



EUROPEAN COMMISSION
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL

Directorate D: Food Safety; production and distribution chain
Unit D.3: Chemical and physical risks; surveillance

Sanco/10754/2005 rev.5
15 April 2005

Guideline developed within the Standing Committee on the Food Chain and Animal Health on the taxonomic level of micro-organisms to be included in Annex I to Directive 91/414/EEC

General view

This guidance document deals with the taxonomic level of inclusion of micro-organisms in Annex I to Directive 91/414/EEC and also gives some guidance on which taxonomic level information is needed in order to be able to perform the assessment necessary to decide on inclusion. Micro-organisms in the sense of this document are those defined in Directive 91/414.

The risk assessment of micro-organisms for the use as active substances in plant protection products is for several reasons not comparable to the risk assessment of chemicals serving the same purpose. Because of the diversity and complexity of micro-organisms, decisions concerning the dossier (requirements) have to be taken on a case by case basis and any guidance for the production and submission of dossier information for micro-organisms must inevitably be of a more general nature. Therefore, it is highly recommended that notifiers, when preparing the dossier, establish and stay in close contact with the respective Rapporteur Member State.

It is a general view that the micro-organisms are to be included in Annex I at strain¹ level, which is also in accordance with the data requirements as laid down in the Directive 91/414/EEC. Consequently, the data requirements as described in Commission Directive 2001/36/EC should be fulfilled at strain level unless the notifier can prove that this is not necessary for the particular strain in question. An example, which clearly demonstrates the importance of studies to be generated on the strain level, is the species complex *Fusarium oxysporum*. This species contains both plant pathogenic and non-pathogenic strains, of which the non-pathogenic strains may be used as plant protection product. In other cases in which the species is known to be relatively homogeneous and well studied it may be decided by experts if certain questions may be handled on a species² rather than on a strain level.

For the more general parts of the dossier, data from different strains of the same species might be used, but only in a situation where a high similarity within a species has been

¹ Note that for the purpose of this document the word "strain" refers to a culture that is specifically linked to a collection number

² Note that for the purpose of this document the word "species" refers to all taxonomic entities higher than strain level

demonstrated. Still strain specific data are necessary for key issues, such as the mode of action and the possible production of toxins.

Large parts of the dossier may consist of data presented in open literature. Such data have to be evaluated in the same way as all other information. However, Member States might conclude that such information is not acceptable for the purpose of a risk assessment in the draft assessment report if it does not meet the quality criteria set out in Directive 91/414/EEC.

Identity and biological properties

Taxonomic identification of micro-organisms is a key element in the risk assessment of any microbial active ingredient, although it is complex and based on comparisons. A document from the OECD provides guidance on taxonomic identification in the risk assessment **(OECD, 2003)**.

The delimitation of microbial species is dependent on changes in new taxonomic insights and/or opinions. The identification of a strain thus needs to be based on the newest available methodologies and knowledge about the species and its genus.

It is noted that the culture procedures and further processing may influence the characteristics of the micro-organism. Therefore all procedures and methods applied, including molecular methods, should be well described and standardised as far as possible.

Different strains from the same species may produce distinct metabolites, possibly with toxic potential. Two aspects should at least be addressed:

- 1) Of all metabolites/toxins known to be produced by (the various strains of) a species, the production of the relevant metabolite/toxin must be investigated for the notified strain. If the notified strain is able to produce the relevant metabolite/toxin, detailed information is required.
- 2) Strain specific mode of action might be exerted by (strain) relevant metabolites/toxins. Since these relevant metabolites/toxins are biologically active, they should be investigated in detail, especially for their toxicity.

Because of the second aspect, the notified strain has to be described in detail regarding the known intraspecies variability in the mode of action and efficacy. Other differences in biological properties between strains of the species in question should additionally be addressed, when data from different strains are used for the general part of the dossier.

In order to be able to waive a certain study based on strain similarity, the (genetical) similarity and identical characteristics of the different strains should be proven where they are relevant for the end-points of the (toxicity) test to be waived. Data on efficacy and monitoring may in a few cases also be species specific, but would normally be strain specific. Depending on the properties of the strain further specific information might be necessary.

