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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)
 - Guidance on the establishment of Acute Reference Doses (2004)
 - IPCS Framework for analysing the relevance of a cancer mode of action in humans (2005)
 - 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
 - <http://www.fao.org/WAICENT/FAOINFO/AGRICULT/AGP/AGPP/Pesticid/JMPR/Download/faom2002.doc>
- 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 $P_{o/w}$
 - 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
 - <http://ec.europa.eu/food/plant/protection/resources/app-i.pdf>
- NAFTA model
 - This statistical procedures provide a good estimate of the 95th to 99th percentile range where there are sufficient data points
 - <http://www.pmr-arla.gc.ca/english/nafta/docs/mrls-e.pdf>
- 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 P_o/w of an individual component of a residue is an initial indicator
- In general
 - when log P_o/w exceeds 4, the compound would be designated fat-soluble
 - when log P_o/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
- <http://www.who.int/foodsafety/chem/gems/en/index1.html>

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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