Question & Answer document for Applicants - EFSA Info session on the updated 2026 Food Additive Guidance - 15 April 2026

This document compiles the questions submitted by participants upon registration and during the "Info session on the updated Food Additive Guidance" organised by EFSA on 15 April 2026, together with the corresponding responses provided by EFSA. The purpose of this document is to clarify the questions discussed during the Info Session and to ensure that all participants have access to the issues addressed. Questions falling outside EFSA's remit, as well as questions already addressed in the context of the EFSA presentation, are not included in this document.

Questions related to Section 3 - Characterisation and specifications of the 2026 Food Additive Guidance

1. **Question:** In cases where there is not enough batch quantity, e.g. if studies need to be repeated, or additional analytical data are required during risk assessment, different batches than the ones initially used may be required for completing these analyses. How flexible will EFSA be in these cases, if different batches are used e.g. for batch variation vs. stability, or vs. impurities?

   Answer: As indicated in the 2026 EFSA Food Additive Guidance, the use of the same individual batches across studies is recommended. Where this is not feasible (e.g. due to insufficient batch quantity, repeat studies or additional data requests during risk assessment), the use of different batches may be acceptable, provided that this is adequately justified. Applicants should demonstrate that all batches used are representative of the proposed food additive and that comparability across datasets (e.g. batch-to-batch variation, stability and impurities) is ensured.

2. **Question:** For additives produced with enzymatic reaction, would an application for authorization of this enzyme be required before the submission of the food additive application?

   Answer: Applicants should indicate whether the food enzyme(s) used in the manufacturing process have been assessed, or are under assessment, by EFSA under Regulation (EC) No 1332/2008, including the relevant EFSA question number(s) and, where available, the corresponding EFSA scientific opinion. Where the enzyme(s) fall outside the scope of Regulation (EC) No 1332/2008 (e.g. enzymes used exclusively in the production of the proposed food additive), data to support the safety evaluation of the enzyme(s) should be provided and will be assessed in the context of the food additive application, following the scientific principles outlined in the relevant EFSA Guidance on Food Enzymes (EFSA CEP, 2021).

3. **Question:** For fermentation derived food additives, will only the 2021 Guidance on Food Enzyme need to be followed, or will the 2025 Microorganism Guidance will also be applied during risk assessment?

   Answer: The EFSA Scientific Committee (SC) Guidance on Microorganisms (EFSA SC, 2025) provides overarching recommendations for applications for products used in the food chain that contain, consist of, or are produced by microorganisms (GM or non-GM) within EFSA's remit, and it supersedes previous guidance on this topic. Therefore, the information requested in the 2025 SC Guidance should be provided for the characterisation of fermentation-derived food additives. Where the manufacturing process involves the use of enzyme(s), applicants should additionally provide the relevant process details as requested in the 2026 Food Additive Guidance, in line with the 2021 EFSA Guidance on Food Enzymes.

4. **Question:** What should be the level of detail required for the description of the production process, especially when it involves proprietary technologies?

   Answer: The description of the production process should be sufficiently detailed to allow the EFSA Panel on Food Additive and Flavorings (FAF) to assess its safety.
   The applicant can use the confidentiality claims to avoid sharing sensitive details, without affecting the assessment by the FAF Panel, who consult the non-confidential dossier for its evaluations.

Questions related to Section 4 – Proposed uses and exposure assessment

5. **Question:** For foods for special medical purpose (FSMP), EFSA asks me to clarify the use levels and to perform exposure calculation including FSMP for two ongoing additive applications. Here, you indicate that supplements and FSMP are not included in exposure calculation. Can you please clarify?

   Answer: Reliable consumption data are not available in the EFSA Comprehensive Database for Foods for Special Medical Purposes (FSMP) in Food Categories 13.2 and 13.3 (FSMP for non-infants and young children). Where applicants can identify the relevant FSMP products/foods, EFSA may use consumption data from corresponding 'standard' (non-FSMP) foods as a surrogate to support a pragmatic exposure estimate. Where an appropriate mapping to standard food categories is not possible, the exposure estimate for FSMP should be supported by the information provided by the applicant (e.g. product description and expected intake). The FSMP-related exposure will then be added to the exposure estimated for the other proposed food categories.

