Post-public consultation stakeholder event

21-22 June 2021

New Food Enzyme Guidance – Part B

Yi Liu

FIP unit

Trusted science for safe food

efsa

European Food Safety Authority

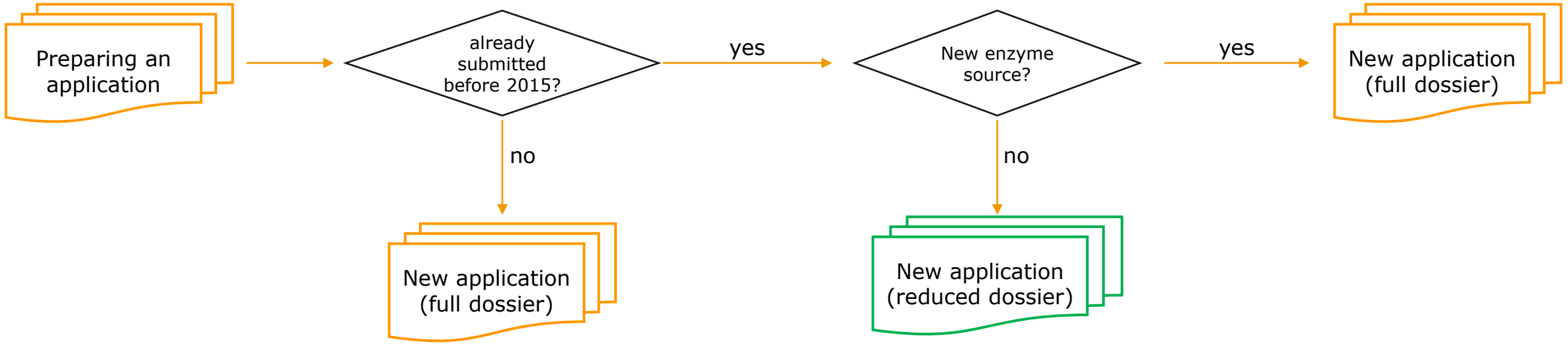
Comments Collected from Public Consultation

Part B **Data** required for the safety assessment of **modifications to an existing authorization**

1) Full dossier *vs* reduced dossier submission

Part B of the New Food Enzyme Guidance

Data required for the safety assessment of modifications to an existing authorisation



Part A
1. Source of the food enzyme
2. Production of the food enzyme
3. Characteristics of the food enzyme
4. Toxicology
5. Dietary exposure estimation

Part B
1. Source of the food enzyme
2. Production of the food enzyme
3. Characteristics of the food enzyme
4. Toxicology
5. Dietary exposure estimation

Post-public consultation stakeholder event
21-22 June 2021

New Guidance for Submission of Dossiers on Food Enzymes

E-submission
Food Chain Platform

Anastasia Livaniou
Scientific Officer APDESK Unit

Trusted science for safe food

efsa
European Food Safety Authority

E-submission Food Chain Platform (ESFC)

FSCAP v.1 **EC web system**, operational since Jan 2018 (Novel Foods/Traditional Foods)

v.2: E-Submission Food Chain Platform

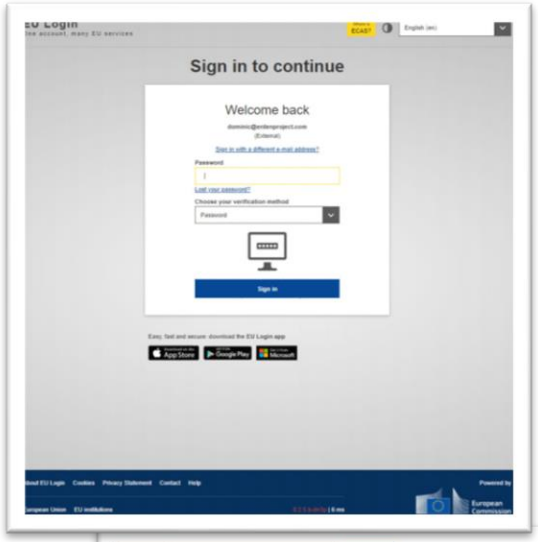
- **TR compliance:** NoS, Confidentiality assessment, Dissemination
- **All Regulated Product** dossiers (excl. pesticides)
- **Single point of entry** for Applicant, European Commission, Member States

6 Food Domains - 37 Application Types (New, Modifications, Renewals)

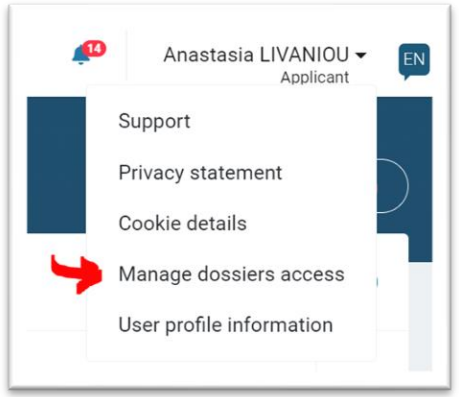
- **Food Contact Materials**: Substances, Active & Intelligent materials, Recycling processes, Cellulose
- **Food Improvement Agents**: Food Additives, Food Enzymes, Food Flavourings, Smoke Flavourings
- **GMO**: Food-feed (Regulation), GMO Directive
- **Nutrition**: Novel/Traditional Foods, Health Claims, Infant formulae, Food allergens, Nutrient sources
- **Biological hazards**: Decontamination substances
- **Feed Additives**

