across process helps maintain robustness and regulatory confidence, especially when uncertainty needs to be kept within acceptable limits.

Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed

Applicability domain of read-across

In this guide

[In this guide](#)

1. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Introduction](#)
2. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Background](#)
3. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Stepwise read-across guidance](#)
4. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Applicability domain of read-across](#)
5. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Conclusions](#)
6. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Questions for the Committee](#)
7. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Abbreviations](#)
8. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - References](#)

This is a paper for discussion. It does not reflect the views of the Committee and should not be cited.

34. The applicability domain of a method refers to the chemical, biological, or functional space where its predictions or measurements are considered reliable. For read-across, EFSA highlights that defining this domain means identifying suitable similar substances.

35. A clearly defined applicability domain is especially important for category-based read-across, which relies on patterns across multiple substances within a category. This allows the same prediction to apply to several target substances, provided they meet the category criteria. In contrast, analogue-based read-across is more limited, as its outcome applies only to the specific target substance unless another substance is very closely related.

36. After identifying similar substances, filters are often applied to refine the selection. These filters help define the boundaries of the read-across and should be explicitly stated. The domain is more clearly established when data interpolation is used.

37. EFSA advises using multiple source substances to strengthen read-across, as this increases the number of matching features and expands the applicability domain. If only one source is used, it must be highly similar to the target, with minimal differences that could affect the outcome.

38. Read-across is always endpoint-specific. Therefore, the applicability domain depends on the availability and density of chemical and biological data for the specific toxicological endpoint.

Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed

Conclusions

In this guide

[In this guide](#)

1. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Introduction](#)

2. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Background](#)
3. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Stepwise read-across guidance](#)
4. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Applicability domain of read-across](#)
5. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Conclusions](#)
6. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Questions for the Committee](#)
7. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Abbreviations](#)
8. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - References](#)

This is a paper for discussion. It does not reflect the views of the Committee and should not be cited.

39. The concept of read-across is based on the principle that structurally or mechanistically similar molecules tend to exhibit similar properties. This methodology involves identifying data-rich source substances that closely resemble a data-poor target substance and using their toxicological data to estimate the potential toxicity of the target.

40. EFSA's guidance provides a structured framework for applying read-across to assess the toxicological hazard of a chemical substance, supporting safety evaluations within the food and feed chain. However, EFSA emphasises that read-across is not a substitute for a full risk assessment. Instead, it serves as a supporting line of evidence within hazard assessment, which itself is a key component of risk assessment. Like other structure-activity relationship-based approaches, read-across alone is generally insufficient for regulatory conclusions—particularly when asserting the absence of toxicity for a specific endpoint. Such evidence is more robust when integrated into a WoE analysis alongside other data sources.

41. The guidance outlines the key steps in conducting a read-across: problem formulation, target substance characterisation, source substance

identification and evaluation, data gap filling, and uncertainty analysis. Each step may introduce varying degrees of uncertainty, which collectively determine the overall uncertainty level—low, moderate, or high. Whether this level is acceptable depends on the context of the risk assessment. Therefore, the risk assessor must define a tolerable level of uncertainty during the initial problem formulation. The guidance also addresses strategies to manage and minimise uncertainty throughout the process.

42. While expert judgement is necessary at certain stages, EFSA stresses that read-across must be conducted transparently, using standardised and unbiased procedures. Scientific justification should be clearly provided to support the overall conclusions.

Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed

Questions for the Committee

In this guide

[In this guide](#)

1. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Introduction](#)
2. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Background](#)
3. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Stepwise read-across guidance](#)
4. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Applicability domain of read-across](#)
5. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Conclusions](#)
6. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Questions for the Committee](#)
7. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Abbreviations](#)

8. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - References](#)

This is a paper for discussion. It does not reflect the views of the Committee and should not be cited.

43. Do Members have any comments on:

- a) The structured workflow to standardise and justify the read-across approach.
- b) Any other comments on this scientific opinion.
- c) Would they be content to use this guidance?

Secretariat

October 2025

Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed

Abbreviations

In this guide

[In this guide](#)

1. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Introduction](#)
2. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Background](#)
3. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Stepwise read-across guidance](#)
4. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Applicability domain of read-across](#)
5. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Conclusions](#)

6. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Questions for the Committee](#)
7. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Abbreviations](#)
8. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - References](#)

This is a paper for discussion. It does not reflect the views of the Committee and should not be cited.

(Q)SAR (Quantitative) Structure–Activity Relationship

ADME Absorption, Distribution, Metabolism and Excretion

AOP Adverse Outcome Pathway

CI Mitochondrial Complex I

CIII Mitochondrial Complex III

COT Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

DART Developmental and Reproductive Toxicity

ECHA European Chemicals Agency

EFSA European Food Safety Authority

FAF Food Additives and Flavourings

GLP Good Laboratory Practice

IATA Integrated Approaches to Testing and Assessment

KE Key Event

LogP Partition Coefficient Logarithm

MHA 2-Methylhexanoic Acid

MoA Mechanism of Action

NAMs New Approach Methodologies

N-NA N-Nitrosamine

OECD Organisation for Economic Cooperation and Development

SC Scientific Committee

WoE Weight of Evidence

Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed

References

In this guide

[In this guide](#)

1. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Introduction](#)
2. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Background](#)

3. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Stepwise read-across guidance](#)
4. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Applicability domain of read-across](#)
5. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Conclusions](#)
6. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Questions for the Committee](#)
7. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - Abbreviations](#)
8. [Summary of the EFSA Scientific Opinion on the Guidance on the use of Read-across for Chemical Safety Assessment in Food and Feed - References](#)

This is a paper for discussion. It does not reflect the views of the Committee and should not be cited.

