PREPARATION AND SUBMISSION OF DATA DOSSIERS TO JMPR BY MANUFACTURERS

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Overview

- Who are the JMPR?
- What do they do?
- Description of data package to be submitted
- Developments
Who are the JMPR?

- Experts in
  - Toxicology
  - Pesticide residues
  - Risk assessment

- Attend in a personal capacity as international experts, and not as representatives of governments, institutes, or any other organization

- Two panels
  - WHO (toxicology)
  - FAO (MRLs/consumer exposure)
What do they do?

- Produce an annual, independent review of pesticide residues
- Using data submitted by
  - manufacturers
  - member governments
  - other interested parties
- Review is in the public domain but may not be used by regulatory authorities for registration purposes
Types of JMPR review

- New active substance review
- Periodic review
  - Substances re-reviewed every 10-15 years
  - Start from scratch to review to current standards
- Evaluation of additional MRLs
- Advice on technical issues referred by CCPR
Toxicology submission – Objectives of JMPR

• To recommend
  – Acceptable daily intake (ADI)
  – Acute reference dose (ARfD)
  – Advise on toxicology of metabolites
  – Advice on other areas of toxicology important for consumer risk assessment
Toxicology – form of submission

- Data list of available data
- Summaries of all available toxicology data excluding
  - Product specific data
  - Data relating to operator exposure
- Proposal for ARfD and/or ADI
- Summaries can be in the form of those submitted to regulatory authorities e.g. dossier submitted to EU under Directive 91/414
Toxicology – time of submission

• Data lists, studies (electronic format) and summaries must be submitted before 1 December the year before the JMPR review is due to take place
  – e.g. for 2008 review (meeting September 2008), information to be submitted before 1 December 2007
Toxicology – recent general considerations

• Examples include
  – Setting the Acute Reference Dose on the basis of haematological effects (2003)
  – Hepatocellular hypertrophy (2006)
Objectives of residues submission

• To recommend
  – residue definitions
  – Maximum Residue Limits (MRLs) in traded commodities
  – Become Maximum Residue Levels if accepted by CCPR
  – Become Codex MRLs if adopted by Codex Alimentarius Commission
Guidelines for residues submission

• FAO Manual
• Published in 2002

• General considerations each year
  – Included as updates in manual

• All available data should be submitted
  – FAO panel to review and decide on relevance
Example submission

- New active substance
- It must be registered and have a label somewhere in the world
- Applicant should provide
  - Overview/summary of studies
  - Proposals for MRLs
  - Assessment of dietary exposure
  - Supporting studies
  - Labels supporting residue trials
Physical and chemical properties

• Basically, background information in tabular format
  – how the pesticide will behave in plants and the environment
  – inform method development

• All available data on active substance should be submitted

• Data on formulated product not required

• Example data
  – Melting point
  – Boiling point/temperature of decomposition
  – Solubility in water and solvents including log Po/w
  – Vapour pressure
  – pKa
  – etc
Environmental data

• Selective data to be submitted (review in 2003)
  – Anaerobic degradation in soil
  – Hydrolysis rate and products (carried out in sterile aqueous buffers)
  – Other data relevant to rice paddys
Good Agricultural Practice (GAP)

- Summary of crops, rates and timings
- Labels must be submitted
  - No label, no GAP!
- Critical GAP concept not used
- Alternative GAP
Metabolism studies

- All data to be submitted
- Summaries of main findings including distribution and amount in crop/animal parts
  - Plants
  - Animals
  - Rotational crops
- Used to determine residue profile in harvested/traded crops and commodities
  - what should be included in the residues definition
Residues data

- Summary of all residues trials data
- OECD template for residues supervised trials data preferable
- Minimum data requirements
  - FAO panel considers all data although generally will not set an MRL on less than 3-5 data points
  - Likely to be rejected by CCPR
Processing data

• Summary of data on the nature and transfer of residues to processed product
  – Processing factor calculated as mean transfer from RAC to processed product

• Processing studies may result in processing factors including both “less than” and real values, or some high values without any identifiable reasons.
  – Use median value as it provides the best estimate as the calculation of the mean provides a biased value.
Rotational crops

- In cases where the residues in follow-on and rotational crops may occur at levels above the LOQ,
  - minimum data requirement as specified in the FAO Manual

- The data submitters should automatically provide information on:
  - Metabolism in root or tuber vegetables;
  - Results of field studies on follow-up and rotational crops carried out at various times after the application of the pesticide;
  - Environmental fate studies, and
  - Any other relevant information, which may assist the comprehensive evaluation of residues in food.
Animal transfer

• Summaries of animal feeding studies where residues are likely to occur at detectable levels in products of animal origin
  – Typically in cattle or goats and chickens
  – Occasionally, pigs

• Need to take account of pesticides which have uses as
  – Veterinary medicines
  – Topical application

• Necessary to take additional uses into account in calculating MRLs
Storage stability

• Summaries of data to demonstrate residues in crops/commodities do not degrade significantly during storage prior to analysis
  – Helpful to relate data to residues studies
Methods of analysis

- Summaries of data including validation data e.g.
  - recoveries
  - linearity
  - specificity
  - limit of quantitation
  - etc

- Relevant to residue definition
  - Monitoring
  - Risk assessment
Available national residues monitoring data

- To be submitted for periodic review compounds
- Generally submitted by member governments
Proposing MRLs (1)

• Eye ball highest residue!

• EU models
  – Rber and Rmax

• NAFTA model
  – This statistical procedures provide a good estimate of the 95th to 99th percentile range where there are sufficient data points

• Processed products only when there is a concentration of the residue in the processed product
Proposing MRLs (2)

- Calculation of dietary burden now using OECD animal diets
  - Adopted in 2007

- Fodder MRLs continue to be evaluated and MRLs recommended as previously.

- Forage residue data would continue to be evaluated and used in the estimation of farm animal
Extrapolation and group tolerances

- Extrapolation and group tolerances are acceptable
- No definitive guidelines
- Expert judgment considering all available data including residues, trails, and GAPs
Fat soluble residues

• The log Po/w of an individual component of a residue is an initial indicator

• In general
  – when log Po/w exceeds 4, the compound would be designated fat-soluble
  – when log Po/w is less than 3 it would be so designated not fat-soluble.

• However it is not the only factor used to assess fat-solubility (2005)
Dietary risk assessment

- Dietary risk assessment should be carried out
- In reality it is likely to change between your proposal and that proposed by FAO panel
  - may derive different ADI, ARfD, HR or STMR to the ones proposed
- However, gives an indication whether dietary intake problems may occur
- Deterministic calculations only
- No probabilistic modeling
Chronic model

- GEMS cluster diets
- 13 diets
- General population only
  - no children
Acute model

- Derived from a number of diets around the world
- Limited spread
- Covers general population and consumers <7 years
- Variability factors
Dates of submissions to FAO panel

• Data lists must be submitted before 1 December the year before the JMPR review is due to take place
  – e.g. for 2008 review (meeting September 2008), information to be submitted before 1 December 2007
  – Allows FAO to allocate compounds to evaluators

• Studies (electronic format) and summaries must be submitted before 1 March in the year the JMPR review is due to take place

• Situation to change from 2009 submissions onwards
  – All info before 1 December in the year before JMPR review to take place
  – Same as WHO panel submission
Examples of new developments

- OECD guidelines
- MRLs for spices
Conclusions

- Clear summaries will help JMPR
  - but remember, its an independent review
- JMPR has an enormous task
  - submission of all relevant data with help the evaluator
- Submission of data at defense hearing can not always be taken into account because of time constraints
- Remember,
  - no label
  = No GAP
  = No MRL!
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