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World Health Organization

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**Agenda Item 11** **CRD02**

**July 2021**

**JOINT FAO/WHO FOOD STANDARDS PROGRAMME**

**CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS**

**25th Session**
**(Virtual)**
**12-16 and 20 July 2021**

# REPORT OF WORKING GROUP ON PRIORITY LIST OF VETERINARY DRUGS REQUIRING EVALUATION OR RE-EVALUATION BY JECFA

## I. Introduction

The working group (WG) on priorities was held in virtual mode on July 6, 2021 and chaired by Dr Dugald MacLachlan (Australia). The Chair reminded the EWG on the prioritization criteria and advised the EWG of documents prepared for the CCRVDF25 that were relevant to the discussion (CL 2020/18-RVDF (Rev 1), CX/RVDF 21/25/3, CX/RVDF 21/25/12, CX/RVDF 21/25/12-Add.1).

**Part I. Veterinary drugs for inclusion in the Priority List for JECFA evaluation / re-evaluation**

1. Amoxicillin: The request is for MRLs to be established for chicken tissues. Amoxicillin is classified by WHO as a critically important antimicrobial (CIA) and by the OIE as a veterinary CIA. Amoxicillin has previously been evaluated by JECFA and an ADI and ARfD set. The nominator has confirmed residue data are being generated for evaluation by JECFA. The working group recommended that amoxicillin should be included Part II Veterinary drugs for which data availability should be confirmed at the next meeting of CCRVDF.

2. Fipronil: The request is for MRLs to be established for cattle muscle, fat, liver and kidney. Fipronil has previously been evaluated by JMPR and an ADI and ARfD have been set (2000). The nominator has confirmed that residue and some toxicology data are available. The working group noted the reliance of the nomination on the JMPR evaluation of toxicology. It was raised by the JECFA secretariat that the lack of availability of original toxicology studies might impact the assessment of the compound. The sponsor was encouraged to obtain access to the full toxicological data package. Some members considered the compound could be used as a pilot to explore the use of JMPR toxicology evaluations by JECFA. The working group recommended that fipronil should be included on the priority list.

3. Imidacloprid: The request is for MRLs to be established for fin fish in muscle and skin in natural proportions. Imidacloprid has previously been evaluated by JMPR and an ADI (2001) and ARfD (2002) have been set. The nominator has confirmed that residue and toxicology data, other than some studies on carcinogenicity, are available. The nominator will explore access to the missing genotoxicity studies. The working group recommended that imidacloprid should be included on the priority list.

4. Ivermectin: Two requests were received. The first request is for MRLs to be established in fin fish (Indian and Chinese carp and catfish etc). The nominator has not indicated if residue data are available. The working group recommended that ivermectin in fin fish should not be included on the priority list. The second request was for MRLs to be established for sheep, goat and pig tissues. The nominator has indicated that residue data in sheep are available. The working group recommended that ivermectin for MRLs in sheep, goats and pigs be included on the priority list.

5. Nicarbazin: The request is for a re-evaluation of the nicarbazin MRLs for chicken tissues (muscle, skin/fat, liver and kidney). Nicarbazin has previously been evaluated by JECFA and an ADI has been set (1998). The JECFA secretariat noted it has been over 20 years since the toxicology was last evaluated. As JECFA now considers whether an ARfD needs to be established and the toxicology may need to be considered. It would be an advantage to have access to the original toxicology study reports. The nominator has confirmed that residue data are available, and the working group recommended that nicarbazin should be included on the priority list.

6. Norfloxacin: The request is for MRLs to be established for cattle, camelids, equines, goats, poultry, sheep and swine tissues. Norfloxacin is classified by WHO as a CIA and by the OIE as a veterinary CIA. Norfloxacin has not previously been evaluated by JECFA. The nominator has not been able to confirm the availability of necessary toxicological and

residue data (original study reports) for evaluation by JECFA but did note they are continuing to work to identify data sources. The working group recommended that norfloxacin should be included Part II Veterinary drugs for which data availability should be confirmed at the next meeting of CCRVDF.

Recommendation 1: Approve the substances recommended in the accompanying table for inclusion on the priority list (Appendix 1).

**Part II. Veterinary drugs for which data availability should be confirmed at next CCRVDF**

- Ethoxyquin: Following inclusion on the priority list at CCRVDF21 (2013), ethoxyquin has been retained on the priority list pending confirmation that data is available to enable an evaluation by JECFA else ethoxyquin should be then removed from the priority list. The working group was informed by India that data are being generated and agreed to retain the compound on the priority list pending confirmation of data availability at the next meeting of CCRVDF.

Recommendation 2: Approve the substances recommended in the accompanying table for inclusion as veterinary drugs for which data availability should be confirmed at CCRVDF26 (Appendix 1).

**Part III. Veterinary drugs for which additional data/information is necessary to complete the JECFA evaluation**

JECFA have reported that additional data is required to complete the evaluation of several compounds (CX/RVDF 21/25/3).

- Ethion: the nominator has confirmed data are relevant available with critical studies to be completed in 2024
- Flumethrin: the nominator has confirmed that relevant data are not expected to be available for another three to four years.
- Fosfomycin: no update received
- Sisapronil: the nominator has confirmed relevant data are not available

Recommendation 3: The meeting notes the updates on compounds currently being considered by JECFA and recommended the removal of sisapronil from the priority list.