URL for ESFC

ESFC –Access & Dashboard

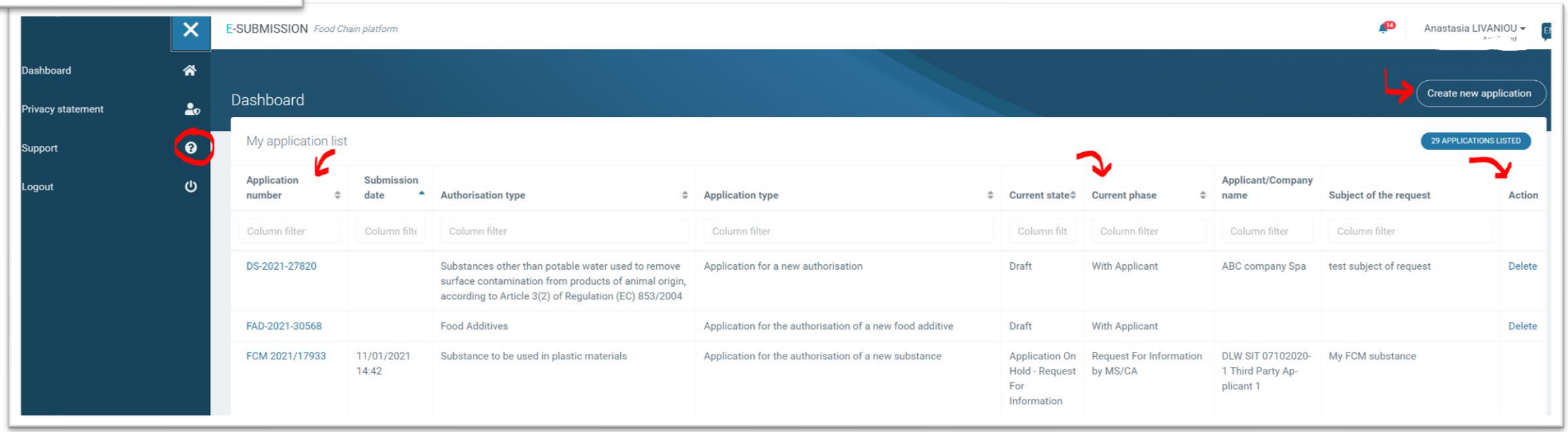


EU-Login needed



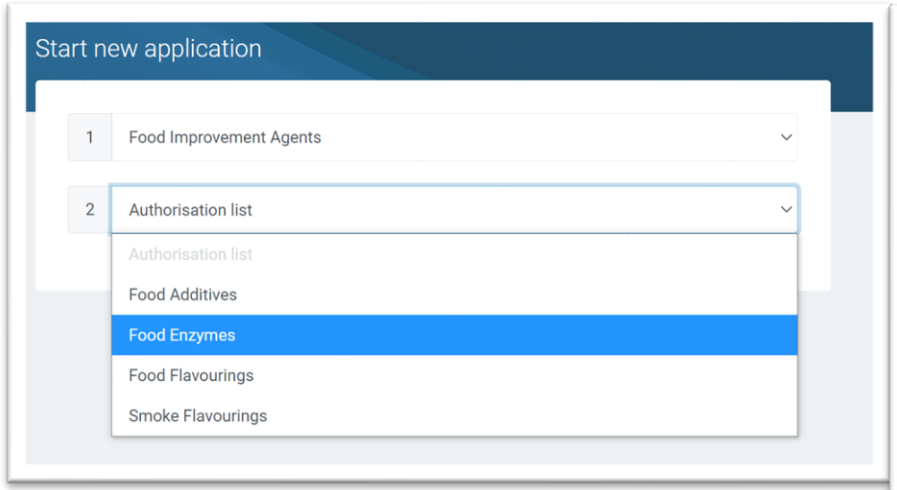
Add dossier owners

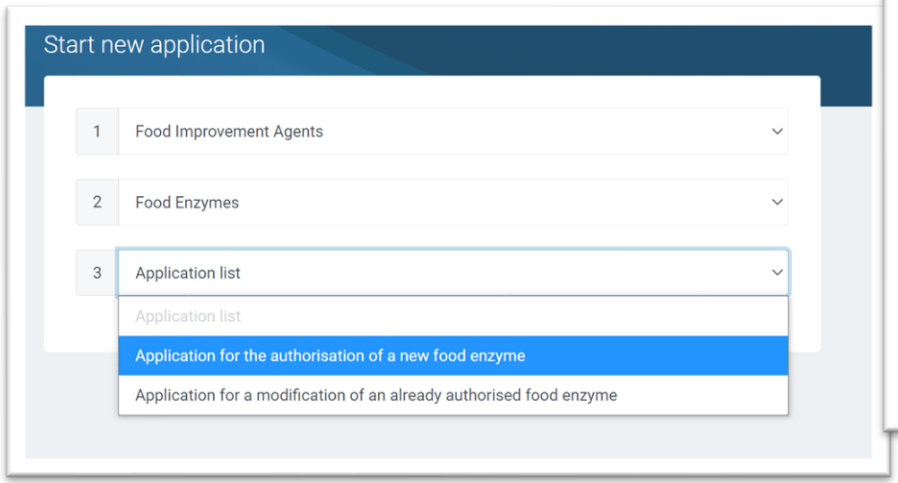
Dashboard

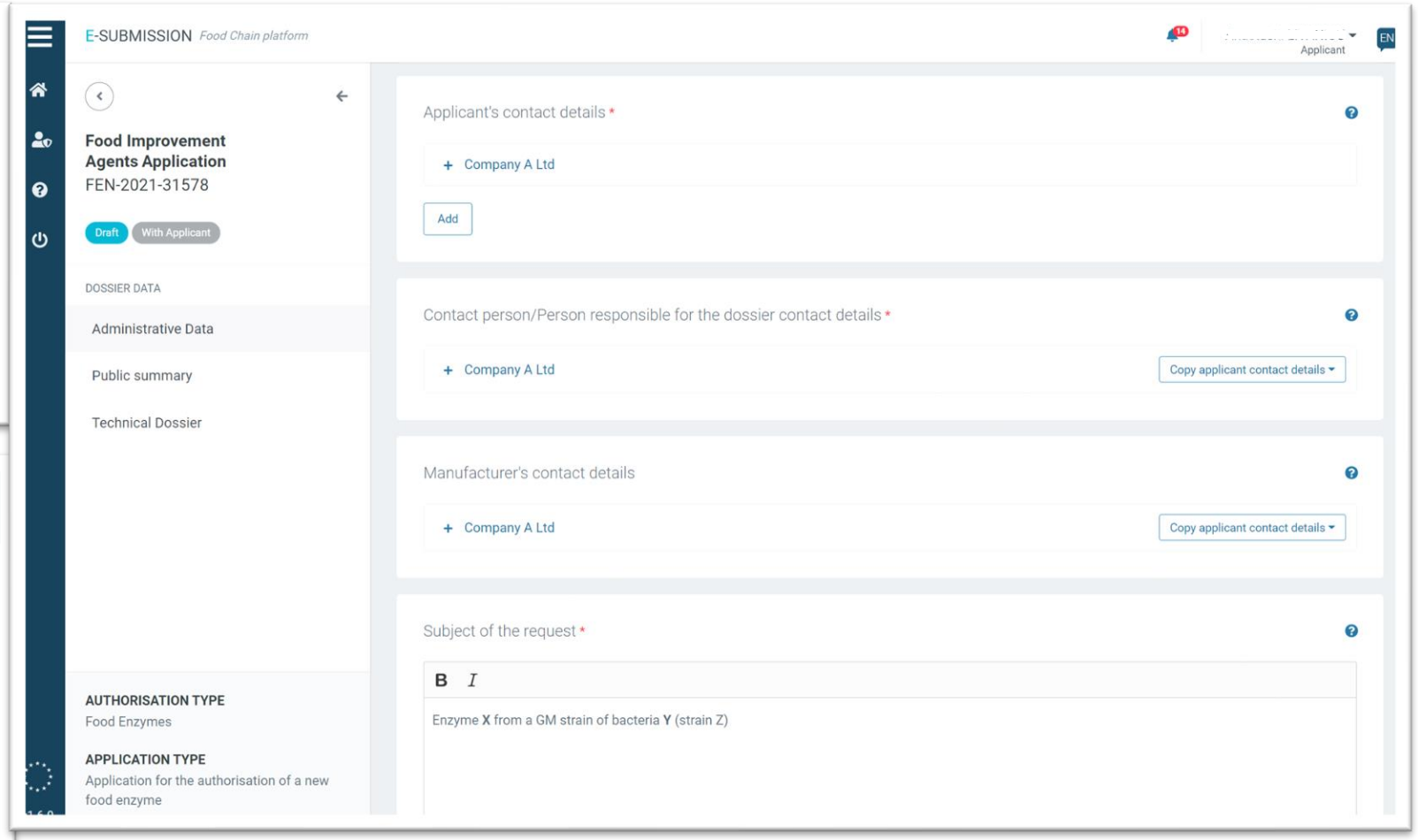


ESFC- Select the Table of Contents

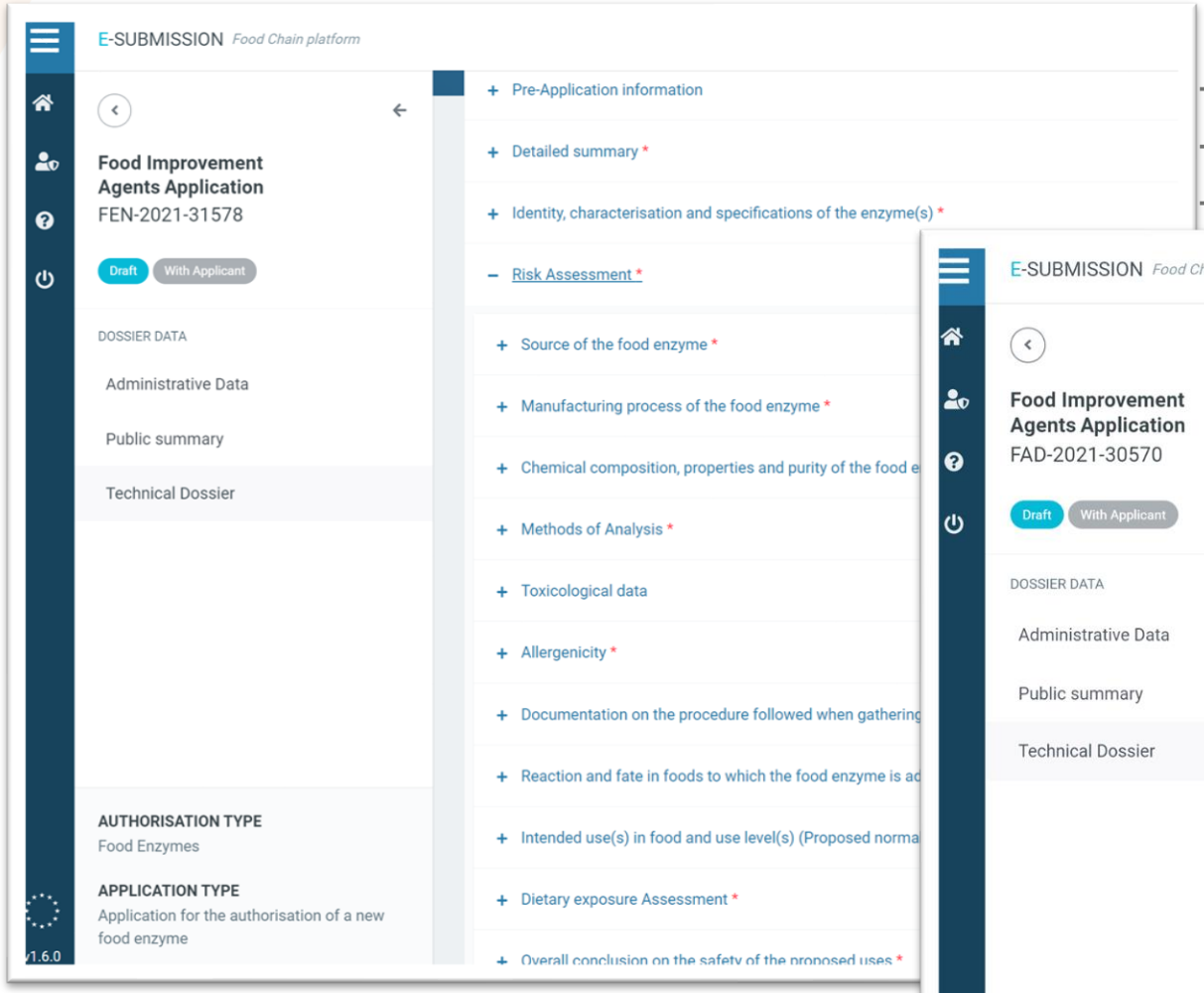
Select Table of Contents (template)







