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Inconclusive opinions: why and how to avoid them

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Trusted science for safe food

European Food Safety Authority

EFSA Scientific Opinions on Food Enzyme Evaluation

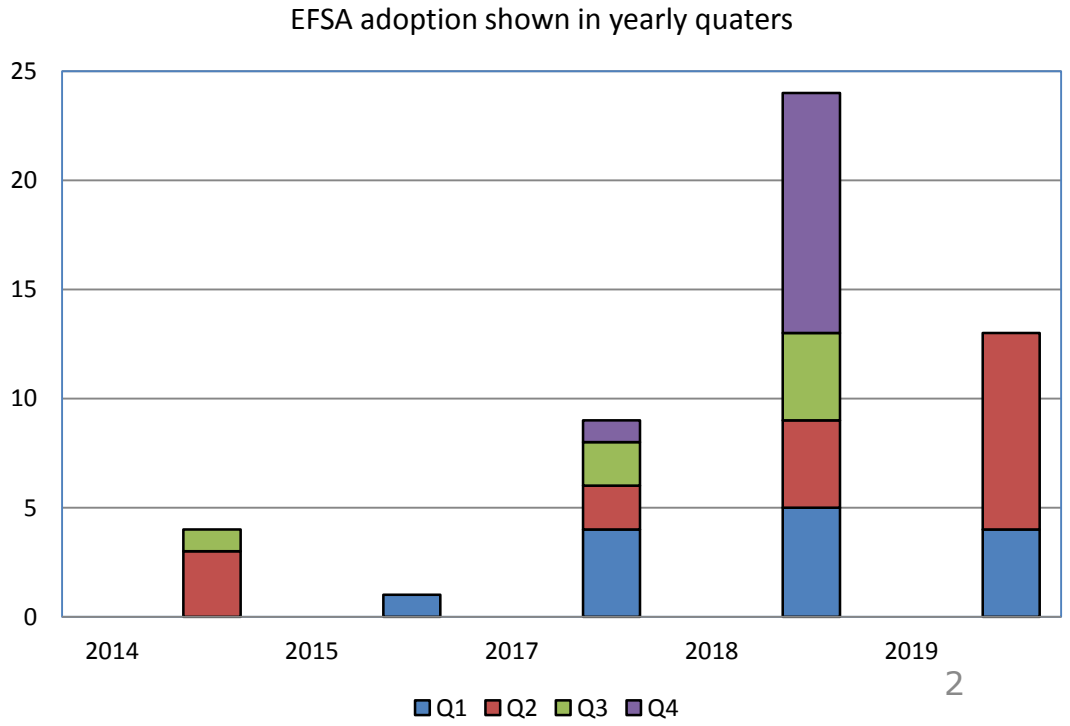
- Among 51 adopted opinions, 4 were inconclusive.

- Undesirable for both applicants and EFSA
  - Applicants —› commercial, reputation
  - EFSA —› resources, customer value

We aim for:

- High efficient and good quality

- Less to zero inconclusive opinion



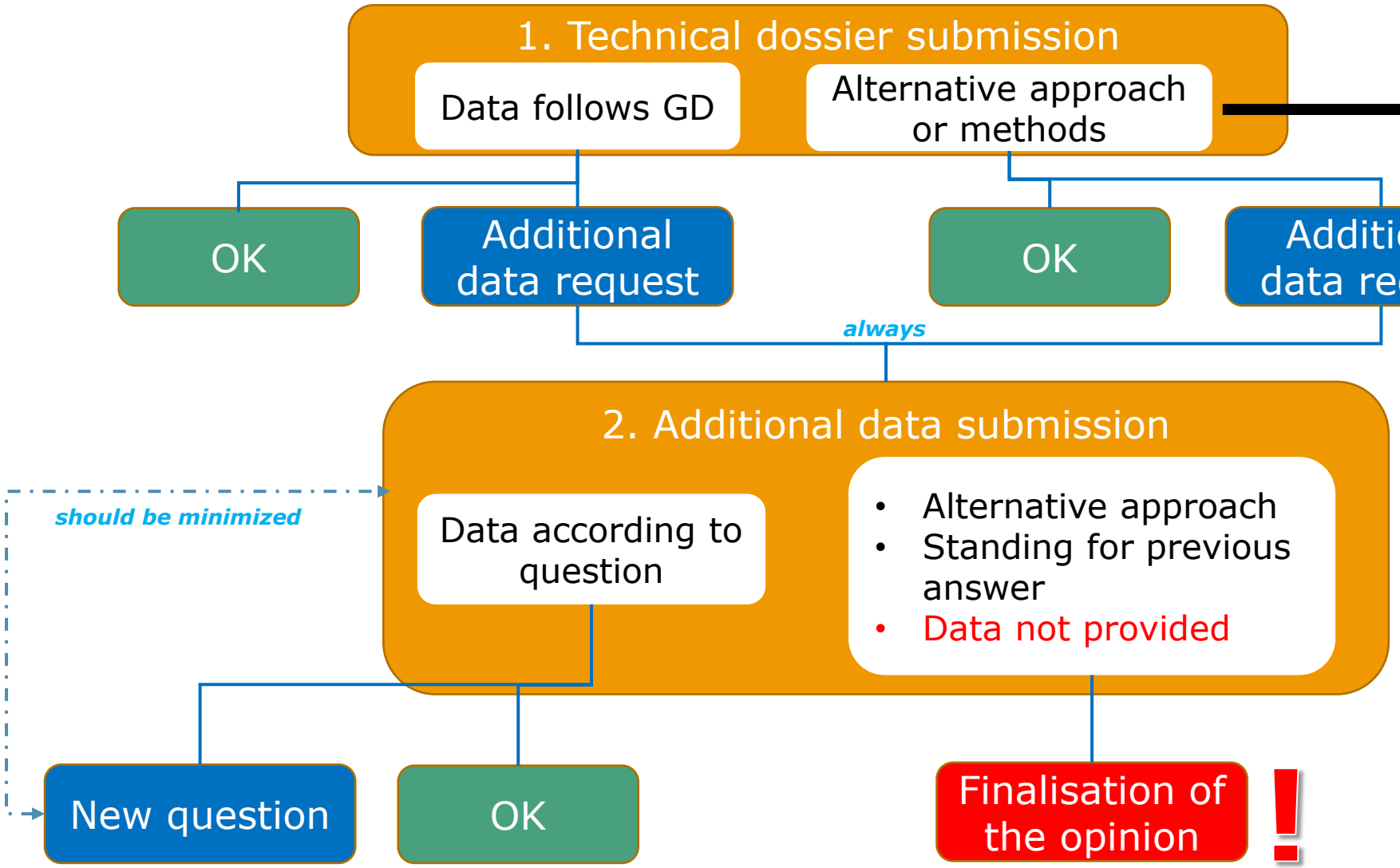
Inconclusive opinions

Problem	Affected opinion	What is missing
Antimicrobial resistance gene	1	Although requested, insufficient information was provided on the methodology applied to show the absence of viable cells.
Quality of the AMES test	1	Although requested, additional test was not provided to rule out false positive.
Incomplete AMES test	1	Missing a strain to evaluate gene mutations by DNA oxidising or cross-linking mechanisms.
Insufficient margin of exposure	1	Missing information on the tox-batch used in 90-day, *"……concentration procedure did not only result in the loss of water, but apparently also led to a loss of TOS constituent…"*

Can they be avoided?

Often not very difficult

Additional Data Request



- Rationale provided
- Full methodology
- Robust dataset

A guiding principle:

Chance to providing missing information and/or clarification should always be given.

