



Food and Agriculture
Organization of the
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World Health
Organization

Joint FAO/WHO Expert Committee on Food Additives (JECFA)

Chronic dietary exposure assessment of compounds used
as veterinary drugs and pesticides

24th session of CCRVDF

Background

- Some agricultural chemicals have a dual purpose: use as a veterinary drug and application to agricultural and/or horticultural crops.
- The resulting residues potentially end up in foods that contribute to the overall exposure of populations.
- JMPR and JECFA use two very different methods to estimate population chronic exposure. Consequently, combining the outputs of the JMPR and JECFA assessments is difficult and has a high level of uncertainty.
- Consequently, there is a need for a solution to ensure that risk managers have sufficient information to set MRLs



Background

- The 81st JECFA meeting identified some additional important issue concerned with the methodologies applied by JECFA and the JMPR to estimate chronic dietary exposures that merit general consideration:
 - Need to develop a combined dietary exposure approach for compounds that are used both as veterinary drug and pesticides
- A Joint FAO/WHO Electronic working group on harmonizing / combining exposure from veterinary drug and pesticide use was established
 - Report the outcomes of the FAO/WHO expert consultation to JECFA and JMPR.



Approach

- **For compounds that have been assessed as both pesticides and veterinary drugs a comparison of dietary exposure methodologies was carried out to assess whether:**
- dual uses for the eight compounds resulted in dietary exposure estimates within the relevant ADIs
- the current JMPR and JECFA dietary exposure methodologies, when applied to dual use compounds, gave comparable estimates
- the current JMPR and JECFA dietary exposure methodologies gave estimates that were sufficiently protective when compared to national estimates of dietary exposure



Approach

- The assessment was conducted for eight compounds previously evaluated by JECFA/JMPR, which are used as both pesticides and veterinary drugs
 - Abamectin
 - Cyfluthrin
 - Cypermethrin
 - Deltamethrin
 - Emamectin benzoate
 - Teflubenzuron
 - Thiabendazole



Less than Lifetime Exposure

- The model is also intended to cover **less than lifetime** dietary exposure. **Acute** is not included in this work
- Exposure can occur over greater than one day but less than a lifetime. Such exposure scenarios may be continuous for a period of time or intermittent over a certain period up to a lifetime
- A few days every so often, a few months every year, or short-term peak exposure, which may be life-stage specific.
- An ADI is based on the most sensitive, relevant endpoint, regardless of duration of exposure and will be protective if usual exposure is below the upper range of this value. However, where chronic exposure is estimated as the life-time (or long term) average, it is possible that less than lifetime exposure will exceed this value.
- The point of departure for sub-sub-acute or sub-chronic studies in experimental animals is often similar to (or even the same as) that observed after chronic (e.g. 2 years) exposure. Hence, less than lifetime exceedances in humans would present a potential health concern.



GECDE- JECFA vet drugs

- For vet drugs the chronic dietary exposure model used is the **Global Estimated Chronic Dietary Exposure (GECDE)**
 - The highest exposure calculated using the 97.5th percentile consumption figure for a single food selected from all the foods plus the mean dietary exposure from all the other relevant foods

$$\begin{array}{ccccc} \text{GECDE} & = & \text{Highest exposure from one} & + & \text{Total mean exposure} \\ & & \text{animal product} & & \text{from all other} \\ & & & & \text{products} \\ \text{(mg/kg body weight per day or mg/day)} & & \text{(mg/kg body weight per day or mg/day)} & & \text{(mg/kg body weight per day or} \\ & & & & \text{mg/day)} \end{array}$$

- Data set used is the FAO/WHO Chronic Individual Food Consumption – summary statistics (CIFOCOss)
 - Currently contains summary statistics of 37 surveys from 26 countries. To be included in CIFOCOss, food consumption surveys must have collected data on at least two consumption days.



IEDI- JMPR pesticides

- The JMPR uses the **International Estimate of Daily Intake (IEDI)** to evaluate chronic exposure to pesticides.
- Uses the average daily per capita consumption of raw and semi-processed agricultural commodities obtained from the GEMS/Food cluster diets (FAO Manual, 2016) and the supervised trial median residues (STMR)



Approach

- **The following dietary exposure estimates were derived:**
 - IEDI (JMPR model) based on the GEMS/Food Cluster diets.
 - GECDE (JECFA veterinary drugs model), extended to cover plant products, using the CIFOCOss data set.
 - National chronic dietary exposure assessments were conducted using food consumption data and national methodologies from Australia, the Netherlands, Brazil, New Zealand, Italy, USA, the Republic of Korea, the People's Republic of China, and 11 European Union (EU) Member States.
- **The estimations were conducted using two different approaches related to the median residues in animal commodities:**
 - Highest median residues from JECFA and JMPR
 - Combined median residues (sum of the JECFA and JMPR medians)
 - Where median residue values were not available MRLs were used as a proxy



Approach

- For chronic exposure estimates, it is preferable to use surveys of more than 1 day's duration to represent “usual” consumption patterns
- Methodologies should take into consideration non-average individuals, such as those who consume large portions of specific food items.
- Exposure was estimated in both children and the general population, for median and high percentile consumers, to cover less than lifetime exposure, where possible. Note that it is not possible to estimate exposure in children or in high percentile consumers using the JMPR approach.
 - It was decided to include separate data on infants and children, because the amount of food they consume in relation to body weight is higher than for older age groups.



Results

- There was no marked difference between dietary exposure estimates based on the highest median residue or summing the median residues.
- In principle, the GECDE is a suitable model for assessment of lifetime and less than lifetime dietary exposure.
- The IEDI is not a suitable model for assessing less than lifetime dietary exposure. However, the IEDI is suitable for estimating chronic (lifetime) exposure from widely and regularly consumed staple commodities.
- The GECDE adequately covers the high percentiles obtained by the national estimates for all compounds for both the adult population and children. It can be noted that the GECDE is more conservative than the IEDI for all compounds.
- For the adult population, the IEDI adequately covers the high percentiles obtained by the national estimates for most compounds. However, the IEDI is not specifically addressing the exposure in children.



Future Work

- For the immediate future, residue concentrations obtained from veterinary use and pesticide use in the same animal commodity should be added together to provide the residue data input for the dietary exposure assessment.
- The model needs to be refined to decrease uncertainty and more accurately reflect national dietary exposure estimates. Consequently, a refined GECDE-based dietary exposure estimates are expected to decrease compared to current estimates.



Future Work

- **In regards to less than lifetime exposure:**
- To appropriately link the exposure assessment with the hazard assessment, sensitive populations and relevant exposure duration need to be clearly identified from the toxicological profile for each compound under consideration. The nature of the toxicological effect and the duration of exposure until the onset of effect should be considered.
- Suggest JMPR consider the use of individual food consumption data when it is indicated by the toxicological end points.



Future Work

- Continue to update the CIFOCCOs database to provide a more complete coverage of a broader range of population groups.
- Wherever possible, collect data based on FoodEx2 classification.
- Develop a conversion table to approximately translate the foods of animal and plant origin for which food consumption statistics have been collected in CIFOCCOs into Raw Agricultural Commodities.



Questions?



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