ESFC– Fill in the template with your documents



- Main text, Annexes, References in the same section
- Define document type
- Request Confidentiality

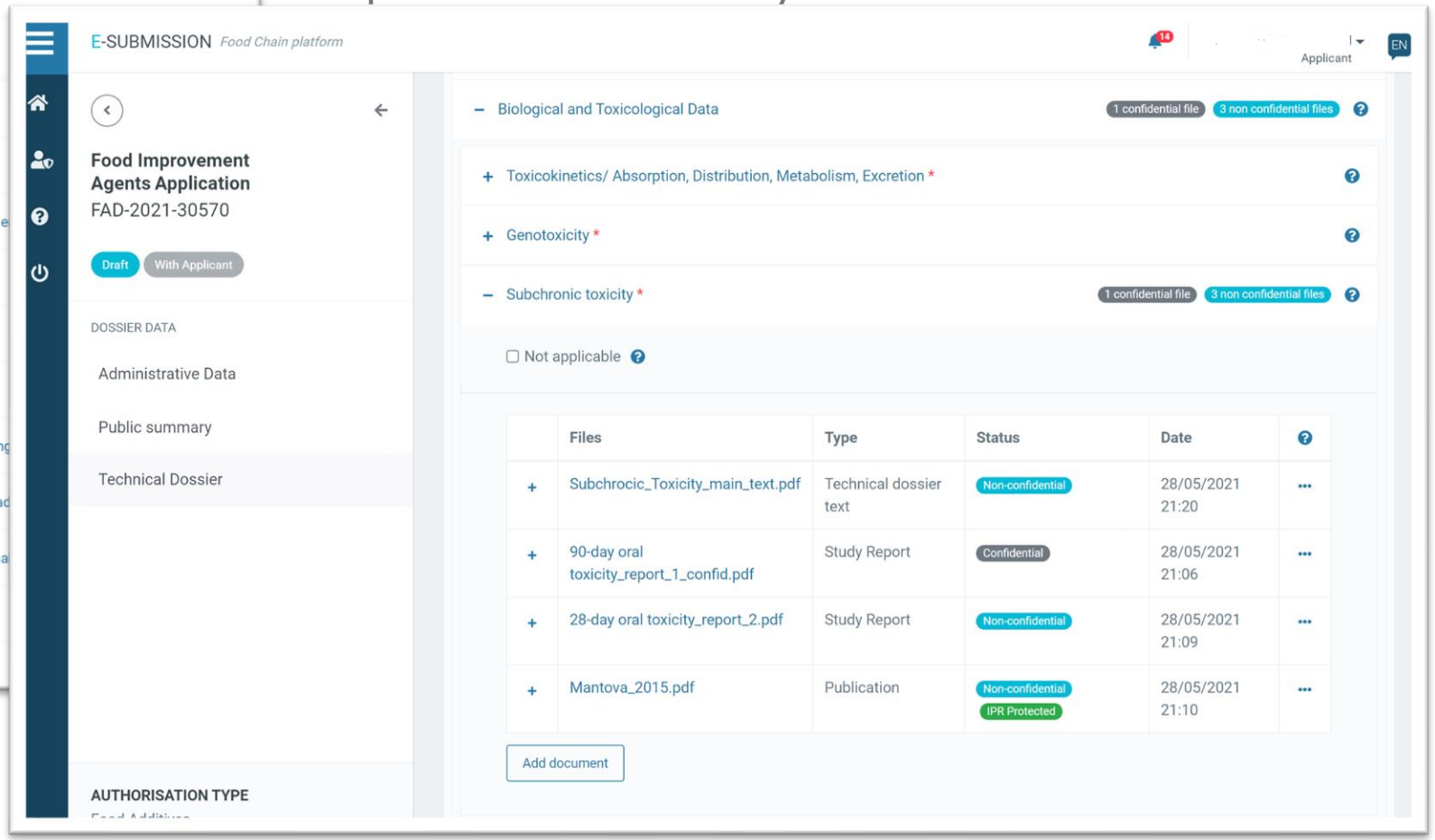
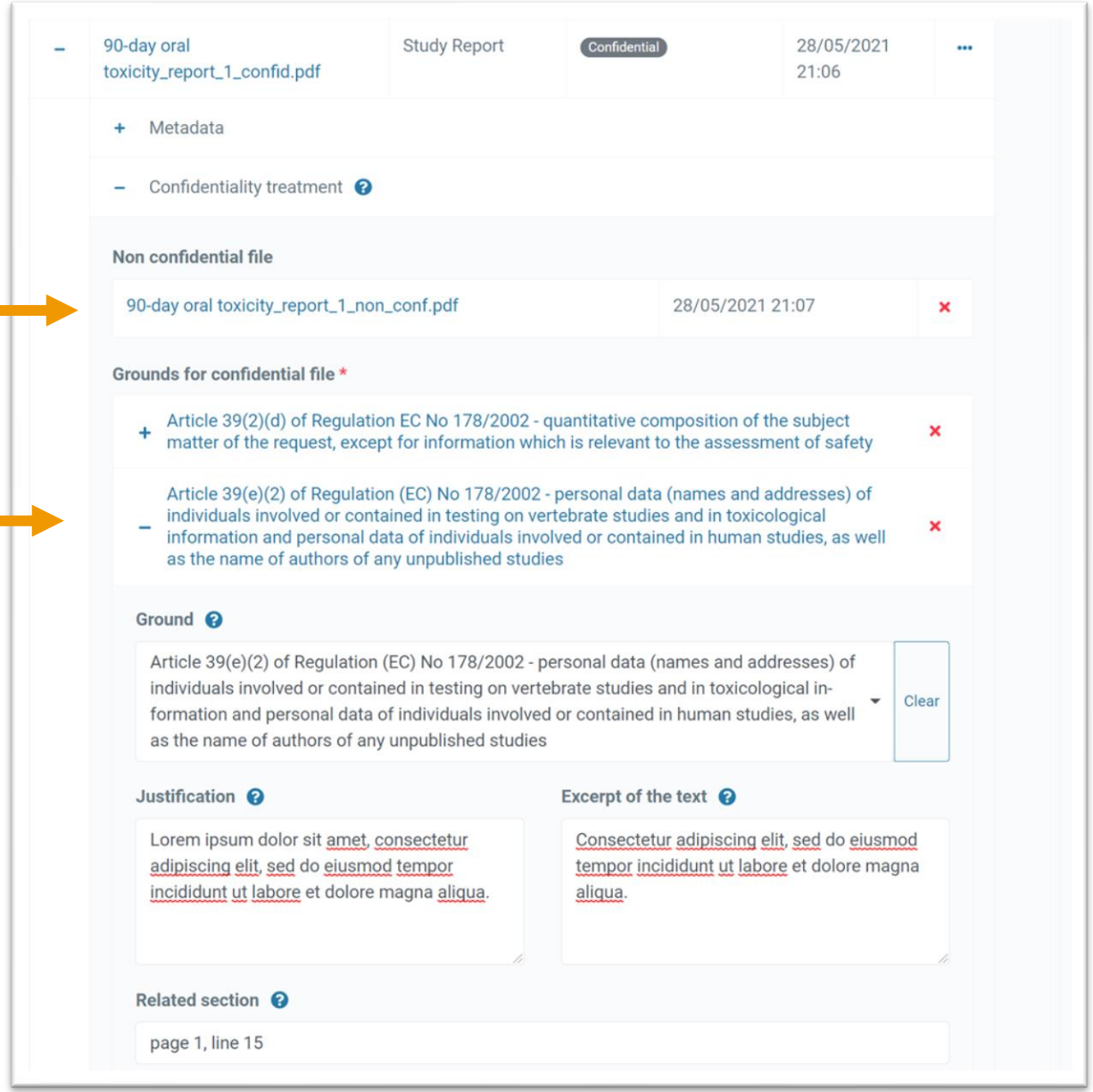