Benigni R, Serafimova R, Parra Morte JM, Battistelli CL, Bossa C, Giuliani A, Fioravanzo E, Bassan A, Gatnik MF, Rathman J, Yang C, Mostrag-Szlichtyng A, Sacher O & Tcheremenskaia O, 2020. Evaluation of the applicability of existing (Q)SAR models for predicting the genotoxicity of pesticides and similarity analysis related with genotoxicity of pesticides for facilitating of grouping and read across: An EFSA funded project. Regulatory Toxicology and Pharmacology, 114, 104658. <https://doi.org/10.1016/j.yrtph.2020.104658>

ECHA (European Chemicals Agency), 2017. Read-Across Assessment Framework (RAAF). European Chemicals Agency. [Read-Across Assessment Framework \(RAAF\) - Publications Office of the EU](#)

ECHA/EFSA (European Chemicals Agency/European Food Safety Authority), 2023. Guidance document on the impact of water treatment processes on residues of active substances or their metabolites in water abstracted for the production of drinking water. EFSA Journal, 21(8), 8194. <https://doi.org/10.2903/j.efsa.2023.8194>

EFSA CONTAM Panel (EFSA Panel on Contaminants in the Food Chain), 2023. Risk assessment of N-nitrosamines in food. EFSA Journal, 21(3), 7884. <https://doi.org/10.2903/j.efsa.2023.7884>

EFSA FAF Panel (EFSA Panel on Food Additives and Flavourings), 2021. Scientific Guidance for the preparation of applications on smoke flavouring primary products. EFSA Journal, 19(3), 6435. <https://doi.org/10.2903/j.efsa.2021.6435>

EFSA SC (EFSA Scientific Committee), 2018. Guidance on Uncertainty Analysis in Scientific Assessments. EFSA Journal, 16(1), 5123. <https://doi.org/10.2903/j.efsa.2018.5123>

EFSA SC (EFSA Scientific Committee), 2019. Guidance on the use of the Threshold of Toxicological Concern approach in food safety assessment. EFSA Journal, 17(6), 5708. <https://doi.org/10.2903/j.efsa.2019.5708>

EFSA SC (EFSA Scientific Committee), 2025. Guidance on the use of read-across for chemical safety assessment in food and feed. EFSA Journal, 23(7), e9586. <https://doi.org/10.2903/j.efsa.2025.9586>

Irwan J, Simetska N, Wehr M, Kellner R & Escher SE, 2024. Read-Across Application for Food or Feed Ingredients. EFSA Supporting Publications, 21(7), EN-8811. <https://doi.org/10.2903/sp.efsa.2024.EN-8811>

OECD (Organisation for Economic Cooperation and Development), 2017. Guidance on Grouping of Chemicals, Second Edition. OECD Series on Testing and Assessment, No. 194, OECD Publishing, Paris. <https://doi.org/10.1787/9789264274679-en>

OECD (Organisation for Economic Cooperation and Development), 2020a. Case study on the use of integrated approaches to testing and assessment for identification and characterisation of parkinsonian hazard liability of deguelin by an AOP-based testing and read across approach (ENV/JM/MONO(2020)22). OECD Publishing. [Case study on the use of integrated approaches to testing and assessment for identification and characterisation of parkinsonian hazard liability of deguelin by an AOP-based testing and read across approach -pdf](#)

OECD (Organisation for Economic Cooperation and Development), 2020b. Case study on the use of integrated approaches to testing and assessment for mitochondrial complex-III mediated neurotoxicity of azoxystrobin - read-across to other strobilurins (ENV/JM/MONO(2020)23). OECD Publishing. [Case study on the use of integrated approaches to testing and assessment for mitochondrial complex-III mediated neurotoxicity of azoxystrobin - read-across to other strobilurins-pdf](#)

OECD (Organisation for Economic Cooperation and Development), 2020c. Case study on the use of Integrated approaches to testing and assessment for read-across based filling of developmental toxicity data gap for methyl hexanoic acid (ENV/JM/MONO(2020)21). OECD Publishing. [Case study on the use of Integrated approaches to testing and assessment for read-across based filling of developmental toxicity data gap for methyl hexanoic acid -pdf](#)

Pestana CB, Firman JW & Cronin MTD, 2021. Incorporating lines of evidence from New Approach Methodologies (NAMs) to reduce uncertainties in a category based read-across: A case study for repeated dose toxicity. Regulatory Toxicology and Pharmacology, 120, 104855. <https://doi.org/10.1016/j.yrtph.2020.104855>