Procedures to set an import tolerance in Europe including data requirements

**Joint Regional Symposium on
Regulation of Pesticide Residues in Food**

Hong Kong, 27 – 28 March 2009

Content

- MRL setting
- MRL application
- Data requirements

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- **MRL setting**
- MRL application
- Data requirements

Procedures (1)

1. MS to evaluate the data
2. Evaluation report send to EFSA via European Commission
3. EFSA to assess the evaluation and give a reasoned opinion on, in particular, the risks to the consumer and where relevant to animals
4. European Commission to draft a proposal

Procedures (2)

5. European Commission to launch SPS notification
6. Standing Committee on the Food Chain and Animal Health to vote
7. European Commission to submit the draft measures for scrutiny by the European Parliament and the Council
8. Publication in the Official Journal

Question

What is needed
to receive a MRL
necessary to import food to Europe?

Content

- MRL setting
- **MRL application**
- Data requirements

Who can apply for a MRL?

- ☑ applicants according to Directive 91/414/EEC
- ☑ parties demonstrating, through adequate evidence, a legitimate interest in health, including civil society organisations
- ☑ commercially interested parties such as manufacturers, growers, importers and producers
- ☑ Member States of the EC

Where to apply for a MRL?

☹ **Member State granting an authorisation**

☺ **for import tolerance:**
Rapporteur Member State responsible for the evaluation of the active substance

When to apply for a MRL?

☑ **When a MRL laid down in Regulation (EC) No. 396/2005 is insufficient**

and

☑ **necessary data for the evaluation are available.**

‼ **Which data are necessary?**

When to apply for a MRL?

Use the application form available on the internet

http://ec.europa.eu/food/plant/protection/resources/publications_en.htm#residues

MRL application form

Content

- MRL setting
- MRL application
- **Data requirements**
  - **Basic principles**
  - **Toxicological and metabolism data**
  - **Methods of analysis**
  - **Residue behaviour**

Data required

- Directive 91/414/EEC, Annexes II (active substance) and III (formulation)
- No need to duplicate data that are available and applicant has access to
- All other data needed have to be presented

!! Basis for evaluation is the Good Agricultural Practice

Toxicology (1)

- Studies on absorption, distribution, excretion and metabolism in mammals
- Acute toxicity (oral, dermal, inhalation, eye irritation, skin irritation and sensitization)
- Short-term toxicity (28- and 90-days, oral)
- Genotoxicity testing (in vitro studies, in vivo studies in somatic and germ cells)

Toxicology (2)

- Long term toxicity and carcinogenicity
- Reproductive toxicity (multi-generation and developmental toxicity studies)
- Delayed neurotoxicity studies
- Other toxicological studies (studies with metabolites, mechanistic studies, …)
- Medical data

Studies to be generated

- ☑ on the basis of test guidelines described in Directive 87/302/EEC and 92/69/EEC based on OECD Test Guidelines

or

- ☑ in accordance with OECD Test Guidelines

Results

- ADI
- ARfD
- AOEL
- Proposals for classification and labelling
- Proposals for the protection of operator, worker and bystander

Methods of analysis (1)

The methods of analysis presented must be capable to determine

- ☑ **the pure active substance and/or**
- ☑ **relevant metabolites.**

Methods of analysis (2)

In general the method of analysis for enforcement purposes should be a multi-residue method and the residue should be determinated

- **by commonly available analytical techniques**
- **using standard matrices**
  - high water, high acid, high fat, dry
  - milk, eggs, meat, (fat)

Residue behaviour (1)

Nature of residues

- Metabolism in plants
- Metabolism in livestock animals
- Nature of residues in processed commodities
- Metabolism in rotational crops

Residue behaviour (2)

Magnitude of residues

- Residues in plants
- Residues in livestock animals
- Residues in processed commodities
- Residues in rotational crops

Residue behaviour (3)

The data and studies required for fixing Maximum Residue Limits should comply with two main aims to be fulfilled

- !! **enforcement**
- !! **risk assessment**

General Requirements

- Formation of metabolites and bound (non-extractable) residues to be reported
- Normally 14C labelling is used
- Necessity to label substances with several important structural elements in more than one place
- Dose rate normally equal to intended use

Plant Metabolism Data

Metabolism studies have to involve

- **crops or categories of crops in which plant protection products would be used,**
- **at least three crops from three different crop categories if a wide range of uses in different crops from different crop groups or in the group of fruits is envisaged.**

Plant Metabolism Data

If the route of degradation is similar in all three categories then it is unlikely that any more studies will be needed unless it could be expected that a different metabolism will occur.

