Regulation on Food Enzymes and Submission of Dossiers
Potential follow-up outreach to suppliers for Dossier Preparation

- **Industry has until March 2015 for submitting dossiers for food enzymes that are presently on the market. When outreaching to their enzyme suppliers some flavouring manufacturers have reported problems in receiving the needed confirmation that the Risk Management Template (as developed by AMFEP and EFFA) will be part of the respective dossier.**
- **The current Information Letter provides additional technical/practical guidance for the compilation of the Risk Management part of the dossiers and for the calculation of the Exposure and Margin of Safety.**

Introduction

Through **EFFA Information Letter 13/20** we informed you about the need to ask the food enzyme suppliers to prepare food enzyme dossiers. With the follow-up **EFFA Information Letter 14/04** we provided some further advice and recommendation and shared the final ***Template* for the *Risk Management*** part of the Food Enzyme dossiers (i.e. "*RM Template*"), which has been completed and reviewed by AMFEP.

The current Information Letter, targeted to both the food enzyme users (flavouring producers) and food enzyme suppliers, aims at providing more technical/practical guidance for the compilation of the Risk Management part of the dossiers and for the calculation of the Exposure and Margin of Safety (MoS).

1. Contacting suppliers

EFFA have already circulated two different types of *supplier query letters* in the context of the establishment of the Union List of food enzymes. These letters were developed for the EFFA membership to contact their respective food enzyme & ingredient suppliers and to make sure that the food enzymes supplied (case a) and/or the food enzymes contained in other purchased ingredients (case b) are identified and notified in due time. These letters were recirculated with the previous EFFA IL 13/20. The last letter is attached again (See Enclosure 1).

EFFA recommended **pursuing the supplier outreach** only (case a) with the updated supplier query (which was attached to IL 14/04) letter including the *RM Template* (see Enclosure 2) in order to prepare the subsequent steps for the identified materials. It is highly recommended to request your supplier to incorporate the relevant risk management aspects (cfr the *RM Template*) in their dossiers.

Attached is a list with the relevant/appropriate contact points for some of the suppliers, as shared with EFFA by AMFEP (see Enclosure 3).

2. Risk management template (See Enclosure 2)

The dossiers to be submitted by the food enzymes producers consist of a **risk assessment** part which will be put together by each applicant in the food enzyme industry and a **risk management** section.

The framework for the **risk management section** has been written by AMFEP and discussed with the EU-Commission and EFFA. Whilst some of it is common to many food enzymes / sectors some sections require input by the users of the food enzymes (e.g. flavouring manufacturers). The attached ***RM Template*** should be used by the suppliers as part of all Food Enzyme dossiers dealing with flavourings.

In the case of joint dossiers (see EFFA IL 13/20), the AMFEP working groups (consortia) will incorporate the template. For all other food enzymes (not subject to joint dossiers, i.e. "individual dossiers") each flavouring manufacturer should send the template to its food enzyme supplier and ask for it to be included in their dossier.

- **Note on the content of the dossier**

Users need to ask their suppliers to certify that the dossier is either submitted by one of the working groups (see Section 7) or will be prepared and submitted as a stand-alone dossier by the respective supplier, including the source (micro-organism strain) and the reference to "flavouring production" or another suitable process (see Section 3).

3. Reference to the process for which the food enzyme is used

AMFEP recommends, where possible, to refer to the process (e.g. baking, brewing, **flavouring production**, potable alcohol production, starch processing, yeast processing, …) rather than to the target material or final product (e.g. "flavouring preparation").

"Flavouring production" should therefore be used as the preferred default. However, in cases where the supplier has indicated that a reference to "flavouring production" is not feasible it is recommended to refer to another suitable process (e.g., potable alcohol production, starch processing, yeast processing, protein hydrolysis…). A non-exhaustive list of those processes is mentioned in Enclosure 4. Some specific examples (from the attached RM Template) are illustrative for the latter case:

- **Figure 3**: use of beta-glucosidase for the production of a flavouring preparation from tea leaves

In this example beta-glucosidase is used to split the terpenes (and other glycosidically bound molecules) from the glycosides. It is also an option to call the process "tea processing" rather than referring to "flavouring production".