The natural occurrence of a specific strain is difficult if not impossible to determine and data on this issue should generally be submitted on species level. For example, the bacterial species *Pseudomonas fluorescens* is commonly occurring in various environments and it may be questioned how relevant such information is for the risk assessment of a specific strain of this species.

Human Health

For the risk assessment of micro-organisms regarding human health, in particular aspects such as toxicity, pathogenicity and infectiveness of the micro-organism, and the possible relevant metabolites/toxins it may produce, need to be addressed. Since in most cases these aspects are strain specific, they are to be considered at the strain level in accordance with 2001/36/EC.

Medical data have to be submitted. These data are often generated at the species level and pooling of such data on the species level may be acceptable.

If there is sufficient evidence that strains do not differ with regard to properties of potential relevance for human health, an existing risk assessment performed for one strain may be applied to another and new studies could be waived.

Environment - Fate and behaviour in the environment

The exposure assessment (environmental fate and behaviour) is preferably performed at the strain level. However, dependent on the function and structure of the micro-organism, pooling of data on the species level rather than on the strain level may be acceptable, as described below.

If there is sufficient evidence that strains do not differ in their environmental fate and behaviour (growth, replication and persistence dependent on pH, temperature, humidity, etc.) the use of several strains for the same risk assessment should be considered, particularly when the data per strain are limited. In general, the fate and behaviour in the environment largely depend on environmental conditions such as temperature, humidity, wind speed, soil type (pH, presence of other micro-organisms which may be antagonistic), presence of suitable hosts for multiplication, presence of vectors for distribution (birds, animals) and shelter (otherwise fast degradation in UV-light). Due to the large possible ranges of the environmental factors, data on fate and behaviour of the micro-organisms will inevitably show large variability. This variability caused by environmental factors could be larger than the possible differences between strains of the same species.

If there is sufficient evidence that strains differ in their environmental fate and behaviour, data on strains should be treated separately.

Environment - Effects on non-target organisms

The assessment of effects on non-target organisms (ecotoxicity, infectivity, pathogenicity) is preferably performed at the strain level. If there is sufficient evidence that strains do not differ in their detrimental effects on non-target organisms, pooling of data at the species level could be considered. If there is evidence that strains differ regarding the effects on non-target organisms, data on strains should be treated separately. This depends on the mode of action, e.g. when a metabolite or toxin is involved.

General conclusions

Inclusion of micro-organisms into Annex I should be at the strain level.

In cases in which the species is known to be relatively homogeneous and well studied it may be decided by experts that certain data requirements may be handled on a species rather than on a strain level. In practice, the core of the dossier will consist of strain specific information, which may be complemented with species specific information. It is recommended that notifiers generate species specific information together wherever possible.

The risk assessment of the micro-organism concerning human health has to be treated at the strain level unless the notifier can prove that data at the species level sufficiently address this issue. If that is the case, data pooling at the species level might be acceptable.

The risk assessment of the micro-organism concerning its fate and behaviour in the environment has to be treated at the strain level, unless it can be shown that strain differences do not relate with the environmental fate and behaviour. If that is the case, data pooling at the species level might be acceptable.

The risk assessment of the micro-organism concerning its effects on non-target organisms has to be treated at the strain level unless the notifier can prove that data at the species level sufficiently address this issue. If that is the case, data pooling at the species level might be acceptable.

In order to prevent duplication of work, notifiers are encouraged to submit information that has already been assessed in earlier evaluations, if this does not interfere with the rules of data protection as set out in Directive 91/414/EEC, e.g. by producing data together on higher taxonomic level, exchanging letters of access to protected data or by using open literature data as well as risk assessments performed in other countries.

The Rapporteur Member State should preferably be the same for all strains of the same species.

It is recommended that the taxonomic level at which data are submitted is addressed during a pre-submission consultation among Rapporteur Member States and notifiers (<http://www.oecd.org/dataoecd/25/43/27772072.pdf> and <http://www.oecd.org/dataoecd/60/6/30919600.pdf>).

References

OECD. Guidance document on the use of taxonomy in risk assessment of microorganisms: bacteria. OECD Series on Harmonisation of Regulatory Oversight in Biotechnology. 2003; ENV/JM/MONO, 2003 OECD.