Livestock Animals

Metabolism studies have to involve

- **livestock animals to be fed with feed contaminated with residues,**
- **lactating ruminants (goats preferred),**
- **laying poultry (chicken),**
- **pigs (if metabolic patterns differ significantly in the rat as compared to ruminants).**

Processing

Metabolism studies have to involve

- **a maximum of three hydrolysis studies for the chosen representative conditions.**
- **More studies have to be conducted if processes other than hydrolysis affect the nature of the residue or if the chosen hydrolysis conditions are not representative.**

Rotational Crops

Metabolism studies are not necessary

- **in permanent crops,**
- **if after 100 days < 10 % of the active substance and bioavailable metabolites can be detected in the soil,**
- **if no uptake of residues will occur.**

Metabolism studies are necessary

- **if metabolites in soil occur, which were not found in plant metabolism.**

Definition of residue (1)

There are three general considerations which are fundamental to the decision as to whether or not specific metabolites/ degradation products should be included in the definition and expression of a residue

- ☑ **their presence in significant amounts,**
- ☑ **their basic toxicology,**
- ☑ **the suitability of the analytical procedure for routine monitoring.**

Definition of residue (2)

Two different residue definitions may occur

- residue definition for enforcement purposes (marker concept)
- residue definition for risk assessment (toxicological relevant compounds)

- ☑ apply to plant, plant products and to products of animal origin
- ☑ will influence the extend of analytical work done in residue trials.

General Principles

- to determine the level of residues
- to assess the consequences of these on the health of humans and animals

- trials should cover realistic worst case conditions
- trials should only cover situations where an authorisation is asked for
- results of the metabolism studies have to be taken into account

Plants

- division between major and minor crops
- consumption and cultivation area/ or production are used for selection
- 8 trials for a major crop and 4 for a minor crop required; reductions are possible.
- extrapolation of results should be used as far as possible

Livestock Animals

Feeding studies are only necessary

- **when significant residues (0.1 mg/kg of the total diet) occur in crops or part of the crop fed to animals**

and

- **metabolism studies indicate that significant residues (>0.01 mg/kg) may occur in any edible animal tissue.**

Livestock Animals

- 4 dose groups (control, 1 x, 3 x - 5 x, 10 x expected residues in animal feed on a dry weight basis)
- lactating ruminants (cows preferred), laying poultry (chickens), pigs (if metabolic pathways differ significantly in the pig as compared to ruminants)

Processing

The decision as to whether it is necessary to carry out processing studies will depend on:

- **the importance of a processed product in the human and animal diet,**
- **the level of residue in the plant or plant product to be processed,**
- **the physico-chemical properties of the active substance or relevant metabolites**

Magnitude of residues (6)

Processing

- cover more likely types of processes
- 11 types of process defined
- two different types of studies proposed
  - ✓ balance studies for the distribution
  - ✓ follow up studies for important food and feed items
- number of trials depends on type of study
  - ✓ 1 balance study
  - ✓ 3 follow-up studies

Rotational Crops

Studies are not necessary

- **in permanent crops or**
- **if no uptake of soil residues via the root system occurs**

Stepwise procedure is foreseen

- **preliminary tests (3 steps) and**
- **main test (2 steps)**

MRL proposal (1)

The evaluation of the results obtained from the different studies will enable to propose

- **MRLs for products of plant origin,**
- **MRLs for products of animal origin,**
- **transfer factors,**
- **values for risk assessment.**

MRL proposal (2)

- ☺ **Statistical methods used to propose MRLs.**
- ☺ **A MRL can only be proposed and set if the residue do not have any adverse effects on human or animal health.**
- ☺ **The proposed MRL will be set to cover the enforcement purpose.**

Thank you for your attention!

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