- **Figure 4**: use of lipase or protease to produce preparations from fish meat

In this example various food enzymes are used (lipases and proteases) to obtain flavourings from fish meat in the raw state treated with the food enzymes. It is also an option to call the process "protein hydrolysis" or "meat and fish processing" – rather than referring to "flavouring production".

4. Calculation of Exposure

Food enzymes contain, apart from the enzyme proteins, organic substances coming from the fermentation process. The sum of all such substances (including the enzyme protein) is normally called "Total Organic Solids", or TOS.

In particular in the case of production of "chemically defined flavouring substances" (**Fig. 2**) the final flavouring substance is purified (applying distillation, rectification and other separation techniques) and there are no traces of enzyme proteins or TOS in the final product (flavouring substance of high purity): therefore in these cases there is no need for an exposure assessment as the food enzyme is removed ➔ consumer exposure of TOS = 0.

An exposure assessment is however required in all other cases, even if the enzyme protein is denatured due to the applied processing (i.e. heating, acid hydrolysis). This is because the safety assessment is not only based on the enzyme protein (which is normally not toxic) but on the TOS, which remains in the final food even if the enzyme protein has been denatured. This is usually the case for the production of "flavouring preparations". In

this case, producers of such flavouring preparations should always explain how they use the food enzyme preparation including the amount used, whether the enzyme protein (even in a denatured form) and TOS are likely to be present in the final flavouring sold to the food industry. This will inform the notifier of the food enzyme (i.e. the applicant of the dossier) whether an exposure assessment is needed or not.

In most cases the flavouring substances or flavouring preparations are diluted before they end up in the final food: hence the dilution factors need to be taken into account for the calculation of TOS and final exposure.

Further information is provided in Enclosure 5.

5. Calculation of "Margin of Safety"

The Margin of Safety (MoS) for human consumption can be calculated by dividing the "No Observed Adverse Effect Level" (NOAEL) derived from a 90-day oral toxicity study on rodents by the Total Theoretical Maximal Daily Intake (TMDI). The calculation of the MoS is in the responsibility of the food enzyme manufacturer.

MoS = NOAEL/Exposure (TMDI)

The MoS should be higher than 300.

6. Deadline for dossier submission

The **deadline** for dossier submission as set in the Food Enzyme regulation is **11 March 2015**. Therefore the flavour manufacturers are highly recommended, if not done yet, to ask their suppliers for confirmation that the dossiers will be submitted before this deadline.

7. Legal implications and set-up of Positive List

At this stage it is far from certain how food enzymes will be entered in the final positive list of Food Enzymes. Where single company submissions are made the entry may be specific but for joint dossiers it is still uncertain how this will be handled. It is also uncertain how specific the permitted applications will be but it is hoped that there will be generic entries referring to the processes such as baking rather than listing all uses – bread, cakes, cookies etc. Regarding the use for the production of flavourings the generic wording "Flavouring Production" has been proposed.. The overview of **Active Working Groups for joint submission of Food Enzymes Dossiers** is available on the Amfep website via the following link:
http://www.amfep.org/content/active-working-groups-joint-submission-food-enzymes-dossiers

It should be noted that discussions between Amfep and the EU-Commission are still ongoing.

Additional Guidance Documents are provided in Enclosures 6-8.

8. Update of EFFA survey on the use of food enzymes

An **updated survey** with the complete list of food enzymes, reported to be used by the EFFA membership, can be found in Enclosure 9. This list has been shared with AMFEP and is also part of the *RM Template*.

If you have further questions, please do not hesitate to contact EFFA at info@effa.eu or AMFEP at amfep@agep.eu.

Overview of Enclosures:

- *Encl 1: Enzyme Supplier Letter from December 2013*
- *Encl 2: Risk Management Template*
- *Encl 3: List with the relevant/appropriate contact points for some of the suppliers*
- *Encl 4: non-exhaustive list of enzymatic processes*
- *Encl 5: Glossary and examples of the production of a flavouring using food enzymes*
- *Encl 6: EFSA Scientific Opinion: Guidance of the CEF Panel on the submission of a dossier on food enzymes*
- *Encl 7: EFSA Technical Report for the Guidance of the CEF Panel on the submission of a dossier on food enzymes*
- *Encl 8: COM Practical guidance for applicants on the submission of applications (**FL/11/69-vs 9**)*
- *Encl 9: Updated survey with complete list of food enzymes used for the production of flavourings.*