EFSA should not reiterate questions

Answer to EFSA Data Request

- Do's
  - Answer all the questions and provide all the requested information
  - If questions unclear
  - If something not understood
  - If problems in obtaining data

  } Contact EFSA

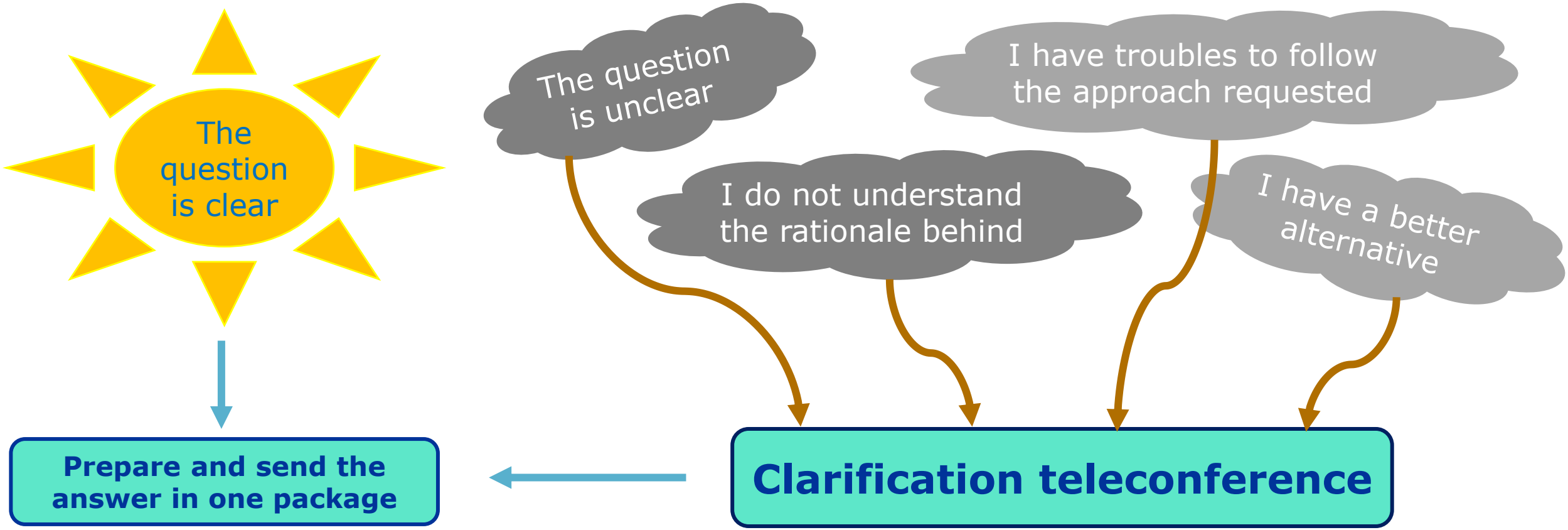
- Suggestions
  - Reject or refute data/information requests, the WG/Panel needs explanations/justifications
  - When providing alternative approaches, to justify and explain clearly

Examples of Challenging Answers Received

- *"the information was already provided in the first submission"* (but in reality, was missing)
- *"[experiments have been made] at the adequate temperature and with the adequate incubation time"* (without explaining the adequacy)
- *"We do not keep records of that study, therefore we cannot provide the data"* (against good laboratory practice)
- *"this request is unjustified and in contradiction to EFSA's own"*
- *"the requested additional tests would be superfluous"*
- methods used to determine metabolites: semi-illegible scan of a paper from the 1970s (most probably obsolete or incomplete in 2019)

Meeting Data Requirement

- Data requirement: follow the guidance documents
- Flexibility: GD requirements may be substituted by **alternative approaches/methods**
  —› **duly justified**



Need more time? –notify asap fip@efsa.europa.eu **– proportionality and justification to be provided**

CLARIFICATION TELECONFERENCE

- Telephone conference with EFSA staff, following a letter from EFSA requesting additional information
- Upon request by the applicant and/or by EFSA
- Exceptionally, participation of EFSA's experts