6. **Question:** How will be managed the assessment of sweeteners? "EFSA will perform a 'consumers only scenario' according to the sweeteners' exposure protocol, i.e. selecting relevant foods that may contain a sweetener based on facets. Indeed, this scenario cannot be calculated with the EFSA dietary exposure tool(s), because these tools do not contain facets." Can you please give more details on this?

   Answer: The 'consumers-only scenario' described in the EFSA sweeteners exposure protocol requires identification of consumers of foods containing the sweetener using

FoodEx2 facet descriptors. At present, the tools made available to applicants (i.e. FAIM and DietEx) do not include facet descriptors and therefore cannot be used to calculate this scenario. As indicated in the Guidance, EFSA will perform the consumers-only scenario internally using facets. Where available, applicants may refer to exposure estimates reported in previous EFSA scientific opinions (e.g. for the corresponding sweeteners) to support the application.

7. **Question:** When I apply for the use of a sweetener, why is it not possible to use EFSA's proprietary exposure assessment model (brand-loyal vs. non-brand-loyal) for sweeteners? EFSA will do their own exposure assessment for sweeteners based on this model. As an applicant I am forced (or only allowed) to use FAIM or DietEx which may give different results. This is not helpful for applicants to check if their application will result in an exposure below the ADI. This issue has been highlighted during the consultation on the draft guidance and in stakeholder meetings with EFSA and the Commission. However, it seems that it has not been addressed in the final guidance.

   Answer: The brand-loyal scenario requires, at the individual consumer level, assigning maximum concentration data to the food category to which each consumer is assumed to be brand-loyal, while assigning typical concentration data to other consumed categories. In the tools currently available to applicants (FAIM/DietEx), individual consumption data are used but only one concentration value (e.g. maximum or typical) can be applied uniformly across individual to a given food category. Consequently, the brand-loyal scenario cannot be implemented in these tools at present.

   EFSA continues to develop and update its exposure assessment methods and tools. In the interim, applicants may use conservative assumptions (e.g. maximum proposed use levels across relevant food categories) to support a screening comparison with the ADI, noting that EFSA's internal assessment will be the basis for the regulatory evaluation.

8. **Question:** While EFSA provides digital tools like FAIM and DietEx for professionals, how does the Authority intend to bridge the gap for the average consumer who lacks the technical capacity to translate an ADI into daily portion sizes?

   Answer: EFSA scientific opinions report the concentrations (mg/kg or mg/L) used for dietary exposure estimates and identify the main contributing food categories. In some cases, illustrative examples may be provided; however, translating an ADI into portion sizes for an individual consumer is generally not straightforward because the ADI refers to total intake from all dietary sources.

   The average consumer can also refer to the foods which contribute the most to the total dietary exposure, this is available in each EFSA opinions. If the food category contributing the most to the total dietary exposure correspond to a food which is highly consumed by this consumer, then he/she can consider reducing his/her own consumption.

   The tools are not only for professional and are available for anyone after registration to EFSA. These are user-friendly (one data to enter by food category) so can be used by anyone. Training material (manual, video tutorials) are also available for all users.

   It is also important to note, that EFSA does not provide dietary advice to consumers. Its mandate is to deliver independent scientific risk assessments, including setting health-based guidance values, such as ADIs. The translation of these into practical dietary

guidance sits primarily with risk managers, i.e. European Commission and national competent authorities.

9. **Question:** Regarding exposure assessment: high consumption for infant< 16 weeks is set to 260 ml/kg bw/day. For follow-on formula for toddlers, could we set this exposure value to 140 ml/kg bw/day, based on what was written in EFSA rapid risk assessment of cereulide? (EFSA provides rapid risk assessment on cereulide in infant formula | EFSA) In other words, is it possible to generalize this value?

   Answer:

   In the case of cereulide's rapid risk assessment, an acute exposure was performed which is different from chronic exposure.

   For chronic exposure FAIM must be used, with the exception of infants < 16 weeks for which the default value of 260 ml/kg bw/day.

   Real consumption data for toddlers (1-3 years old) are available in the EFSA Comprehensive Database; these data are reliable, thus, a default value is not needed for this population group for formulae. In the draft guidance on default values currently under public consultation (https://connect.efsa.europa.eu/RM/s/consultations/publicconsultation2/a0lTk000007kRij/pc1861), there is no such default value for formulae consumption for toddlers.

