HOW TO USE GUIDANCE DOCUMENTS

For whom is the guidance?

For AMFEP members to ensure they put safe final products on the market and for downstream users so they have appropriate safety measures to minimise the risk of exposure to a minimum.

Due to the risk of respiratory allergy when exposed to high levels of airborne enzyme dust, AMFEP members have committed themselves to working towards eliminating dusty enzyme products from the market – to reduce the risk of sensitization by inhalation to an absolute minimum (AMFEP Statutes article 8c). As an association, AMFEP wants to demonstrate responsibility towards any potential safety risk towards downstream users. The guidance is readily available on the AMFEP website.

Why do we publish this guidance even though there are only few national laws and regulations?

The aim is to prevent health risks caused by dusty enzyme products, to offer guidance on necessary safety controls and ensure appropriate product stewardship.

Note: there are several cases where national laws and regulations exist in the form of Occupational Exposure Limits (OELs). Please see the industry specific guidelines for safe handling of enzymes on the AMFEP website where these OELs are listed. OELs for subtilisin exist in most EU countries as well as worldwide.

Downstream users have sufficient measures to maintain safe exposure levels of solid enzymes/products. Do we still need to determine the SRS-value?

Yes, the SRS-value will either confirm to your downstream user that the right safety controls are in place, or will advise which safety controls should be in place when handling a specific enzyme product.

Downstream user's products containing enzymes will be used at B2B downstream user outside EU. Do they still need to inform them or recommend performing the determinations of SRS-value/exposure measurements for these products?

The guidance is directed towards AMFEP members who are committed to follow the AMFEP statutes. However, the guidance may also be used by downstream users if appropriate.

The guidance targets the dustiness of enzyme products and does not relate to whether these products are handled or produced within or outside the EU.

Will the supplier (AMFEP member) take over or share the costs for these dustiness measurements? (downstream user's question)

This guidance is for AMFEP members and it is assumed AMFEP members will do the Heubach I testing. How they decide to fund such testing is up to individual AMFEP members.

What is the target audience for the layman's guide?

The guide is primarily aimed at people in direct contact with downstream users or downstream users themselves to provide them understanding and broader explanation on the guidelines.

Will the guidelines be made publicly available?

The guidance has been published on the AMFEP website.

Can the complete guideline be shared with the downstream user on demand?

The guidance has been published on the AMFEP website and is thus available to all.

Who is responsible for compliance with the guidelines?

AMFEP members are responsible for the products that they put on the market. Although AMFEP has no authority to ensure compliance, members should be aware of the potential risk they may cause to the enzyme industry, such as the potential increased risk of enzyme allergy among workers if such products are not handled correctly. This is part of the continuous work that AMFEP has been doing to improve product stewardship throughout the past 50 years. This enables enzymes to bring sustainability benefits to the market and to continue contributing to the EU Green Deal.

TECHNICAL QUESTIONS FOR CLARIFICATIONS FOR MEMBERS

Is SRS-value mandatory for all products?

SRS-value is only applicable to solid enzyme products in particulate form, such as powders or granules which may or may not be encapsulated. SRS-value is not mandatory, but simply serves as a guideline to aid in identifying which products have a high exposure potential and which products are fairly safe.

What is the relation between SRS-value and P-sentences?

Strictly speaking, there is no relationship. P-sentences are related to the hazard of the substance (inherent properties), SRS pertains to the risk.

P-sentences provide safety measures and guidance for communicating with downstream users. However, they may not always be sufficient alone, so additional guidance on how to implement these measures might be necessary.

How is FAEP expressed?

FAEP stands for “Fraction of Active Enzyme Protein”. In the context provided, it refers to measurements by weight, not volume.

Should members share SRS-value with downstream users?

It should be foreseen that downstream users may ask for the SRS-value. However, it is up to each AMFEP member whether they want to post the SRS-value on the downstream user’s site or in SDSs.

However, if the SRS-value is above 10, it is advised to put certain safety measures in place. This should clearly be communicated to downstream users.

Will the SRS value be given by the enzyme supplier on the SDS ?

Not necessarily. The enzyme supplier will decide how to communicate the information in line with the guidance. An SRS score is given in some cases, but values might vary from batch to batch.

More commonly, enzyme suppliers provide a range, indicated by the colour codes included in the guidance. You can expect the SDS to include guidance on how to handle this according to these colour codes.