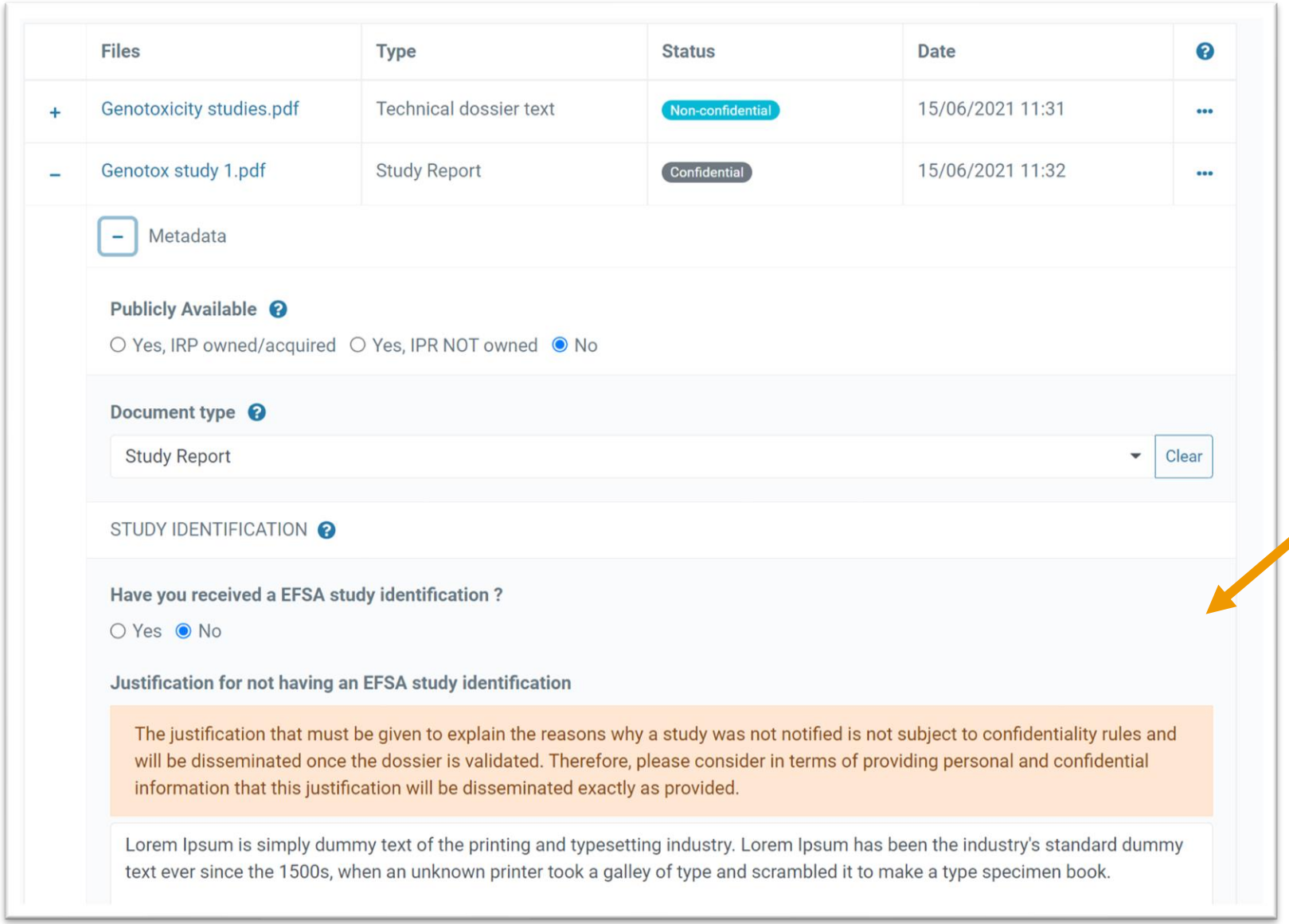
Table of Contents
based on Guidance documents

ESFC – Building a Confidentiality Request

- Provide non-confidential file
- Define your request:
  - Legal ground
  - Justification
  - Excerpt
  - Location in text
- Add request, as required



ESFC – Study reports



Study Reports:
- NoS id, or
- Justification if not notified

ESFC- Published studies

European Food Safety Authority

– Subchronic toxicity * 1 confidential file 3 non confidential files

☐ Not applicable

	Files	Type	Status	Date	
+	Subchrocic_Toxicity_main_text.pdf	Technical dossier text	Non-confidential	28/05/2021 21:20	•••
+	90-day oral toxicity_report_1_confid.pdf	Study Report	Confidential	28/05/2021 21:06	•••
+	28-day oral toxicity_report_2.pdf	Study Report	Non-confidential	28/05/2021 21:09	•••
–	Mantova_2015.pdf	Publication	Non-confidential IPR Protected	28/05/2021 21:10	•••

– Metadata

Publicly Available

○ Yes, IRP owned/acquired ◉ Yes, IPR NOT owned ○ No

IPR Reference

For publications already available to the public (e.g. studies published in scientific journals which may be accessible upon payment of fees) for which the applicant does not have or cannot obtain IPRs for the purposes of the proactive public disclosure requirements (i.e. reproduction of the study on EFSA's website), the applicant must provide:
(a) a copy of the relevant publication. The copy of the relevant publications will be used for assessment purposes only.

(b) and in this free text section the relevant bibliographic references/ citations (indicating where these publications are available to the public and their web links for public dissemination on EFSA's website.

Mantova, A. L., Benoit, J. N., Barrowman, J. A., Harper, S. L., Kvietys, P. R., & Granger, D. (2015). Repeated Dose 28-day Oral Toxicity Study in Rodents. American Journal of Toxicology, 247(5), G486-G493.