   The EFSA Comprehensive Database being regularly updated, consumption levels of follow-on formula for toddlers should be calculated for each exposure assessment.

Questions related to Section 5 – Toxicological data

10. **Question:** Is the read-across approach applicable to the FA itself, or only to the impurities?

    Answer: Read-across may be applicable also to the food additive itself, but it has to be justified by the applicant based on the principles outlined in the EFSA Scientific Committee Guidance on the use of read-across in food and feed risk assessment (EFSA SC, 2025). The toxicological and toxicokinetic endpoints covered by read-across should be compliant with the data requirements as prescribed in section 5 of the 2026 EFSA Food Additive Guidance.

11. **Question:** What is the impact of the current revision of the 2021 EFSA Nano RA Guidance (EFSA SC, 2021) on the 2026 EFSA Food Additive Guidance? The same question could be applicable to all horizontal guidance documents and administrative guidance cited in the 2026 EFSA Food Additive Guidance, when they will undergo a revision.

    Answer: The revised guidance on food additives will not be updated to reflect any new horizontal guidance update.

    Once horizontal guidance documents, especially the Scientific Committee guidance, are updated or new guidance documents become available, then these updated or new guidance are considered applicable horizontally to the relevant EFSA food domains.

Please refer to section 1.5. General principles (first bullet point) of the 2026 EFSA Food Additive Guidance for further details.

12. **Question:** When the EFSA Genotoxicity Guidance has been updated, will any differences and/or additional studies mentioned in that guidance supersede the genotoxicity strategy in the food additive guidance?

    Answer: Yes, please refer to the reply to Question n. 11 of this Q&A document. In general, once horizontal and cross-cutting guidance documents, such as the EFSA Scientific Committee Guidance on Genotoxicity, are updated or new guidance documents become available, these updated or new documents are considered applicable horizontally to the relevant EFSA food domains.

13. **Question:** ToxTracker is an emerging in vitro genotoxicity assay that is highly specific and sensitive, as well as providing mechanistic information. It should soon have an OECD TG. Would EFSA accept this study in Tier I?

    Answer: As indicated in the 2026 EFSA Food Additive Guidance, the data required to assess the genotoxic potential of a food additive should follow the principles of the genotoxicity testing strategy recommended by the EFSA Scientific Committee (SC) (EFSA SC, 2011, EFSA SC, 2017 and EFSA SC, 2021). At the moment ToxTracker is not listed among the recommended in vitro genotoxicity testing by the SC, although in the future this may change, considering that the SC Guidance on Genotoxicity is currently under revision (EFSA-Q-2025-00166). On the other hand, as recommended by the EFSA Food Additive Guidance (2026), any relevant non-animal data informing on the safety of the proposed food additive can be submitted by applicants under Tier I. Validated and standardised methodologies endorsed by an official body (e.g. OECD, JRC) should be preferred, when available. If these data are not sufficient to reach a conclusion, they can be used to support the decision making in the risk assessment process and/or they may contribute to the overall weight of evidence.

14. **Question:** EFSA mentions the transgenic mutation rodent assay in the recent opinion on berberine. I understood based on previous exchange with EFSA that this test may be requested more frequently. Would this concern food additive?

    Answer: As mentioned in reply to question n. 16 of this document and as indicated in the 2026 EFSA Food Additive Guidance, the data required to assess the genotoxic potential of a food additive should follow the principles of the genotoxicity testing strategy recommended by the EFSA Scientific Committee (SC) (EFSA SC, 2011, EFSA SC, 2017 and EFSA SC, 2021).

15. **Question:** Is an in vivo absorption study mandatory to confirm lack of absorption shown in vitro? How does this align with what was mentioned earlier that it is possible to conclude on safety without in vivo data?

    Answer: As described in the updated 2026 EFSA Food Additive Guidance, the evidence of lack of absorption is a pivotal element of the tiered toxicity testing strategy. Where the in vitro absorption studies provide no evidence of absorption, the Guidance nevertheless recommends an in vivo study of limited duration (e.g. 2 weeks, up to the limit dose) to (i)

assess potential local effects in the gastrointestinal tract and (ii) confirm the lack of systemic absorption.
Where available, existing data from the published literature may be used to address concerns regarding potential local toxicity in the gastrointestinal tract and/or to support the lack of absorption observed in vitro. This is consistent with the principle that, where adequately justified, it may be possible to conclude on safety without the need for in vivo toxicity testing.