Should members communicate guidelines with downstream users?

Guidelines are intended to be a tool for manufacturers, the communication obligation concerns safety. Once the guideline is published on the AMFEP website, it is for each member to decide whether they want to share the guideline with their downstream users upfront.

What is the timeline for implementing these guidelines?

The goal was set at the General Assembly 2020 for completion by 2025. While AMFEP will not enforce compliance, member commitment is crucial to avoid issues such as enzyme allergies.

The SRS-value of your product is above 250. Can we still consider it safe?

The exposure is determined by how safely the product is handled. If the material is handled carefully and the equipment is appropriate to the risk (please consult Table 2 of the guidelines), exposure should be controlled, upon confirmation by the appropriate exposure measurements.

If an AMFEP member as supplier does the Heubach testing; will the SRS-value be sufficient, or does a downstream user still need to carry out an exposure measurements?

Whereas the AMFEP member will determine the SRS-value, the downstream user has the obligation to ensure a safe working environment in their facility. This might include that exposure measurements will have to be made. In cases where the measured SRS-value is >250, the guidance recommends to conduct exposure measurements to see whether the risk can be adequately controlled.

Is staff required to wear personal protective equipment (PPE) such as special clothing and/or respirators? What about new technologies?

This depends on the safety assessment made for the product itself, the way it is handled, and of engineering controls. The need for PPE should be based on your own enzyme exposure measurement or safety assessment. In some cases (e.g. SRS-value below 10) engineering controls and good handling practices may suffice.

Do we need specific antibodies to measure FAEP?

No, the fraction of active enzyme protein (FAEP) can be calculated using the information in the SDS (Safety Data Sheet) on the percentage of active enzyme protein (%AEP). As AMFEP member this information needs to go into the SDS for all your products, either as a specific number or as a range. If a range is given in the SDS, the highest end of the range should be used when calculating the SRS. Examples on calculating %AEP into FAEP are given in the guidance document.

The SRS is delimited at 10 and 250. Is there a reason for this?

Please see Annex IV of the guidance document.

Is there a contact point for consultation on measurements?

AMFEP cannot provide the contacts directly, but recommends to look for them online.

Heubach I seems to give very variable results, even for same sample being measured. Is there a way to minimise variation between Heubach I measurements?

To minimize variation, repeat each measurement 5 times per product or according to data providers procedures.

How many batches do you recommend testing using Heubach I ?

It is recommended to perform testing in triplicate (3-5 times for an initial assessment). The Heubach method is relatively rough, so a single measurement is not sufficient. At a minimum, conduct duplicate tests, and consider increasing the frequency depending on purpose, available time, resources and variance (csv).

Does AMFEP recommend any CROs that can offer this Heubach I measurement or companies who help with occupational health and safety issues?

AMFEP cannot provide the contacts directly, but recommends to look for them online. Supply conditions are in the domain of the members and cannot be addressed by the trade association.

What to do if my SRS-value remains above 250 ppm and my enzyme distributors/provider do not have an analytical method to measure a possible enzyme exposure?

Try a combination of the following:

- You can ask for packaging in small quantities instead of one large container. Small packages can be handled in a contained environment safer, easier and cheaper than large quantities
- You can try to reduce the active enzyme concentration by dilution/mixing as the first step in the process, reducing the SRS-value in following steps
- You can consider other ways of reducing the SRS-value, for example, using a dust binding agent in the formulation of the product or reformulating the product completely to a non-dusty form.
- More details can be found in the Annex section.

Can the SRS calculation model be used for enzyme containing material where the inclusion of enzyme is below 0.01% AEP as this will give the possibility of a very dusty product (100.000 ppm would give a SRS-value of 10 when containing 0.01% AEP) or should a factor be applied in these cases? Or can products below a certain AEP limit be regarded as safe without testing with Heubach I?

Yes, it can be used even for products that have very low AEP%. In these cases, the dust generated mainly consists of some other formulation ingredient, like flour or other carriers.

Is the SRS model industry specific or can it be applied across all industries handling granulates and powder products? The data behind this model is based on baking products. Is the model is suitable for coated and other types of granulates/pellets found in other industries.