Published studies:
Give full citation

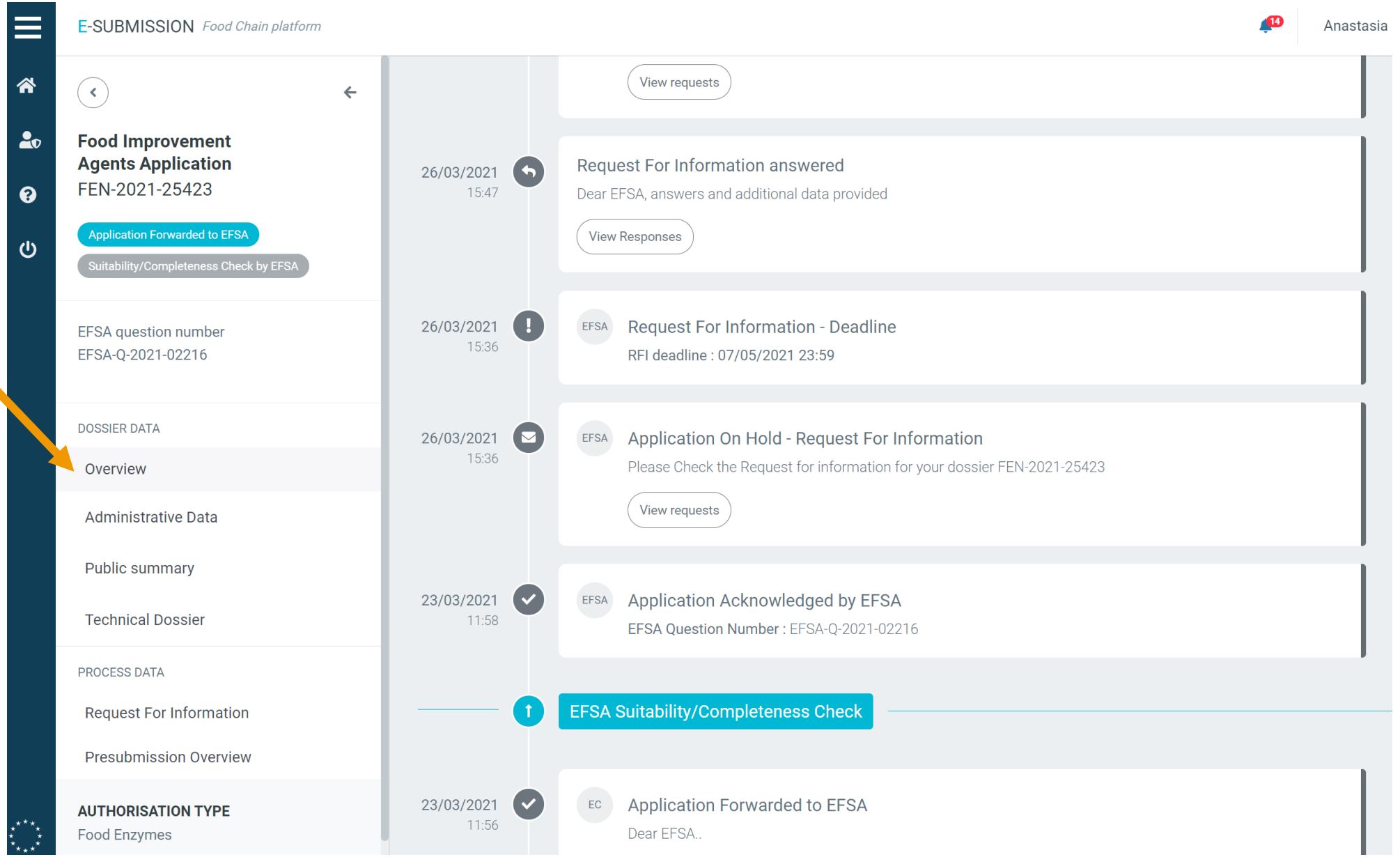
ESFC – Submit and Follow-up

European Food Safety Authority

Timeline Overview

[Video Tutorials]

[User Guide]



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Post-public consultation stakeholder event
21-22 June 2021

New Guidance for Submission of Dossiers on Food Enzymes

Suitability check of food enzyme applications

Costanza Casiraghi

Applications Desk Unit (APDESK)

Trusted science for safe food

efsa
European Food Safety Authority

Scope of the suitability check

Suitability check in a nutshell

"check if all relevant data needed for the risk assessment (as indicated in the EFSA scientific guidance) have been provided in a clear and consistent manner in the entire technical dossier"

Scientific evaluation of the data provided is out of the scope of the suitability check performed by APDESK

If some of the data stipulated in the guidance are not considered by the applicants as relevant for their product, they may be omitted, provided that this omission is fully justified.

During the suitability check, APDESK checks the presence of justifications, if data are omitted.

The declaration of validity of an enzyme application is in the remit of the European Commission

Suitability check: Pre-application information

This check is only applicable to studies commissioned/started as of March 27th 2021

- Presence of Notification of studies (NoS) IDs for the studies included in the application
  - Have the studies included in the dossier been notified?
  - Have they been notified before the starting date?
- Presence of NoS justifications for
  - Non-notification of a study included in the application
  - Notification submitted after the starting date of a study
  - Non-inclusion in the application of a notified study
  - Withdrawal of a notified study

*For further information see EFSA Q&A on practical arrangements (here – Q&A 1-7 and 33-46)

Common missing data found during suitability check
Source of the enzyme

Source of the enzyme

- Microbial origin (MO)
  - Characterisation and taxonomic identity of the MO
    - Certificate of deposit
    - WGS for bacteria and yeasts
    - If genetically modified: characterization of the modification
    - WGS methods Presence of WGS raw data
  - QPS vs non-QPS (toxigenicity and pathogenicity)
  - Viable cells and DNA from the production strain (depending on the nature of the MO), with full methods described
- Plant origin
  - Identity of the plant
  - Secondary metabolites
  - Specifications and quality of raw materials
- Animal origin
  - Identity of the animal
  - Animal tissue and if suitable for human consumption
  - Quality control and risk of infectivity

Common missing data found during suitability check
Manufacturing process

Manufacturing process with flowchart

Actual raw materials used

Microbial origin (MO)	Plant origin	Animal origin
Fermentation	Extraction	Extraction
Methods to eliminate the microbial mass and microorganisms	Methods to eliminate the plant biomass and microbes	Methods to eliminate the animal tissue and microbes

Common missing data found during suitability check
Enzyme properties and purity

Chemical composition, properties and purity

Amico acid sequence, molecular mass, subunits, protein pattern (e.g. SDS-PAGE)

Methods of analysis in full with LODs and LOQs, even if carried out by third parties

Certificates of analysis:
- 3 batches (same ones for all parameters)
- For all parameters measured (activity, TOS and impurities)

Analysis of the batch used in tox studies

Microbial origin (MO)

Chemical purity/presence of impurities as indicated in the guidelines – different requirement depending on the nature of the fermentation process and the MO

Plant origin

Impurities relevant to plant products as indicated in the guidelines

Animal origin

Microbiological purity

Common missing data found during suitability check
Toxicological studies and references

Toxicological studies

- If not present, APDESK checks the presence of a justification as indicated in the guidelines "exemptions from toxicity testing"
- Full and signed reports
- Characterization of the enzyme batch used in tox studies

References

- Full text of the cited references is included

Post-public consultation stakeholder event
21-22 June 2021

New Guidance for Submission of Dossiers on Food Enzymes

EFSA's updated catalogue of support initiatives

Margherita Guidi

Communicatios officer, APDESK unit

Trusted science for safe food

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European Food Safety Authority

The Catalogue

European Food Safety Authority

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Applications helpdesk

All the resources you need to assist you with the submission and the monitoring of an application for regulated products, substances and processes, and the substantiation of claims submitted for authorisation in the European Union.

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Check out our updated Administrative guidance for the processing of applications for regulated products

Update:

- Webinar series to support applicants - Read the news
  - First webinar on: Application procedure for food enzymes, food flavourings and food additives (04/06/2021)

Featured

New rules on transparency: detailed arrangements for stakeholders

The new regulation aimed at increasing the transparency of risk assessment in the food chain becomes...

Dedicated support for small and medium-sized enterprises

EFSA has launched new support initiatives dedicated applicants from small and medium-sized...

No ha de

https://www.efsa.europa.eu/en/supporting/pub/en-6472

EFSA's Catalogue of support initiatives during the life-cycle of applications for regulated products (update 2021)

Published: 3 March 2021

EFSA Journal on the Wiley Online Library

Read the article

Access the PDF

DOI: https://doi.org/10.2903/sp.efsa.2021.EN-6472

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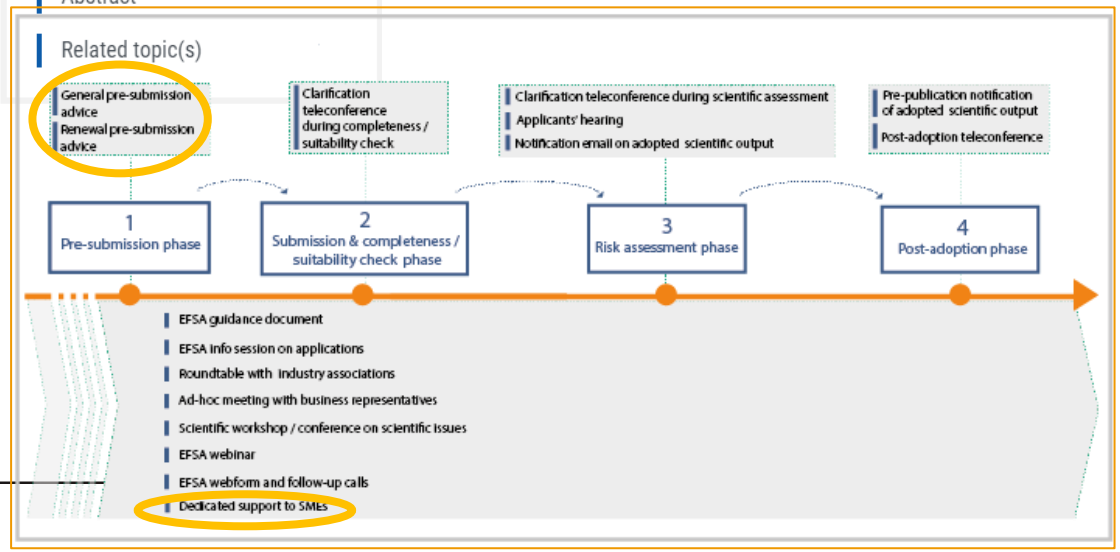