16. **Question:** Since gut microbiota play a critical role in the biotransformation of chemical 'cocktails,' how can EFSA guarantee the safety of these mixtures when the 'first line of defense'—the microbiome—is excluded from formal safety integration?

    Answer: As noted in the 2026 EFSA Food Additive Guidance, section 5.4.5.5., the scientific research in the area of gut microbiota is rapidly evolving, however the knowledge is not yet sufficiently consolidated to be translated into specific data requirements.

    EFSA is following the latest developments in the area. For example EFSA has on ongoing project on the evaluation of microbiome-relevant human biomarkers and in vitro models for xenobiotic risk assessment https://ec.europa.eu/info/funding-tenders/opportunities/portal/screen/opportunities/tender-details/4bdf9e8e-884e-4a5a-ac75-db17bcc84f0b-CN

17. **Question:** We would be interested to understand the lack of harmonization between the Flavouring Guidance and the Food Additive Guidance in terms of data requirements, especially concerning the tiered approach for toxicokinetic and toxicity testing. Is there any intention by EFSA to further harmonize these requirements?

    Answer: The 2026 Food Additive Guidance builds on EFSA's experience with food additive applications and aims at reflecting substance-specific data needs.
    Alignment with the 2022 Flavourings Guidance has been achieved across several sections such as characterisation and specifications, proposed uses and exposure assessment, parts of toxicological data requirements (e.g. genotoxicity testing strategy).
    The tiered approach for toxicokinetics and toxicity testing beyond genotoxicity is not fully aligned between the two guidances, reflecting differences in regulatory context and the evidence base used to develop sector-specific guidance. In particular, since the publication of the 2022 Flavourings Guidance, EFSA has not received any applications for authorisation of food flavourings under Regulation (EC) No 1331/2008, which limits the opportunity to evaluate and refine the practical implementation of the tiered approach for flavourings on the basis of the practical experience.
    As a general principle, EFSA monitors guidance implementation in line with its internal procedure (SOP-003) and may revise sectoral guidance at any time after its publication when needed.

18. **Question:** Thank you for this insightful presentation. In the updated EFSA guidance, the toxicological testing strategy for food additives appears to have evolved somewhat differently from that for novel foods. However, from a purely intrinsic hazard perspective, the toxicological endpoints and underlying principles should theoretically be similar, regardless of the regulatory category.

Answer: The core toxicological endpoints and scientific principles underpinning hazard identification and hazard characterisation (including evaluation of genotoxicity, toxicokinetics (ADME), systemic/target organ toxicity, reproductive and developmental toxicity and, where relevant, carcinogenicity) are broadly applicable across EFSA's different regulatory domains. This is consistent with the approach described in both the 2026 EFSA Guidance on Food Additives and the 2025 EFSA Guidance on Novel Foods (EFSA NDA, 2025).

However, the tiered testing strategies may differ between sector-specific guidance because the problem formulation, the nature of the material and the key uncertainties to be addressed are not identical. For example, in the case of a food additive, EFSA aims at identifying the most sensitive reference point from a range of toxicological hazards and their dose-response relationship, which is used to derive a health-based guidance value (i.e., Acceptable Daily Intake, ADI) that should be protective for all age groups of the general population, theoretically exposed to the additive on a chronic basis and life-long. As outlined in the 2026 EFSA Guidance on Food Additives, the derivation of an ADI requires an adequate dataset to identify an appropriate reference point and to characterise all the relevant toxicokinetic and toxicity endpoints with sufficient confidence.

On the other hand, the 2025 EFSA Guidance on Novel Foods covers a broad range of materials that may include complex matrices and foods with variability in composition, for which considerations such as history of use and nutritional impact may be central and can influence the selection and interpretation of toxicological data. In addition, certain novel foods may be proposed for use in specific food categories such as food supplements, for which the intended target population may be restricted to particular population groups (e.g., excluding children or pregnant and lactating women), rather than the general population.

Therefore, differences in testing strategies between regulatory areas should not be interpreted as differences in the underlying hazard principles, but rather as tailored implementations to address domain-specific decision needs, data availability and uncertainty.

