EFSA Draft Guidance for Public Consultation: on the submission of data for the evaluation of the safety and efficacy of substances for the removal of microbial surface contamination of foods of animal origin

Section 4

In this guide

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10. EFSA Draft Guidance for Public Consultation: submission of data for the evaluation of the safety and efficacy of substances for the removal of microbial surface contamination - Annex A

Assessment of safety to humans (Section 4, page 11)

17. This provides a more detailed overview of the safety assessment requirements. This is a general summary, and specific requirements and procedures may vary depending on the nature of the decontaminating substance and the specific circumstances of the application.

18. For chemical substances, consumer exposure and toxicological assessments are required as part of the safety assessment.

Consumer Exposure Assessment (Section 4.1.1, page 11)

19. The updated guidance provides further information on exposure assessment methodologies and details the use of exposure assessment tools available.

Determining Residue Levels

20. Conservative Approach: applicants are required to estimate the amount of the substance and its reaction products remaining on the food based on the amount of decontamination solution applied per unit of food mass or surface area.

21. More Refined Estimation: Determine the amount of solution retained on the food surface more precisely through gravimetric analysis using small food specimens with a high surface-to-mass ratio.

22. Consider Reaction Products: applicants should account for any potential reaction products formed in the food during or after treatment.

Utilising EFSA Tools

23. Applicants should use the EFSA Comprehensive Food Consumption Database: This database provides detailed information on food consumption patterns across different population groups in EU Member States.

24. The applicant is required to use the Pesticide Residue Intake Model, revision 4 (PRIMo 4) exposure assessment tool. This online tool, designed for pesticide residue assessments, can be used to estimate consumer exposure by combining individual consumption data with residue data for the decontaminating substance. It considers individual dietary habits, body weight, and food consumption patterns.

25. An uncertainty analysis on data availability and exposure assessment should also be provided in line with the recommendations of the EFSA Guidance on Uncertainty Analysis in Scientific Assessments (EFSA SC, 2018).

Toxicological Assessment (Section 4.1.2, page 12)

26. The toxicological assessment of decontaminating substances requires a comprehensive approach, beginning with a detailed description and justification of the chosen testing strategy. This involves explaining the rationale behind including or excluding specific types of *in vitro* or *in vivo* toxicity studies, while applying a tiered approach and the principles outlined in the EFSA FAs guidance (EFSA FAF Panel, 2024). The basis for the assessment thereby lies in the toxicological data for each component of the decontamination solution, including not only the main substance but also any impurities and reaction products that might remain in the treated food. These data are required for both hazard identification and hazard characterisation and should include dose-response relationships derived from full study reports. However, a complete hazard characterisation may not be necessary for reaction products and impurities if a Threshold of Toxicological Concern (TTC) approach is applicable.

27. While assessments conducted under other regulatory frameworks (e.g., ECHA, EMA, FSA, or FDA) can be valuable, EFSA requires the submission of the original data and guaranteed data ownership. If only summaries are available, they can serve as supportive information but not as the basis for the risk assessment.

28. For substances already authorised for direct addition to food within the EU, such as Food Additives, the assessment can often use existing toxicological

data. In these cases, the applicant must confirm compliance with relevant EU specifications and provide information on existing authorisations and evaluations. This information should include the evaluating body, the date of evaluation, a summary identifying critical studies and their no observed adverse effect levels (NOAELs), lowest observed adverse effect level (LOAELs) or benchmark dose lower confidence limit (BMDL) values, and any health-based guidance values (HBGV) along with the uncertainty factors (UF) applied and any other uncertainties noted in the evaluation. For already authorised substances, any changes in the manufacturing process, specifications, or conditions of use will require safety concerns to be addressed, either through new data or a scientific justification explaining why new data are not required.

29. When dealing with substances not authorised for use in food within the EU, a more extensive toxicological assessment is required. This includes data to evaluate genotoxicity, toxicokinetics, and other forms of toxicity beyond genotoxicity. This includes subchronic, chronic, reproductive and developmental toxicity, and carcinogenicity. These endpoints are typically assessed through *in vitro* and *in vivo* experimental studies. Full reports of these studies, along with epidemiological studies, their compliance with international or national guidelines or Good Laboratory Practice (GLP), and any deviations from these, should be submitted. In line with the 3R principles (replacement, reduction, and refinement), the tiered approach should be applied for toxicokinetic and toxicity testing, using animal testing only until sufficient information is available for hazard characterisation.

30. Genotoxicity testing, referred to as Tier 0, should follow the specified testing strategy and be conducted for each individual component of the decontamination solution. Substances that raise concerns about genotoxicity are not assessed further. For those that do not, a minimal dataset is required under Tier I. If the Tier I data are sufficient for toxicity assessment and no triggers for higher tiers exist, no further studies are needed. However, substances that are absorbed or demonstrate toxicity in Tier I tests will require Tier II testing.

31. Tier III testing is reserved for a case-by-case basis to investigate specific endpoints needing further clarification from Tier I and II results. Additional studies, including human data if available, can be incorporated into the evaluation. It is important to note that the testing strategy for toxicokinetics and toxicity offers more flexibility compared to genotoxicity testing due to the wider range of potential datasets. This entire approach aims to identify a Reference Point (e.g., NOAEL or BMDL) and derive an HBGV using appropriate uncertainty

factors. For risk characterisation, human exposure to the decontaminating substance is compared to the HBGV. If an HBGV cannot be derived, a margin of exposure (MoE) approach could be considered.

32. For reaction products and impurities with an available Reference Point or HBGV, potential exposure is calculated based on a limit value and then prorated to the exposure estimates for the decontaminating substance. This estimated exposure is then compared to the available reference point or HBGV of the undesirable impurity. When sufficient toxicological data are lacking, non-testing methods such as read-across, computational methods (structural activity relationship, SAR; quantitative structural activity relationship, QSAR), and the TTC approach can be used for a preliminary assessment. If the TTC approach is used and the worst-case consumer exposure estimate is below the TTC of the relevant Cramer class, and genotoxicity can be ruled out, no further data are needed. For genotoxic compounds without carcinogenicity data, or if genotoxicity cannot be ruled out, consumer exposure should not exceed the TTC for genotoxic and carcinogenic compounds. For reaction products and impurities that are both genotoxic and carcinogenic, the MoE approach may be applied.

33. For biological agents proposed as decontaminating substances the EFSA guidance on the risk assessment of microorganisms (EFSA Scientific Committee, 2024) should be consulted. If multiple formulations are proposed, all should be tested. For bacteriophage-based solutions, requirements include characterising the bacteriophage and/or production strain, demonstrating the absence of viable cells and, if applicable, DNA from the production strain in the final product, and evaluating the impact on the gut and food/feed microbiome. Finally, the applicant must describe the reactions and fate of the decontaminating agents on treated foods, including quantifying residual levels of the active agent.

34. Allergenicity assessment is also required for bacteriophages or their components. If a component of the decontamination solution is a potential allergen, specific data requirements should be followed.