Metadata

EFSA Journal 2021;18(3):EN-6472

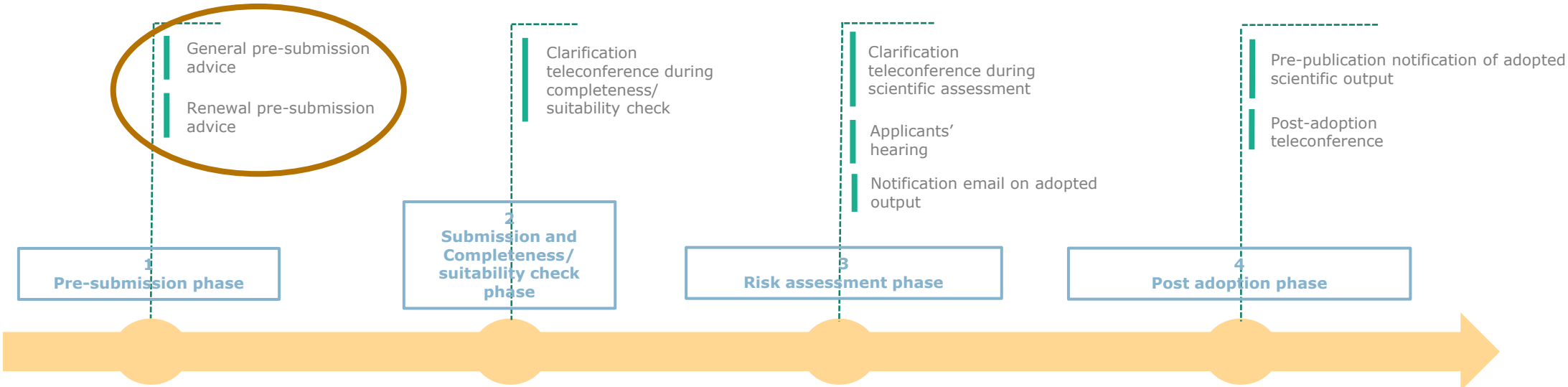
On request from: European Food Safety Authority

Question Number: EFSA-Q-2020-00363

Contact: apdesk.applications@efsa.europa.eu

This publication is linked to the following EFSA Supporting Publications articles: http://onlinelibrary.wiley.com/doi/10.2903/sp.efsa.2021.EN

Overview of the initiatives



- EFSA Guidance documents
- EFSA Info session on applications
- Roundtable with industry associations
- Ad-hoc meeting with an industry association
- Scientific workshop/ conferences
- EFSA webinar
- Web form & follow-up phone calls
- Dedicated support to SMEs

Overview of the initiatives

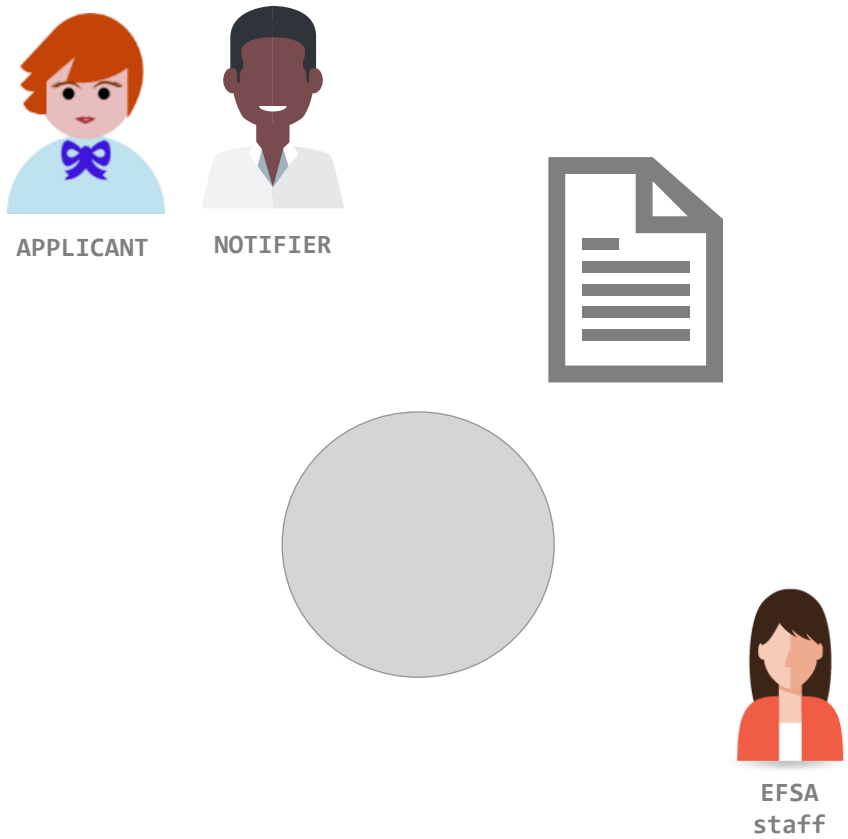
- General pre-submission advice
- Renewal pre-submission advice

1
Pre-submission phase

1 Click to add text

- Guidance docs
- Info session on applications
- Scientific workshop/ conferences
- Roundtable with industry associations
- Ad-hoc meeting with an industry association
- REPRO webinar
- Web form & follow-up phone calls
- Dedicated support to SMEs

General pre-submission advice (GPSA)



Potential applicants or notifier

Indication on the rules applicable to, and the content required for, the application.

Potential applicant/notifier, EFSA staff

Anytime, preferably at least six months before submission.
Max two advice per application:
- Written advice is provided within 15 working days;
- In a meeting, it is organized within 20 working days as of the acceptance (max 1h)

Filling in the dedicated 'GPSA form'

Applicable rules and the required content of an application

Summary sent to the potential applicant and made public together with the non-confidential version of the application dossier once the application is declared valid.

Background

Transparency regulation Article **32a**

1. **Applications meet the applicable specifications** in order to ensure the best quality scientific assessment

2. **Rules** applicable to, and the **content** required for, the application, prior to its submission. Should not address the design of the studies to be submitted

3. Small and medium sized enterprises **-SMEs-**

Regulation (EC) No 178/2002 as last amended by Regulation (EU) 2019/1381 of the European Parliament and of the Council of 20 June 2019 on the transparency and sustainability of the EU risk assessment in the food chain

General Pre-submission Advice - Business Operators

Sarah

Potential applicant may **request** general pre-submission advice at **any time**

Requests for general pre-submission advice

Submit to EFSA

HOW?

Link requests to the individual or joint pre-application ID

Fill in the general pre-submission advice form available on the EFSA's website

Submit questions

Up to 2 G-PSA per pre-app ID

General Pre-submission Advice form

Conditions of use/intended uses

Background information on the subject

List of questions

General Pre-submission Advice - EFSA

Receipt of the general pre-submission advice form

Step 1
Administrative Check

EFSA verifies that the related questions **fall within the scope**

Within **15 working days** from the receipt, EFSA informs the requester as to whether the request is **accepted or rejected**.

Step 2
Written or meeting

Where possible, EFSA shall answer the questions in **writing**

A meeting might be organised by EFSA

Step 3
Provide the Advice

The written advice shall be provided within **15 working days** as of the date of the acceptance of the request;

The meeting shall be organised within **20 working days** as of the date of the acceptance of the request

Step 4
Summary of the PSA

EFSA draws up a **summary** providing an overview of the advice and sends it to the requester for information

Webinar recordings on NoS and GPSA

16/02/2021	Notification of Study and Pre-submission Advice	Business Operators	Webinar (recording and supporting material)
25/03/2021	Notification of Study and Pre-submission Advice	Business Operators	Webinar

New videos/training material will be shared soon

- General pre-submission advice
- Renewal pre-submission advice

1 Pre-submission phase

- Guidance docs
- Info session on applications
- Scientific workshop/ conferences
- Roundtable with industry associations
- Ad-hoc meeting with an industry association
- REPRO webinar
- Web form & follow-up phone calls
- Dedicated support to SMEs

Administrative support to SMEs

Potential applicants

Direct assistance provided by APDESK staff on any administrative aspects related to the preparation of an application of a regulated product

EFSA staff, SME applicant

1hour up to 2 hours

Dedicated email: SMEoffice@EFSA.europa.eu

Support on applicable EFSA guidance documents, workflows, procedures, information needed, etc.