Questions related to Section 6 – Safety for the environment

19. **Question:** We are interested in the expected testing strategy for persistence and biodegradability. If a substance is initially assessed using non-testing approaches (e.g., (Q)SAR or physico-chemical data) and indicates potential persistence, to what extent are standard screening tests for biodegradability (e.g., OECD 301) considered sufficient to refine this assessment? Under which conditions would applicants be expected to go beyond screening tests and generate higher-tier or simulation studies (e.g., OECD 308/309)?

    Answer: As reported in the guidance, the need to perform a full environmental risk assessment for a proposed food additive and its possible metabolites and/or related products should be considered on a case- by- case basis. The purpose of the conditions i-iv is to define in which cases and environmental risk assessment would be needed on the basis of considerations on the potential exposure to the food additives or its related products in the environmental compartments. In this view, the condition ii should be interpreted as a screening to identify substances which are not expected to be degraded

in a STP. A substance readily biodegradable according to an OECD TG 301, it is generally considered not persistent. In cases in which there is an indication of potential persistence using non testing approaches the Applicant is advised to define a test strategy on a case-by-case basis considering the type of data already available, the existing guidance on environmental risk assessment and test guidelines.

20. **Question:** Are already any available examples of environmental safety assessment of additive/ingredient in literature you suggest?

    Answer: This part of the assessment is new and there are no examples of a full environmental risk assessment performed at EFSA level in the context of new food additive applications. As part of the re-evaluation of the already authorised sweeteners, the related EFSA opinions have included a section on environmental considerations in which the available data from the literature on the environment are reviewed. In all cases this section was drafted before the development and/or entry into force of the EFSA Food Additive Guidance (2026). This section does not describe a full risk assessment but could still serve as an example of the assessment of already available data to identify cases in which further assessment would be appropriate. In the latest published opinion, i.e. re-evaluation of sucralose (E 955) (EFSA FAF, 2026), the environmental considerations section was drafted bearing in mind the principles of the 2026 EFSA Food Additive Guidance since the development of this opinion went in parallel with the drafting of the guidance.

Question related to pre-submission and services to applicants

21. **Question**: Are there any new opportunities for pre-submission advice or structured discussions with EFSA to avoid incomplete submissions?

    Answer: EFSA has launched a call to support SMEs and first-time applicants in preparing a complete food additive application following the publication of the 2026 EFSA's updated Food additive guidance document. This initiative was presented during the info session (see slides 86-88 of the presentation), and more information on the call can be found on EFSA's website.

22. **Question:** Will be there any changes to the E-Submission Food Chain (ESFC) platform to address the new Guidance?

    Answer: The new table of contents (ToC), reflecting the 2026 EFSA Food Additive Guidance, is available in ESFC and it can be already used by applicants when starting to draft their applications. The previous table of contents is not available anymore. However, the applicants can use the new ToC following the requirements of the previous 2012 EFSA Food Additive Guidance (that is still into force until 19 July 2026), as explained in slide n. 15 of the presentation given by EFSA during the Info session. The new ToC will not block the submission of applications that are still following the previous EFSA's guidance in these 6 months of transition from the old to the new requirements.

Questions of generic nature:

23. **Question:** Will this guidance apply to the ongoing re-evaluation process of the food additives?

    Answer: This revised guidance document addresses primarily data requirements for new food additive applications submitted under Regulation (EC) No 1331/2008.
    While the re-evaluation context differs from that of new applications (e.g. number of operators involved, availability of a complete technical dossier versus data collection via interested business operators (IBOs), EFSA recommends that business operators take into account the principles of this guidance when submitting information in the context of re-evaluation.

24. **Question:** EFSA continues to base its safety opinions largely on non-peer-reviewed studies funded and conducted by the applicants themselves. Considering the inherent 'funding bias,' how can EFSA claim to provide a truly independent risk assessment when the raw data behind these 'cocktails' remains proprietary and hidden from independent academic scrutiny?

    Answer: Under EU food law, applicants are required to generate and submit the data necessary to demonstrate the safety of substances intended to be placed on the market. The evidence provided by the applicant constitutes the starting point for EFSA's scientific assessment andit is subject to independent scrutiny and critical appraisal.

