Feed Additive Registrations – the Post-Transparency and BREXIT Era

In 2021, the European animal nutrition and health market is facing two important regulatory changes that impact how feed additives are registered. The first challenge is the application of the Transparency Regulation and subsequent changes to the European Food Safety Authority (EFSA) risk assessment of such products. The second one is the withdrawal of the UK from the European Union (EU). The main consequence of these changes is that applicants now need more time and investment to achieve feed additive approval in two different and increasingly divergent geographical and regulatory markets. In the case of the Transparency Regulation, applicants must now comply with complex pre-application activities that did not exist before. There are new stringent EFSA rules on permitted claims for confidentiality and protection of intellectual property, as well as the obligation to redact out personal data covered by the EU General Data Protection Regulation (GDPR). In relation to BREXIT, a separate application is required by the UK authorities, who perform their own risk assessment under a new and independent framework.

In the EU, EFSA is responsible for the risk assessment of all food chain REgulated PROducts (REPRO) and all GMOs, including feed additives. Since 27 March 2021, EFSA applies the provisions of the recent Transparency Regulation (1, Regulation (EU) 2019/1381 of the European Parliament and of the Council of 20 June 2019). Two of the main objectives of this regulation are:

- To increase the transparency of the EU risk assessment in the food chain.
- To strengthen the reliability, objectivity and independence of the studies used by EFSA for their assessment.

To achieve these objectives, EFSA and EU authorities have developed a series of new requirements and procedures with which applicants must comply when developing feed additive dossiers, particularly those related to pre-submission activities.

Notification of studies using the EFSA Connect Portal (Transparency Regulation, Article 32B)

All studies performed after 27 March 2021 for supporting feed additive applications must be notified using the EFSA Connect Portal (2) before the study start date. For each study, applicants must notify the following information:

- Title of the study.
- Scope (intended study area, study type, study international standard certification, study objective, test item).
- Name of the laboratory/contract research organisation (CRO) where the study will be performed.
- Study planned start and end date.

Additionally, laboratories/CROs located in the EU, Iceland, Liechtenstein, Norway and Northern Ireland must co-notify studies and, therefore, should also be registered on the EFSA Connect Portal. This notification obligation will not only apply to studies performed before dossier submission, but also to those studies submitted in reply to a request for supplementary information made by EFSA (e.g., during dossier validation or as a result of an EFSA "clock-stop") or as part of an applicant's spontaneous submission.

The notification requirement has generated considerable anxiety and uncertainty within the industry, since, in addition to the logistical implications (e.g., access to the EFSA database may take 3–4 weeks; only 6 EFSA accounts per company are allowed; there are difficulties to establish the exact start and end date of studies; there is no test platform so applicants can learn how the system works), applicants may incur time penalties affecting EFSA's risk assessment process if studies are not notified properly,[1,3] as illustrated below:

- If the study is not notified but is included in the dossier submitted to EFSA (and there is no acceptable justification for the failure to notify): the dossier must be resubmitted after notification and the assessment of the validity of the resubmitted application will be delayed for 6 months.
- If the study is notified but not included in the dossier submitted to EFSA (and there is no acceptable justification for non-inclusion of the study): the dossier must be resubmitted including all studies notified and the assessment of the validity of the resubmitted application will be delayed for 6 months.
- If a notified study is submitted only partially to EFSA (e.g., there are missing data in the report with no acceptable justification): the assessment of the validity of the application will start 6 months after submission of the pending information/data.

EFSA is still pending to clarify if applicants could incur consecutive time penalties if, for example, they do not notify a study and there is also missing data/information in a study report. Regarding public access to study data for transparency purposes, the regulation establishes that the notified information for each study will be made publicly available once EFSA receives a valid application and after EFSA's confidentiality assessment, which will be performed following an applicant's request.

Renewal of feed additive authorisations: pre-submission advice after public consultation (Transparency Regulation, Article 32C-1)

EU feed additive authorisations must be renewed every 10 years, and the renewal dossier must be submitted 1 year before the expiry date. For renewal dossiers, the Transparency Regulation requires applicants to pre-notify intended new studies and to request renewal pre-submission advice, as follows:

- Prepare a list of intended studies: for each study, applicants must provide the study title, study scope (study intended area, study type, study objective, test item), study guideline to be followed (if applicable) or study design description (including the study hypothesis).
- Submit the study list using the EFSA Connect Portal.
- EFSA conducts an administrative check (10 working days) to confirm that the list is compliant with EFSA's new rules (Transparency Regulation and Practical Arrangements) and may seek clarifications. Afterwards, EFSA launches a

public consultation within 10 working days of completion of the administrative check. The public consultation remains open for 3 calendar weeks, and all interested parties can provide comments using the EFSA Connect Portal.
- After completion of the public consultation, EFSA "without delay" publishes all valid comments received from stakeholders.
- EFSA's renewal pre-submission advice (PSA) is provided to applicants within 30 working days after closure of the public consultation, mainly in written format.
- The PSA provided by EFSA contains information on the content of the application and study design, and a summary PSA is published once the application is considered valid. EFSA PSA is non-binding to both EFSA and applicants.