Acknowledgment email with main points discussed

Fast processing of queries submitted by SMEs

- Any SME interested in the area of regulated products established in the EU
- Front office and support desk on regulated products related matters targeted to SME
- SME applicant
- Responses to web form requests are provided within 7 working days
- Fill-in the web form available on EFSA's Applications web section
- Administrative and scientific issues, EU regulatory framework, guidance documents requirements, procedural steps, status of specific applications
- Individual answer to requests within 15 working days from receipt

Engagement with stakeholders & applicants

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Transparency Regulation and stakeholder engagement

Regulation', until entry into application in accordance with an engagement framework jointly agreed and aligned between EFSA and DG SANTE. This interaction has been separate and in addition to the Stakeholder Engagement Approach (SEA), which continued to be carried out in line with the Management Board Decision on the criteria for establishing a list of stakeholders and the establishment of the Stakeholder Forum and Stakeholder Bureau.

Following the conclusion of the main implementation phase leading up to the entry into application of the Transparency Regulation, EFSA will continue its stakeholder engagement on the Transparency Regulation through the fora foreseen by the Stakeholder Engagement Approach (SEA).

During the main implementation phase leading up to the entry into application of the Transparency Regulation, EFSA followed the following engagement framework.

Applicable principles/framework during the main implementation phase

- **Independence**: No undue influence has been allowed at any time during the implementation. DG SANTE and EFSA have informed stakeholders about the implementation of the Transparency Regulation in dedicated fora. No details regarding the implementation have been discussed with stakeholders, nor has any material been produced jointly with stakeholders. No substantive reply has been provided to individual stakeholder input outside the dedicated fora.
- **Transparency**: Full transparency will be ensured throughout the process. DG SANTE and EFSA will address stakeholders' questions, positions, comments or feedback in the relevant fora in full transparency. A calendar of planned events will be communicated to stakeholders.
- **Openness**: DG SANTE and EFSA have provided timely and clear information on the implementation to all stakeholders.
- **Inclusiveness**: The dedicated fora in which the implementation has been discussed has been inclusive and stakeholders have been treated equally in the discussions. In meetings of a general nature all stakeholder categories have been invited. In technical meetings where expertise of one or more specific stakeholders' categories was needed, other categories have also been invited as observers.
- **Flexibility**: Physical and/or on-line meetings will be complemented by dedicated public consultations where needed.
- **Non-duplication**: There has been, as far as possible, no duplication between the existing stakeholder engagement fora and the fora dedicated to implementation of the Transparency Regulation.

Main engagement fora during the main implementation phase

EFSA has engaged with stakeholders on the implementation through two main channels - the Sounding Board and technical groups.

- **Sounding Board**: The objective of the Sounding Board was to keep stakeholders informed about the state of play of implementation in general, to collect comments stakeholders may have and to address questions where possible. It was composed of the Stakeholder Bureau members and up to one additional member per stakeholder category, Advisory Forum representatives and the European Commission.
- **Technical groups**: The objective of technical groups is to inform stakeholders about the implementation process and to gather

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Transparency Regulation Implementation Training Programme

Date	Title	Target audience	Material
20/11/2020	Implementing the Transparency Regulation: Requirements, tools and services	All	Webinar
20/11/2020	Transparency Regulation: What's new for business operators and applicants?	Business Operators	Video Introduction
20/11/2020	Table of Contents (TOC) for application submission	Business Operators	Video Introduction
13/01/2021	Account registration / AskAQuestion	All	Video Introduction Video Tutorial
22/01/2021	Public Access to Document (PAD)	All	Video Tutorial
30/03/2021	OpenEFSA Portal: Features implementing the Transparency Regulation	All	Video Introduction

Webinars per food sector area

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Regulated products: webinar series to support applicants

Published: 20 May 2021

https://www.efsa.europa.eu/en/news/regulated-products-webinar-series-support-applicants

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Transparency Regulation Implementation Training Programme

04/06/2021	Application procedure for food enzymes, food flavourings and food additives	Business operators, small and medium-sized enterprises, laboratory/testing facilities	Webinar
July 2021	Application procedure for feed additives	Business operators, small and medium-sized enterprises, laboratory/testing facilities	Webinar
September 2021	Application procedure for pesticides active substances and MRL	Business operators, small and medium-sized enterprises, laboratory/testing facilities	Webinar
October 2021	Application procedure for novel food	Business operators, small and medium-sized enterprises, laboratory/testing facilities	Webinar
November 2021	Application procedure for GMO	Business operators, small and medium-sized enterprises, laboratory/testing facilities	Webinar
December 2021	Application procedure for smoke flavourings	Business operators, small and medium-sized enterprises, laboratory/testing facilities	Webinar
January 2022	Application procedure for health claims	Business operators, small and medium-sized enterprises, laboratory/testing facilities	Webinar
February 2022	Application procedure for Food Contact Materials	Business operators, small and medium-sized enterprises, laboratory/testing facilities	Webinar

Hyperlink

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Post-public consultation stakeholder event
21-22 June 2021

New Guidance for Submission of Dossiers on Food Enzymes

Confidentiality decision making after the Transparency Regulation in the food enzymes sector

Simone Gabbi

Team Leader, Legal & Assurance Services

Trusted science for safe food

European Food Safety Authority

Underlying principles

Assessment of confidentiality requests

- Proactive disclosure of application dossiers
- Confidentiality as exception to transparency
- Burden of proof on applicants
- Non-disclosure of information claimed confidential pending decision-making

Procedural requirements

- Submission through E-Submission Food Chain Portal
- Including verifiable justifications, a confidential and a non confidential version of the document
- Providing clarifications ONLY if requested to do so by EFSA
- Submit clarifications within the deadline set by EFSA
- Modifications of submitted requests not allowed, unless requested by EFSA
- No fees

Procedural requirements – follows

only on items on closed positive list. For this sector:

- information provided in detailed descriptions of starting substances and starting preparations and on how they are used to manufacture the substance subject to the authorisation, and detailed information on the nature and composition of the materials or products in which the applicant intends to use the substance subject to the authorisation, except for information which is relevant to the assessment of safety;
- detailed analytical information on the variability and stability of individual production batches of the substance subject to the authorisation, except for information which is relevant to the assessment of safety;
- the manufacturing or production process, including the method and innovative aspects thereof, as well as other technical and industrial specifications inherent to that process or method, except for information which is relevant to the assessment of safety;
- commercial links between a producer or importer and the applicant;
- commercial information revealing sourcing, market shares or business strategy of the applicant;
- quantitative composition of the subject matter of the request, except for information which is relevant to the assessment of safety

Non-disclosure of Personal Data

The non-confidential version of the application dossier shall not contain personal data of any kind, with the exception of:

- name and address of the applicant
- names of authors of published/publicly available studies supporting the application
- names of all participants and observers in meetings of the Scientific Committee and the Scientific Panels, their working groups and any other ad hoc group meeting on the application

Submit confidentiality requests for other personal data to be withheld from disclosure including names and addresses of individuals involved in testing on vertebrate animals or in obtaining toxicological information.