Explanations

Analysis

Warnings

Can't

X Anticipate Panel/WG decisions
X Conduct assessments
X Discuss beyond additional information requests

Margin of Exposure

MoE = NOAEL / Dietary exposure to FE-TOS

- Generally NOAEL corresponds to the highest dose tested

The chances are ↗ Dose level tested, ↗ NOAEL

- Exposure estimates = use level of FE-TOS X food consumption

The chances are ↙ use level, ↙ dietary exposure

Spontaneous Information

At submission, an application should be complete, *i.e.*, all relevant information are included. Spontaneous Information should, therefore, be limited to new data.

- submit spontaneous information as early as possible, and explain how it may influence the risk assessment
- To be considered:
  - Needed? —› addressing safety concerns
  - May delay adoption —› further assessment is needed
  - Follow-up data for inconclusive opinions ≠ spontaneous information —› wait until the procedure is clear

Confidentiality: final decision to be taken by the EC

Reg. (EC) 1331/2008

Article 12

Confidentiality

1. Among the information provided by applicants, confidential treatment may be given to information the disclosure of which might significantly harm their competitive position.

Information relating to the following shall not, in any circumstances, be regarded as confidential:

(a) the name and address of the applicant;

(b) the name and a clear description of the substance;

(c) the justification for the use of the substance in or on specific foodstuffs or food categories;

(d) information that is relevant to the assessment of the safety of the substance;

(e) where applicable, the analysis method(s).

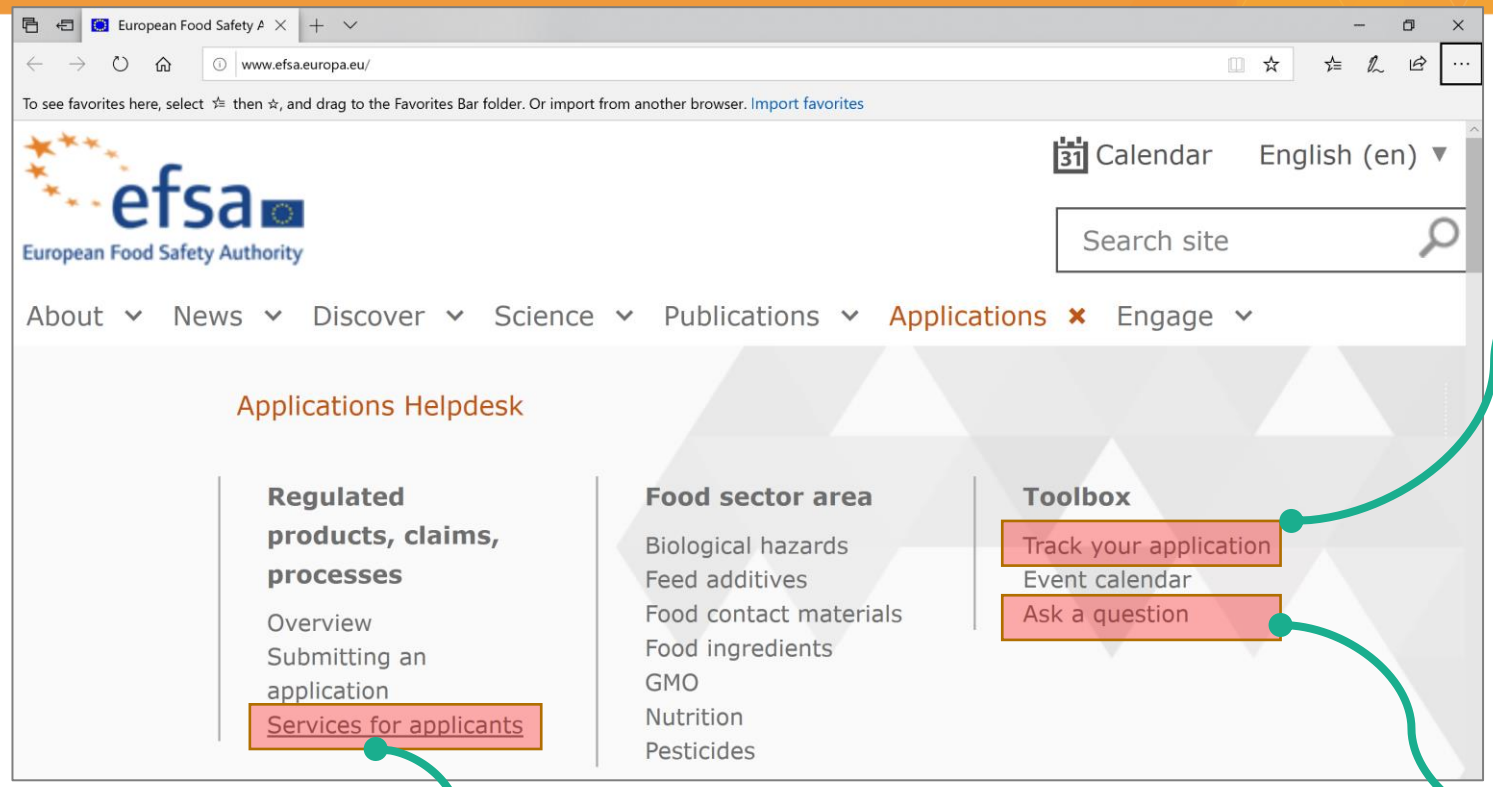
2. For the purposes of implementing paragraph 1, applicants shall indicate which of the information provided they wish to be treated as confidential. Verifiable justification must be given in such cases.