Pre-submission advice for new applications (Transparency Regulation, Article 32A)
Applicants may choose to request PSA for new feed additive dossiers. This is limited to:

- The applicable rules considering the feed additive's characteristics and intended use.
- The dossier content required.

Notably, advice on study design, a key area of interest to applicants, is excluded for new applications. Again, EFSA provides advice to applicants mainly in written format, and a summary is made public after the application is validated.

Confidentiality assessment (Transparency Regulation, Article 39; Annex I, EFSA Practical Arrangements)
An important novelty of the Transparency Regulation is the switch from the EU Commission to EFSA in relation to decision making on confidentiality requests. For feed additive dossiers and upon request of the applicant, EFSA may grant confidentiality only to:[1,4]

- The study plan for studies demonstrating the efficacy of a feed additive in terms of the aims of its intended use.
- Specifications of the impurities of the active substance and the relevant methods of analysis developed internally by the applicant, except for impurities that may have adverse effects on animal health, human health, or the environment.
- 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 or the authorisation holder, where applicable.
- 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.
- Personal data (names and addresses) of individuals involved in testing on vertebrates or in obtaining toxicological information.
- Any other personal data, except for the name and address of the applicant, the names of authors of published or publicly available studies supporting such requests and the names of all participants and observers in meetings of EFSA's Scientific Committee and Scientific Panels, their working groups and any other ad hoc group meeting on the subject matter.

For each piece of information claimed as confidential, applicants must provide an acceptable written justification.

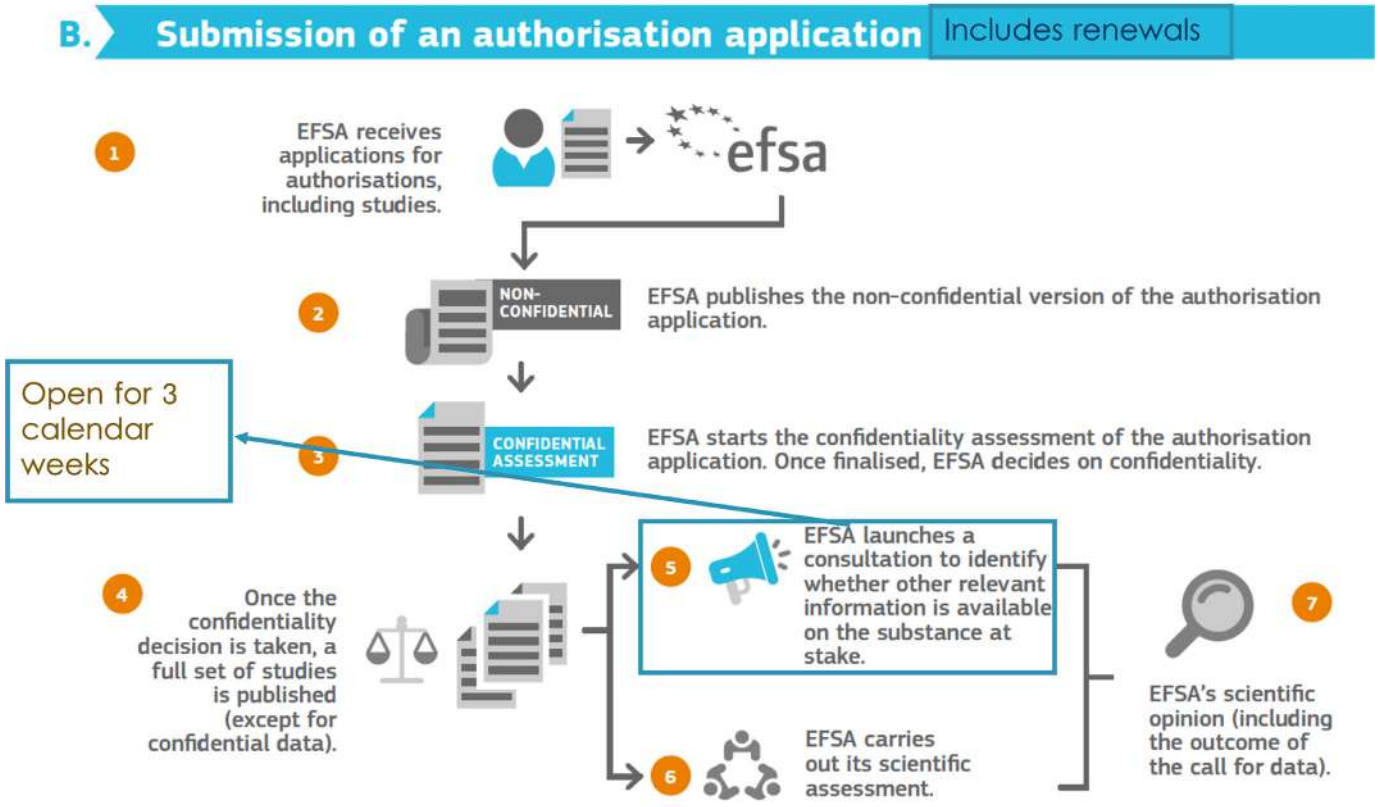

Figure 1. Submission of an authorisation application (European Commission factsheet at https://ec.europa.eu/food/safety/general_food_law/transparency-and-sustainability-eu-risk-assessment-food-chain_en)

The main justifications acceptable to EFSA are outlined in Article 10 of EFSA's Practical arrangements concerning transparency and confidentiality,[4] e.g.:

- The data for which confidential status is requested are not publicly available.
- The data are known only to a limited number of persons.
- Public disclosure of the data may harm the interests of the applicant to a significant degree.