The model can be applied to products in all industries. The SRS-value relates to the product and the product's characteristics rather than to a specific industry. Coated and very robust enzyme granulates are expected to give a very low number when tested in Heubach I.
A safety assessment needs to be carried out by the downstream users to confirm that the robustness of the enzyme granule is strong enough to remain intact in the downstream user's process even when the SRS-value level shows that the product falls in the low risk category.

Should the guidance only be used for formulators or is it also applicable to companies using granulates as processing aids? Or should another risk calculation tool (e.g. ART) be applied?

The SRS-value can be applied to every product and whoever is using the product. The ART tool has been used for setting the safety limits of the SRS-value. Risk calculation based on tier 1 tools, such as EcetocTRA, is not suitable for enzyme exposures.

If an enzyme containing products contains multiple enzymes belonging to the same enzyme class (e.g. alpha amylase) should the SRS-value be calculated for each of them or should the sum of the total enzyme protein be used?

This will depend on the specific product and should be addressed case by case. In case of enzyme blends, calculate SRS-values for each enzyme individually.

Example: An enzyme blend contains fungal alpha-amylase and lipase. The Active Enzyme Protein (AEP) for the fungal alpha-amylase is 3% (equal to FAEP: 0.03), and the AEP for the lipase is 1% (equal to FAEP: 0.01). Heubach I has been measured to be 800 ppm.
SRS for fungal alpha-amylase will be: 800 ppm x 0.03 = 24 ppm
SRS for lipase will be: 800 ppm x 0.01 = 8 ppm
Due to the higher AEP of the fungal alpha-amylase in the blended product this enzyme ingredient brings the blended product into the yellow group where assessing and communicating specific risk controls to downstream users are needed.

The Dutch "newly" established OEL for fungal alpha amylase (10 ng EP/m^3) should the SRS-value be a factor 6 less for products containing this type of enzyme or can the established limits of 10, 10 – 250 and >250 ppm still be applied for this type of enzyme to identify the safety profile of the product?

The Dutch OEL of 10 ng/m3 for fungal alpha amylase is established as an average personal exposure during an 8 hour working day. The SRS-value is product related and unfortunately not useful for documenting compliance to this OEL.

In table 2, PROC 6 and PROC 14 are not listed. How come?

We covered the most relevant enzyme handling operations within the industries where dusty enzyme preparations are used.

If a non-dusty food enzyme preparation with a SRS below 10 is then diluted/formulated with a more dusty carrier and ends with a fictive SRS-value above ten, how should we deal with that. The only reason the SRS is above ten would be due to the carrier and therefore would not be directly related to food enzymes preparation. Can it be possible to calculate an SRS-value of a food enzyme containing product based on the SRS of the raw material?

The SRS-value will refer to the fraction of active enzyme protein in the product. If the non-dusty enzyme product has been diluted with a dusty carrier, and the carrier do not contain enzyme, then the SRS-value of the diluted product will be even lower than the undiluted product.

Is it necessary to perform the SRS-value/exposure measurements for each product containing solid enzymes (different recipes)? Or is it sufficient to consider only 1 average/representative value?

It is advised to measure each product separately as the different recipes/formulations can have significant impact on the SRS-value. Otherwise, use a reasonable worst case dustiness (e.g. 90th percentile) value and not mean/average value. Similar for batch variability.

Why is the focus only on active enzymes?

Step I (SRS calculation) focusses only on active enzymes. This is because step I is supposed to be a simplified approach for screening purposes. The amount of active enzymes in the product is in most cases much higher than inactive enzymes. In addition to this, from an analytical standpoint it is easier to measure only active enzymes. However, this does not mean that only active enzymes may cause adverse health effects.

Enzymes are large proteins with a specific structure. Enzyme activity depends on both chemical composition and this structure. The enzyme activity may be removed while sensitization potential is retained if the enzyme unfolds, i.e. the structure is damaged or changed, but certain sensitizing chemical groups, called epitopes, remain intact.

Enzyme concentration can be measured in several ways. An activity assay will measure only the concentration of protein with the right chemical formula and structure capable of catalyzing a certain reaction. A very common other method is the ELISA assay. This method, which makes use of binding to antibodies, measures the actual sensitization potential. Other methods tend to be less specific and measure higher concentrations, so would give more conservative answers. Hence, AEP measured with ELISA is the most representative method, but AEP in general is a good representative measure and the parameter always known to the manufacturer.