

ECPA questions on the implementation of the Regulation (EU) 2019/1381 on the transparency and sustainability of the EU risk assessment in the food chain

ECPA is supportive of the overall objective to increase transparency and consumer confidence in the risk assessment process, but note that it will entail major changes to the procedures applicable to the evaluation of active substances for plant protection products in Europe.

This paper describes the key questions which remain unanswered or newly identified questions since our first document from 3rd September 2019. The questions are intended to provide constructive input into the implementation process. As we get closer to the entry into force date of the Transparency regulation it is essential that applicants get as much clarity as possible on all the questions listed below so as to prepare internal resources accordingly – and avoid any disruption in the EU regulatory processes after end March 2021.

1. Notification of studies

Q1: What is considered a study?

- ECPA suggests that studies (commissioned/carried out to support regulatory applications in the EU) which fulfil the OECD definition of a study are to be notified. According to the OECD definition, study “means an experiment or set of experiments in which a test item is examined under laboratory conditions or in the environment to obtain data on its properties and/or its safety, intended for submission to appropriate regulatory authorities”. This definition is also captured in the EU Directive 2004/10/EC of the European Parliament and of the Council¹. The criteria in the definition fits with the information that EFSA is considering for notification (e.g. Study starting date, Study planned completion date, etc.). There is information submitted by the applicant in the format of reports that are not studies per se and therefore fall outside of notification obligation.
- It is therefore suggested that position documents, reports containing risk assessments or for instance exposure predictions should not require a notification process. What level of detail is needed at which stage?
- Exposure calculations and Effect Modelling work should be out of scope of the notification obligation:
 - In a regulatory context they fundamentally differs from experimental work in one key aspect: With the same input parameters and the same model version, the results of any model calculation (e.g. the PEC values) can be exactly reproduced again and again. In fact, it is common practice that model calculations reported by the notifier are repeated by the regulatory authority. Over that, a stop and re-start of a model calculation will not change the result. This removes in the case of model calculations the main reason for the notification requirement under GFL, i.e. to prevent the intermediate stop and non-reporting of intended studies.
 - Model calculations are exactly reproducible because they are purely an application mathematical equations. These equations always yield the same result when used with the same parameter values.
 - It is also important to note that model calculations do not deliver regulatory endpoints. Instead they use endpoints from experimental studies to predict exposure and effects under real-world conditions. Since those endpoints are ultimately defined by the regulatory authorities, so are the model input parameters. In most cases, the model calculations will therefore have to be repeated once the endpoints were fixed by the regulatory authorities, based on their interpretation of the experimental data.

Q2: How will EFSA manage the relationship between the list of studies intended for renewal and the list of notified studies? Often this is not a 1 to 1 relation.

3 – 4 years prior to submission, quite limited information is available not allowing to nominate individual studies. About one year ago, the ECPA team developed an Excel sheet giving an indication what kind of information is available for public commenting 1 (PC-1). The information might allow to provide a generic description e.g. “Residue behavior in target crops”. Such a description would result that one item in the renewal list is later

linked to more than one study. Is such a procedure foreseen? Any 1:1 relationship of a study identifier with a study would not allow such a procedure.

Q3: Is there a deadline by which a study may be entered in the EFSA database as a 'commissioned study' without triggering the need for a valid justification of non-compliance?

Q4: Will there be clarifications on how to handle studies conducted first for submissions in other regions and later intended for EU submission (either active substance or MRL, applies to all import tolerances for actives not registered in the EU).

Q5: Can a study whose report is already available be entered in the EFSA database as a 'commissioned study'?

Q6: What will be considered as a valid justification? And will it apply per submission or per individual study?

Q7: Will multiple applicants generating information on the same active substance use the same 'test item'?

Q8: Will there be an interface to electronically submit the notifications information in bulk as required and in a structured format?

- We would suggest using xml with excel formats being a potential alternative. This could avoid inconsistencies between the notification and Dossier, which would certainly occur when the applicants need to manually retype that information directly into the Notification database. The interface should additionally allow for download of the data, to also facilitate reimporting the structured information provided by the database into the in-house systems.

a. List of intended studies for renewal – link to notification database

Q9: What will be the mechanism of commenting on the intended list of studies? And what is EFSA's rationale for proposing picklists for test items?

Q10: What happens if an applicant decides to cancel a study or it needs to be repeated for technical/other reasons? Will the database allow multiple notifications over time? If so, will there be an EFSA review and public commenting every time a change is notified?

Q11: For studies on metabolites or impurities is "coding" acceptable or should the applicant list the chemical name/CAS number? How is confidentiality applied then?

Q12: How to handle triggered studies? The conduct of any intended study for renewal will / might result in the need of further investigation. Will it be enough to nominate such triggered studies exclusively in the EFSA notification database once commissioned? A process for such studies is considered essential.

b. EFSA Notification Database

Q13: Is it confirmed that laboratories of the business owner (independent of site, or different legal entity) do not need to co-notify?

- ECPA wants to point out that business operators may have different legal entities operating in several countries, and therefore the legal entity may not be the same as the legal entity acting as lab/testing facility. However, all legal entities would be under the same company umbrella. ECPA understands that if legal entities fall under the same company umbrella, in such case there is also no need for co-notification.

Q14: Will there be a clear description of the scope of the EFSA database? E.g.