EFSA's decision on confidentiality is taken within 10 calendar weeks after receiving the request and before the risk assessment starts. However, another notable change applied by the Transparency Regulation is that confidentiality requests will be assessed twice – after dossier validation and when EFSA finalise their scientific evaluation (i.e., before publication of EFSA's opinion). This means that EFSA can change its original decision on confidentiality and mandate the release of additional information from the dossier to the public.

Public consultation after dossier submission (Transparency Regulation, Article 32C-2)
Applicants must prepare two dossiers for EFSA: a confidential and a non-confidential version. The latter excludes all claimed confidential information by applicants and is released to the public for consultation. Apart from the key objective of transparency, EFSA also seeks to identify other relevant information (e.g., scientific data, studies) for EFSA's assessment. EFSA will publish the outcome of this data call in addition to EFSA's scientific opinion. If EFSA rejects any of an applicant's confidentiality requests, this information is also released to the public after discussing with the applicant. The public consultation remains open for 3 calendar weeks and is carried out in parallel to EFSA's risk assessment (Figure 1). EFSA will make available the information for the public on their website, in an electronic format that can be downloaded, printed and searched.

Standard data formats (Transparency Regulation, Article 39F)
EFSA will draft standard data formats for submission of documents such as dossier templates, replies to the authority, and submission of supplementary information. These standard data formats will be available online, will allow search, copy, and print functions, and will comply with EU regulatory requirements.

Verification studies (Transparency Regulation, Article 32D)
If not convinced by data supporting an application dossier, EFSA may commission studies to verify the evidence, and such studies may have a wider scope than that considered in the original application.

Fact-finding missions (Transparency Regulation, Article 61A)
A commission of experts selected by EFSA may visit laboratories and CROs involved in studies supporting application dossiers with the objective of assessing:

- Compliance with relevant quality standards.
- Compliance with notification of studies to the EFSA Connect Portal.

In addition to EU locations, these fact-finding missions may visit facilities in third countries who have agreements with the EU (e.g., Iceland, Liechtenstein and Norway).

New platforms for pre- and post-submission activities
In addition to the EFSA Connect Portal, applicants must use another 2 platforms for feed additive registrations: the E-Submission Food Chain Platform (ESFCP, 5) and Portalino.[6]

The ESFCP is web-based and allows applicants to build the dossier, track progress of EFSA's risk assessment, reply to questions from EU authorities (EFSA, EU Commission), withdraw applications, as well as to provide comments on draft EFSA opinions and EFSA's confidentiality assessment. Portalino is a platform for submitting confidentiality requests related to datasets and documents supporting mandates that EFSA receives, or that are submitted to EFSA in response to EFSA's calls for data. Portalino is not used for data submitted via ESFCP, but is used for certain cases, e.g., submitting confidentiality requests related to mandates issued by the EU Commission after EFSA issues an inconclusive opinion.

Implications of BREXIT for feed additive registrations
All feed additives that had an EU authorisation prior to 1 January 2021 are also authorised in the UK as part of EU retained law. Applications for new feed additives, renewals or modifications of authorisations that were under EFSA risk assessment, or had a positive EFSA opinion that was not processed to EU approval, must submit a dossier to the UK Food Standards Agency (FSA, 7) for authorisation in Great Britain (GB). The GB approval covers England, Scotland and Wales. Northern Ireland continues to adhere to EU legislation. To date, GB dossier content and structure follows EFSA guidelines, and GB submissions are made via a secure internet link available on the FSA website[8]. Applicants do not need to be based in the UK and, as in the EU, the dossier can be submitted by a manufacturer, a user, a trade association, or a consultant acting for the applicant. To date, no fees for dossier evaluation are required, though this may change in the future (e.g., the UK FSA may mirror the EURL (European Union Reference Laboratory) and implement fees for an official UK laboratory report assessing the methods of analysis for feed additive active substances/agents).

The UK FSA indicates that their risk analysis may take up to a year and is performed by the FSA and Food Standards Scotland (FSS) in consultation with external experts from independent UK Scientific Advisory Committees and Joint Expert Groups. The outcome will be used by UK ministers to decide if the feed additive is authorised or not. An Excel file containing the list of the applications received by the FSA can be found on the UK Register of regulated product applications.[9] Lastly, it is important to note that the EU Transparency Regulation does not apply in the UK.

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