In EFSA opinion:

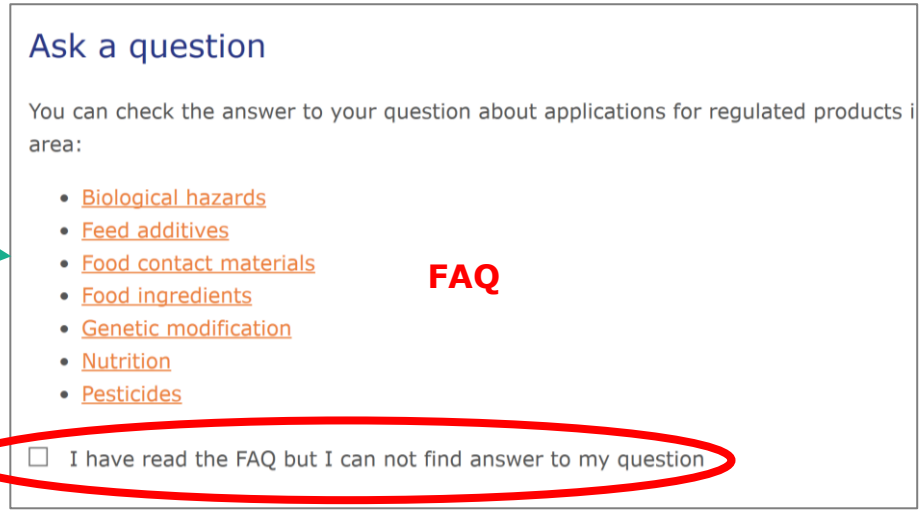
- **No redaction to the following**
  - Information relevant to the assessment of the safety of the substance
  - Potential hazard

- **Redaction is applied to the know-how of individual applicants**, e.g.
  - Names of parental and recipient strains
  - Genetic modification leading to the creation of a production strain
  - Technical details in the food enzyme manufacturing process
  - Specific technical yield factors
  - Name of study directors