    All studies submitted to EFSA are subject to a robust and independent scientific evaluation by EFSA's Panels and their Working Groups. This includes appraisal of the study design and conduct, compliance with internationally recognised test guidelines and quality standards, the adequacy of the statistical analyses, and the relevance of the findings for human health risk assessment. Identified uncertainties, limitations and potential sources of bias are explicitly considered in the weight-of-evidence evaluation and are reflected in EFSA's conclusions.

    With regard to transparency and confidentiality of proprietary data, EFSA operates under Regulation (EU) 2019/1381 (Transparency Regulation), which provides for proactive publication of the non-confidential information and data underpinning EFSA's assessments. Confidentiality can be granted only for specific items and only when duly justified; it is assessed case-by-case within the applicable legal framework. This approach aims to maximise public access to the evidence while protecting business-sensitive information.

25. **Question:** While EFSA advocates for 'Open Science,' the specific toxicological datasets used to justify the new Mixture Assessment Factor (MAF) are often protected by commercial confidentiality. Does this 'black box' approach not undermine the very principle of peer review, making it impossible for the broader scientific community to replicate your findings or verify if the proposed 'cocktail' limits are based on political precaution rather than reproducible science?

    Answer: The safety assessment of food additive is conducted by EFSA using substance specific methodologies. A generic Mixture Assessment Factor (MAF) has not been applied in EFSA scientific opinions on food additives. The scientific rationale and the supporting evidence used to conclude on the safety of the food additive are made publicly available in EFSA's scientific opinions on food additives, in line with Regulation (EU) 2019/1381.

26. **Question:** Is EFSA willing to override confidentiality claims for any data used in cumulative risk assessments, or will the 'Additive Cocktail' policy remain a black box where safety limits are calculated using hidden variables that the public is simply asked to trust?

    Answer: Please refer to the reply given to question n.23 of this document.

27. **Question:** While your slides highlight 'Stakeholder Engagement,' the high cost of producing GLP-compliant studies essentially ensures that the scientific narrative is controlled by large commercial entities. In the interest of preventing a systemic conflict of interest, is EFSA prepared to mandate that any study used to justify a Mixture Assessment Factor (MAF) must be fully open-source and hosted in a public repository for truly independent, third-party scrutiny?

    Answer: The Transparency Regulation (Regulation (EU) 2019/1381), amending the General Food Law (Regulation (EC) No 178/2002), introduced the principle of proactive disclosure and transparency of information, studies and data submitted to EFSA for scientific evaluation. The non-confidential version of an application is made publicly available in Open.EFSA and stakeholders and interested parties are encouraged to share insights, studies, data, and other useful feedback to ensure that EFSA has access to all relevant scientific data and studies available on the subject matter.
    Article 5(7) of Commission Regulation (EU) No 234/2011 on the general provisions on data for risk assessment of food additives requires that toxicological studies shall be conducted in facilities which comply with principles of good laboratory practice. Further details on the acceptability of GLP studies can be found on EFSA's website. The use of any testing methods differing from internationally agreed test guidelines and/or not carried out according to GLP, should be duly justified by the applicant before it can be considered by EFSA in the risk assessment.

28. **Question:** How aligned are EFSA's requirements with other international regulatory bodies when it comes to food additive evaluation? How should legacy or non-GLP data be addressed? Could you please discuss the new toxicity requirements in context of other jurisdictions - for example, a company starting in the US will have conducted a 90-day dietary feeding study and the new guidance could lead to this not being accepted in the EU.

    Answer: EFSA's data requirements for the safety assessment of food additives are based on internationally agreed scientific principles and are, to a large extent, aligned with approaches used by other regulatory bodies (e.g. through the use of OECD Test Guidelines (TGs) and the OECD Principles of Good Laboratory Practice (GLP)). Nevertheless, differences may occur because EFSA's guidance is developed to meet the specific decision needs under EU food law.
    Regarding legacy and/or non-GLP data, EFSA can consider all relevant evidence, including published studies and older studies not conducted under GLP, provided that the study design, conduct and reporting allow an adequate appraisal of reliability and relevance for risk assessment. In line with the applicable legal provisions for food additive dossiers, GLP compliance is expected for toxicological studies where GLP is applicable (see the answer given to Question n. 26 of this document). However, for studies not

conducted according to standard protocols or quality systems, applicants should provide a transparent description of methods and results, access to raw data where available, and a scientific justification of the study's suitability. Any limitations should be clearly identified and addressed.