- Type of submissions and related studies
 - New active substances (ai data, representative formulation)
 - Renewal of active substances (ai data, representative formulations)
 - MRL submissions ("domestic" use, import tolerance: ai data, several formulations, but not limited to representative formulations)
 - Other types of applications leading to an EFSA output? (i.e. confirmatory data)

Q15: Will there be clarifications on how to handle studies responsibilities – especially in OECD multi-site (GLP) studies where several CROs are involved (who does what?)

Q16: Will there be clarifications on how to handle studies and workable “timelines” (when?)

Q17: Will there be clarifications on how to handle studies being submitted in more than one process (e.g. AIR process of one or more substances, MRL application)

Q18: Will there be clarifications on how to handle studies where the scope / designs have been changed depending on the outcome of a previous study (compared with intended study).

- Which fields will remain editable in the system once a notification has been raised? What changes will be allowed to a notification, and is that dependent on the lifecycle status of the study?

Q19: During new active substance development (research phase), the timeline between conduct of a study and a potential submission of such study may be several years. A high number of candidates fail during research and early development or the company decides not to market such active in EU. However, very few studies conducted in early phases may be relevant for a later (5-15 years) dossier submission/evaluation in EU.

- Do applicants need to notify all early studies on all potential development candidates in order to allow later evaluation of such early studies (e.g. mechanistic studies to elucidate mode of action of a specific new chemical structure in research phase) while it is not known yet if or if not they will be used in the EU to support applications?
- Or can industry consider studies relevant for notification under GFL from the date when a first positive decision is taken by the applicant that the development of a new active substance is striving for an application for use in EU? From that point in time all existing relevant studies with this active could be notified and all future studies as well.

Q20: Regulation 844/2012 applies for substances where the dossier was submitted before 27 March 2021, and GFL procedures don't apply. If a study is conducted after this date for such a substance, should it be notified in the database e.g. if it would be submitted in a stop the clock period, which would be after 27 March 2021?

2. Pre-submission advice

Q21: When is the earliest time point prior to dossier submission that pre-submission advice can take place?

Q22: How will pre-submission advice be managed for renewals in cases of multiple Applicants?

Q23: How will coordination be ensured between EFSA and the RMS in the pre-submission advice provided to Applicants and in the subsequent evaluation by the RMS of the dossier submitted?

Q24: Will Applicants be given the opportunity to review and comment on the summary of the presubmission advice prior to this being made public by EFSA under Article 38(2) (at the time “application” is considered admissible)?

3. Stakeholder and public consultation on dossier

Q25: What will be the duration of the consultation on the dossier made available under Article 38(1)(c)?

Q26: Will EFSA manage this consultation in the same manner as the existing consultation on the RMS Draft Assessment Report/Renewal Assessment Report where a response to comments and summary on the consultation are prepared?

Q27: How will the consultation be managed in cases of multiple Applicants? Will a separate consultation be opened for each Applicant or will the consultations be coordinated?

Q28: How will coherence be ensured between EFSA and the RMS? [EFSA is responsible for launching the consultation, the RMS is responsible for preparing the Draft Assessment Report/Renewal Assessment Report taking into account the comments received during the consultation].

4. Making public, Article 38 and confidentiality

Q29: While Article 38(2) provides some guidance on how dossiers (“scientific data, studies and other information supporting applications...”) will be made public under Article 38(1)(c), what will be the system and procedures established by EFSA to disclose this information?

Q30: What safeguards will be put in place to prevent commercial including regulatory misuse of the information in the EU and worldwide?

Q31: Will Applicants be allowed to submit the (non-)confidential versions of the dossier with watermarks on each page highlighting that the content may be subject to copyright and other IP protection and that misuse for commercial, including regulatory purposes is prohibited worldwide?

Q31: Will EFSA maintain a register of persons seeking access to the studies in order to identify the person, so that in cases where the studies have been mis-used without permission, an Applicant is able to enforce its rights?

Q32: Will the undertakings mentioned in the text of the GFL revision contain a legal note that the person accessing the studies consents to the data submitter/owner pursuing effective remedies in court for misuse of information?

Q33: When submitting a request for confidentiality does a reasoning for each item of confidential information need to be submitted by the Applicant? In which format should such requests be submitted and to what level of detail?

Q34: Is ECPA’s understanding correct that personal data can be redacted, and that this redaction applies to all studies submitted and is not limited to confidential information or vertebrate studies?

Q35: Is a difference expected in the procedure for the assessment of confidentiality requests between new applications and renewal applications?

Q36: On confidentiality claims, on which parameter will the potential damage to a significant degree be assessed (Art 39(2))? The approach seen so far is far too vague for business operators to be able to prepare accordingly. Subset questions can be for illustration: will it be calculated on the basis of the turnover of EU based affiliates? On the basis of global turnover? Will it be related to active substance in cases where the manufacturing know-how is concerned and to the product in cases where the product composition is concerned?

5. Other elements

Q37: Will the EFSA own commissioned studies be notified in the database and will there be consultation on the protocol or mandate before?

Q38: Regarding the IUCLID format, it is clear the upcoming regulation on renewals for PPPs will include a provision asking formally the format for future renewals. What about submissions for new active substances and MRL (new, renewal, Import tolerances)? Which document will formalize this obligation and as from when will it apply ? Does the March 27th effective date apply to the IUCLID requirement for these dossiers?