Substantive requirements

Identifying clearly the information claimed confidential, possibly references

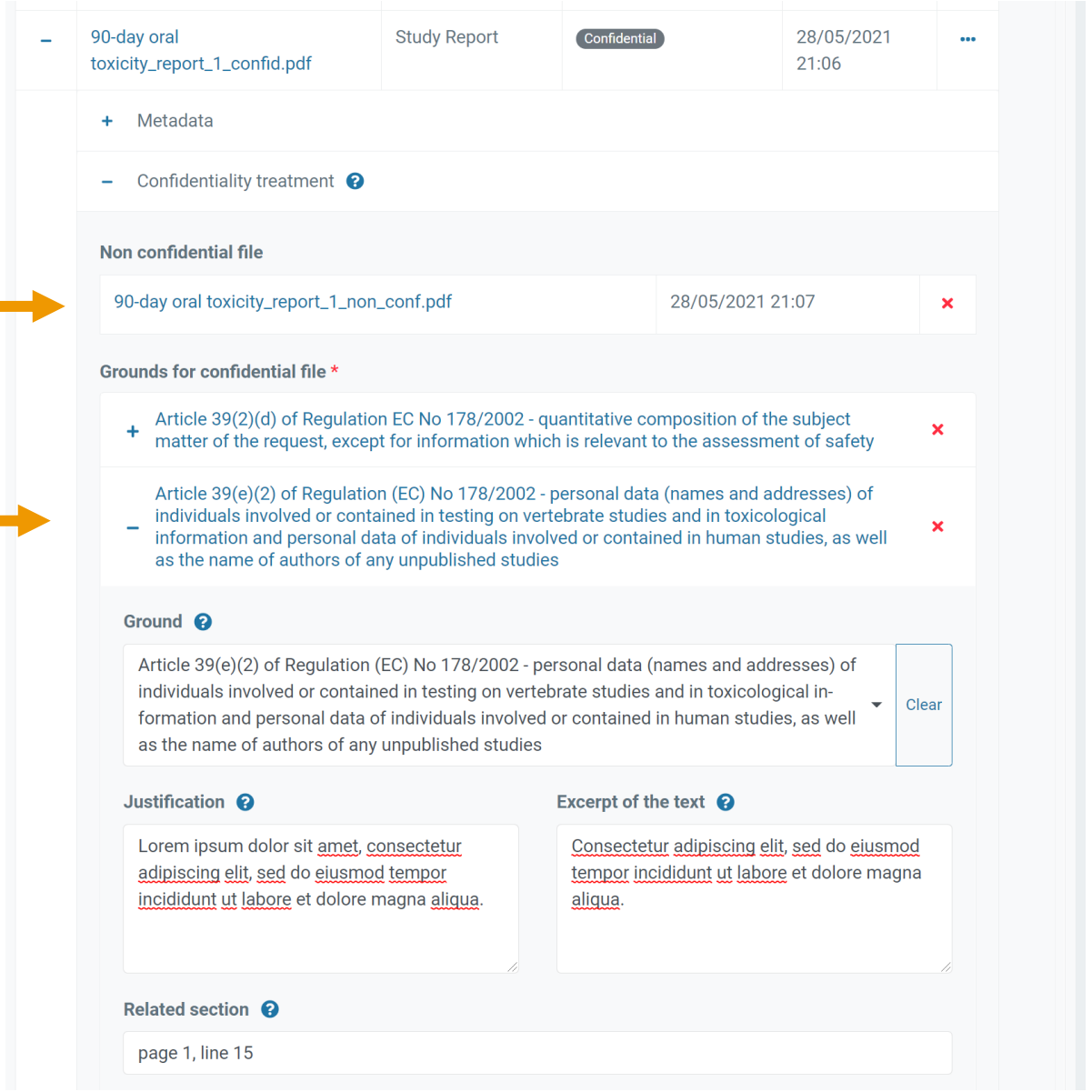
Indicating the legal basis (grounds)

Explaining why the item should be kept confidential:

- Information not publicly available
- Potential harm to a significant degree
  - Information acquired legitimately
  - Negligible harm – rebuttable presumption
  - Novelty – rebuttable presumption
- Clarification on whether «environmental information»

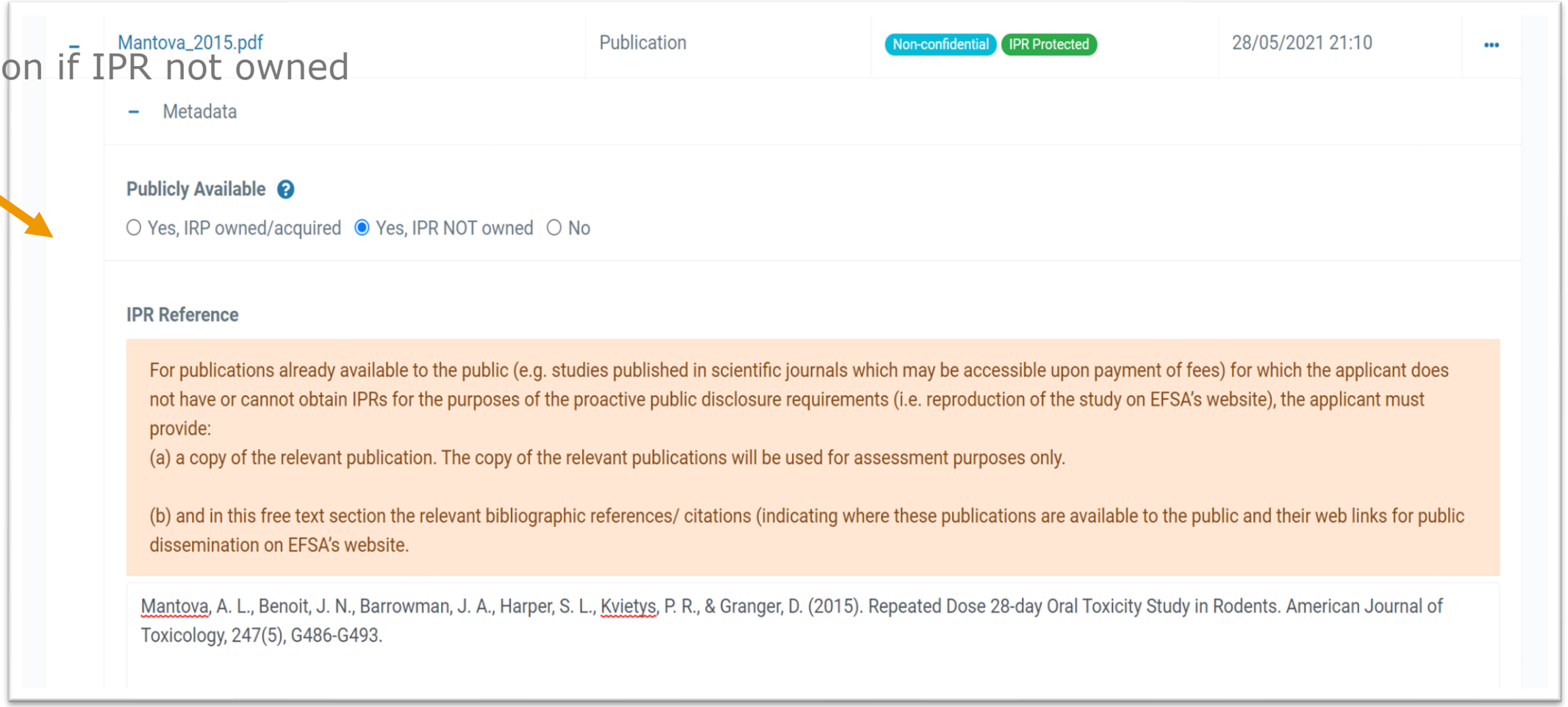
Building a Confidentiality Request

- Provide non-confidential file
- Define your request:
  - Legal ground
  - Justification
  - Excerpt
  - Location in file
- Add requests, as required



Published studies

Give full citation if IPR not owned



Procedural steps EFSA confidentiality assessment

STEPS

Mandatory notification of draft decision to the applicant for comments

Notification of the final decision to the applicant

Possibility to file confirmatory application via tool or email to

Confidentialityconfirmatory application@efsa.europa.eu

Implementation of confidentiality decisions - sanitisation

EFSA may review its decision in case output identifies foreseeable effects on human health, animal health or the environment *(Art 39c GFL)*

Useful documents

Legal documents

- TR: Regulation (EU) 2019/1381
- General Food Law: consolidated text of Regulation (EC) No 178/2002
- Food Additives, Food Enzymes and Food Flavourings Regulation: consolidated text of Regulation (EC) No 1331/2008
- PAs on transparency and confidentiality: Practical Arrangements concerning transparency and confidentiality

Guidance/training materials

- Q&As on PAs: Questions and Answers on the EFSA Practical Arrangements
- Updated administrative guidance for the preparation of applications on food improvement agents (food enzymes, food additives and food flavourings)
- Training material, including video introductions/tutorials and webinar recordings, are available under the dedicated section "Transparency Regulation Implementation Training Programme" on the EFSA website