**Part IV. Parallel review – Evaluation of a new compound**

- Selamectin: the nominator has confirmed relevant data are available

Recommendation 4: The meeting notes the update on the parallel review compound currently being considered by JECFA.

| Name of Compound | Question(s) to be answered | Registration status | Proposed by | Comments | When will data package be available |
|---|---|---|---|---|---|
| **PART I: Veterinary drugs for inclusion in the Priority List for JECFA evaluation / re-evaluation** | | | | | |
| Fipronil | Request for MRL for cattle tissues. | Nominator notes that relevant MRLs are established in Argentina and Uruguay. Use is approved in Brazil. | Brazil | ADI set by JMPR at 0-0.0002 mg/kg bw (2000), ARfD 0.003 mg/kg bw (2000), scheduled for periodic review by the 2021 JMPR. | Residue data available from July 2021. |
| Imidacloprid | Request for MRL for fin fish in muscle and skin in natural proportions. | Nominator notes that relevant MRLs are established in the EU. | Norway | ADI set by JMPR at 0-0.06 mg/kg bw (2001), ARfD 0.4 mg/kg bw (2002). | Residue and toxicological data available July 2021. |
| Ivermectin | Request for re-evaluation of MRLs for sheep, goat ad pig tissues. | MRLs are established in many countries. | EU | ADI set by JECFA at 0-10 µg/kg bw (2015), ARfD 0.2 mg/kg bw (2015). | Residue data on sheep are available. |
| Nicarbazin | Request re-evaluation of MRLs for chicken tissues. | Nominator notes that relevant MRLs are established in many countries. | Argentina/Malaysia | ADI set by JECFA at 0-0.4 mg/kg bw (1998). | Residue data available July 2021. |

| **Part II. Veterinary drugs for which data availability should be confirmed at the next CCRVDF** | | | | |
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| **Name of Compound** | **Question(s) to be answered** | **Proposed by** | **Comments** | **When will data package be available** |
| Amoxicillin | Request for MRLs for chicken tissues. | Chile | ADI set by JECFA at 0-0.07 µg/kg bw (2011), ARfD 0.005 mg/kg bw (2017). Classified by WHO as a CIA and by the OIE as VCIA. | Residue data expected available July 2024. |

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| Ethoxyquin<br>(feed additive use) | Request to establish MRL in shrimp muscle. | Philippines/India | Carried over from CCRVDF21 (2013).<br>ADI 0-0.005 mg/kg bw (2005 JMPR). The ADI and the ARfD are applicable to ethoxyquin and its metabolites/degradation products methylethoxyquin (MEQ), dihydroethoxyquin (DHEQ), dehydrimethylethoxyquin (DHMEQ)<br>ARfD 0.5 mg/kg bw (2005 JMPR). | India advised data are being generated. |
| Norfloxacin | Request to establish MRLs for cattle, camelids, equines, goats, poultry, sheep and swine tissues. | Peru | Norfloxacin is classified by WHO as a CIA and by the OIE as a veterinary CIA. | Peru to advise at next CRVDF if data are available. |
| **Part III. Veterinary drugs for which additional data / information is necessary to complete the JECFA evaluation** | | | | |
| **Name of Compound** | **Information required by JECFA** | | **Comments** | **When will data package be available** |
| Ethion | Additional data/scientific argument to enable MR and MR:TRR to be determined, analytical method. | Argentina (Costa Rica, Uruguay) | From JECFA85, ADI 0-0.002 mg/kg bw, ARfD 0.02 mg/kg bw for general population and 0.002 mg/kg bw for women of child-bearing age. | Metabolism studies to identify compounds of concern, validation of an analytical method and a radiolabel study to enable MR and MR:TRR to be determined are expected to be completed in 2024. |
| Flumethrin | Additional data/scientific argument to enable MR and MR:TRR to be determined, residue depletion data, identity of metabolite in milk and toxicological profile. | EU | ADI set by JECFA at 0-0.004 mg/kg bw (2017), ARfD 0.005 mg/kg bw (2017). | Additional data not expected to be available for 3-4 years. |

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| Fosfomycin | Additional data/scientific argument to enable a mADI to be set, additional data/scientific argument to enable MR and MR:TRR to be determined, analytical method. | Argentina/Paraguay | | |
| **Part IV. Parallel review – Evaluation of a new compound** | | | | |
| **Name of Compound** | **Information required by JECFA** | | **Comments** | **When will data package be available** |
| Selamectin | Additional data/scientific argument to enable MR and MR:TRR to be determined, analytical method, information on GVP, stability of radiolabel in tissues. | Canada/US | Sponsor intends to submit:<br>•Characterization of the residues in tissues in order to establish an MR:TRR.<br>•An MR depletion study under conditions of use, conducted in a laboratory.<br>•Information on an analytical method suitable for monitoring purposes.<br>•Information on the proposed withdrawal period.<br>•Confirmation of the stability of the radiolabel in tissues.<br>•Revised chronic toxicology study report (rat). | Available. |