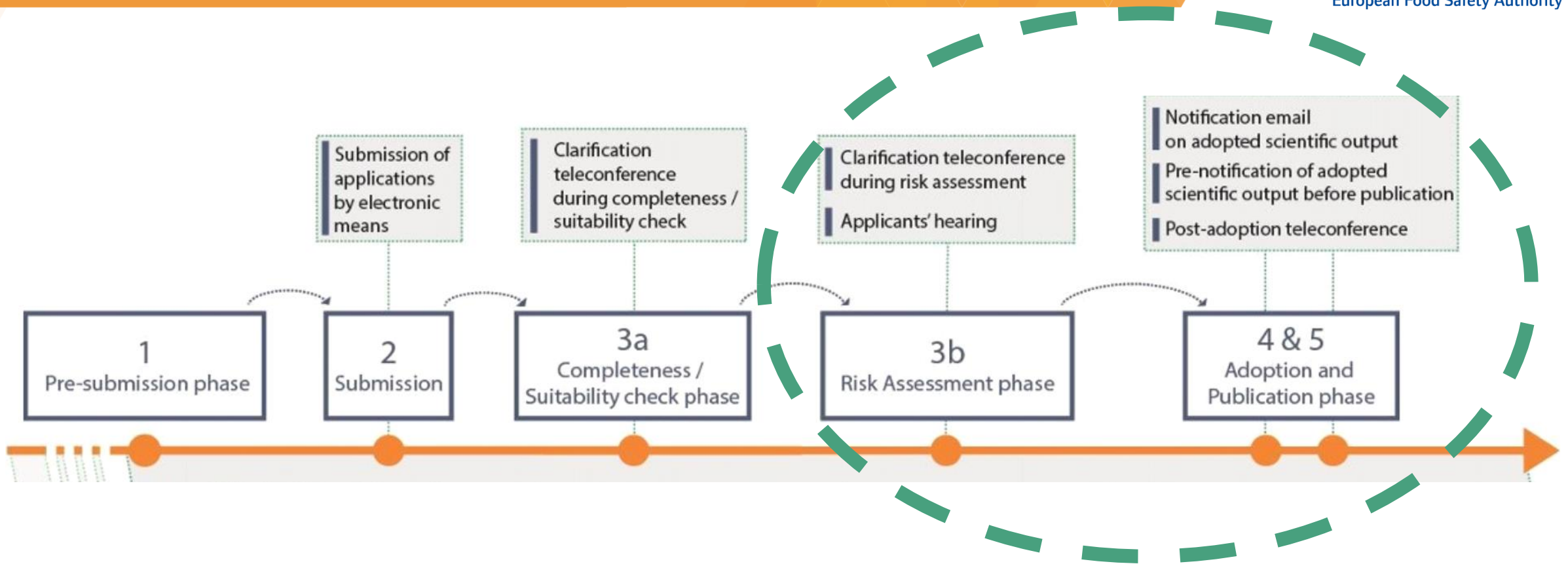
Interaction with EFSA – Multiple Channels



Searchable by question number, key words



Catalogue of Services for Applications



- ✓**Clarification teleconference** – frequent in dealing with Add Info request
- ✓**Applicant hearing** – only for complex issues
- ✓**Pre-notification** – 36 hours prior, for administrative purpose, only editorial comments
- ✓**Post-adoption teleconference** – to explain why inconclusive

Principle in Processing Food Enzyme Applications

TECHNICAL REPORT

APPROVED: 15 December 2017

doi:10.2903/sp.efsa.2018.EN-1362

Administrative guidance for the processing of applications for regulated products

European Food Safety Authority

- **Transparency, Impartiality & Independence**
- **Efficiency, Dialogue, Equal treatment**
- **Data protection / confidentiality compliance**

Take Home Message

- EFSA does not issue an inconclusive opinion upon first submission
- EFSA endeavors to send all questions once or twice (not unlimited number of times)
- EFSA asks the same question only once. Answers may trigger further questions/clarifications, but lack of answer will not.
- EFSA endeavors to explain rationale behind the request, and is open to clarify via tele-conferences
- EFSA shall not warn beforehand the possibility of an inconclusive opinion
- The more adherence to GD and additional requests —› the less chance of inconclusive opinion