With respect to studies generated for submissions in other jurisdictions, EFSA generally accepts studies conducted according to internationally recognised standards (e.g. OECD TGs) and expects that the test item used is representative of the material to be placed on the EU market and that the study addresses the relevant endpoints and exposure route.
The 2026 Food Additive Guidance foresees the possibility to deviate from the standard data requirements where this is scientifically justified. Therefore, applicants with existing datasets are encouraged to map available studies against the 2026 data requirements and to provide a reasoned justification where studies differ from EFSA's recommendations, including an explanation of how the available evidence addresses the relevant uncertainties. Where gaps remain, additional targeted studies (or well-justified alternative approaches, where appropriate) may be needed to support an EFSA assessment.

29. **Question:** Your 'Transparency & Engagement' roadmap highlights public consultations and stakeholder meetings, but it does not mandate the release of raw toxicological data in an interoperable format for independent re-analysis. Is EFSA's definition of transparency merely about 'showing the process' rather than 'sharing the evidence,' and doesn't this effectively prevent the scientific community from identifying potential flaws in the industry-funded studies you rely on?

    Answer: Please refer to the answer given to Question n. 23 of this document.

30. **Question:** Regarding the evaluation process, how does the updated guidance address the 'cocktail effect' (combined exposure to multiple additives)? Does the new guidance incorporate harmonized methodologies for assessing chemical mixtures, such as dose addition or response addition, as outlined in the MIXTOX framework? I would appreciate a discussion on how EFSA plans to bridge the gap between single-substance testing and real-world combined exposure.

    Answer: The 2026 EFSA Food Additive Guidance provides data requirements for new food additive applications for which an authorization process is in place, according to Regulation (EC) No 1331/2008. Systematic assessment of combined exposure to multiple chemicals (including potential additivity/synergy) is not performed as part of the safety evaluation for a new food additive application.

31. **Question:** Since EFSA groups additives based on pure chemical data, how can you claim these safety limits are realistic considering the 'Matrix Effect'? Does your model account for how real food components—like fats or proteins—might actually trigger synergy and turn a safe 'cocktail' into a toxic one?

    Answer: Please refer to the answer given to Question n. 29 of this document.

32. **Question:** If exposure models (FAIM/DietEx) are built on historical data and single-additive limits. Since these datasets do not account for synergistic 'cocktail' effects, how can EFSA justify using these legacy assessments to ensure that real-world, multi-substance exposure remains within safe biological limits?

    Answer: Exposure to multiple chemicals is not conducted as part of the safety assessment of new proposed food additives. Please also refer to the answer given to Question n. 29 of this document.

33. **Question:** Since most published studies focus on single substances in isolation, how does EFSA ensure that this 'Non-Testing' approach doesn't miss unique synergistic risks that only emerge when these additives are combined in a consumer's diet?

    Answer: As mentioned in the reply to Question n. 29 of this document, the safety evaluation for a new food additive application does not include a systematic assessment of combined exposure to multiple additives or other chemicals in the diet.
    Where there is a specific scientific rationale or evidence suggesting that an additive may interact with other substances (e.g. shared mode of action, common target organ, known metabolic inhibition/induction, or co-occurrence at high exposure), such information can be submitted to EFSA and will be considered in a weight-of-evidence evaluation.
    Of note, as explained in the presentation given by EFSA during the Info session, for some endpoints, e.g. genotoxicity of mixtures, testing individual components is considered more informative on the identification of the potential hazards than testing of the whole mixture.

34. **Question:** Since synergistic effects often manifest as subtle metabolic shifts rather than immediate organ weight changes, how does EFSA justify relying on this single-substance protocol to predict the cumulative impact of additives on human immunotoxicity and endocrine health?

    Answer: Please refer to the answer given to Questions n. 29 and n. 32 of this document.

35. **Question:** If a food additive is not metabolized, it is not "biologically neutral"—in fact, the lack of metabolism is often the very reason it poses a unique risk to both the gut and the environment. How does EFSA account for the synergistic stress these 'active' non-metabolized additives place on the human microbiome and renal filtration systems when consumed as part of a daily multi-additive diet?

    Answer: please refer to the answers to Questions n.16, n. 29 and n. 32 of this document.