



ANALYSIS OF AGENDA ITEMS IN PREPARATION FOR THE 25th SESSION OF CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOOD (CCRVDF25)

12 – 16 and 20 July 2021 Virtual Meeting

Substances/MRLs Submitted for Approval

Agenda Item 5: Maximum Residue Limit for Flumethrin (Honey) at Step 7

Objectives

This document offers an analysis of agenda items to support participation to the 25th session of the Codex Committee on Residues of Veterinary Drugs in Food (CCRVDF25), taking place virtually in July 2021. The document is intended for possible use by the Codex communities of practice promoted by [GFORSS](#) and [PARERA](#), as part of their contribution to enhancing awareness and supporting effective participation in international food standard setting meetings (Codex meetings) by representatives from members and observers, in particular in **the Middle East and North Africa**.

The analysis provided in this document offers a factual review of agenda items, their background and a discussion of some considerations. This analysis is indicative in nature and does not represent an official position of the organizations mentioned above ([PARERA](#) and [GFORSS](#)), their membership or their management.

This analysis is prepared as part of the [Codex Initiative for the Middle East and North Africa: MENA Codex Initiative](#), implemented by [PARERA](#) and [GFORSS](#) and funded by the US Codex Office, US Department of Agriculture.

**It is important to note that experts – members of the Expert Working Group (EWG) – do not represent the organizations and / or jurisdictions to which they are affiliated. The selection and participation in the EWG proceedings is based on each expert's own credentials and experience which should not be misconstrued as the country's / delegation's / organization's position to which they belong.*

Agenda Item 5: Maximum residue limit for flumethrin (honey) at Step 7*Documents: REP18/RVDF-App. IV and CX/RVDF 21/25/5***Background**

A proposed draft MRL for Flumethrin in honey was recommended by JECFA85 (2017). This MRL was based on **twice the limit of quantification** of the most reliable analytical method used in the residue studies.

At CCRVDF24 (2018), some members raised concerns that the method used as a basis for the development of the MRL was deemed expensive and not readily available in developing countries. It was noted that some trade problems may occur due to the lack of laboratory capacity to measure such low levels.

The JECFA Secretariat noted that when Flumethrin was used according to Good Veterinary Practice, the amount of residue that could be expected in honey is at or below the limit of quantification of current methods and that there was little risk that residues would move from the wax to the honey due to Flumethrin's highly lipophilic properties.

The CCRVDF24 (2018) agreed to forward a proposal to the Codex Alimentarius Commission (CAC) that an MRL was 'unnecessary' for adoption at Step 5 (allowing for another round of comment and consideration by the Committee). CAC41 (2018) adopted the CCRVDF proposal at Step 5. The draft MRL was circulated for comment at Step 6 and will be considered by CCRVDF25 (2021) at Step 7.

Summary of the Scientific Evaluation of Flumethrin

Chemical Name: (RS)-cyano-4-fluoro-3-phenoxybenzyl 3-(β ,4-dichlorostyryl)-2,2-dimethylcyclopropanecarboxylate.

CAS number:69770-45-2

JECFA number: 85

JECFA Evaluation year: 2017

Functional Class: Veterinary Drug - **pyrethroid (type II) insecticide**

Flumethrin is registered in several countries for the **diagnosis and control in honeybee colonies of varroosis** (also known as varroosis), a disease caused by parasitic mites. Previous approved uses include the external treatment against parasitic insects and ticks on cattle, sheep, goats, horses, and dogs.

Although a synthetic pyrethroid, pyrethroids were developed from natural pyrethrum extracts (Chrysanthemum flowers).

Highlights of the Chronic Toxicity Assessment

ADI: 0–0.004 mg/ kg bw

Health Based Guidance Values (HBGV) based on skin lesions in parental animals and reduced survival and body-weight gain in pups in a two-generation toxicity study in rats. NOAEL from the 2-generation study was **0.37 mg/kg bw/day** (standard 100-fold UF).

Inflammatory ulcerative skin changes were consistently noted in short term toxicity studies. *Flumethrin is not considered to be genotoxic or carcinogenic.*

Highlights of the Acute Toxicity Assessment

ARfD: 0.005 mg/kg bw based on the rat developmental toxicity study.

The NOAEL for maternal toxicity was 0.5 mg/kg bw per day based on clinical signs at 1.0 mg/kg bw per day. The NOAEL for embryo/fetal toxicity was 1.0 mg/kg bw per day based on reduced placental weight, reduced fetal weights and an increase in the incidence of skeletal variations at 2.0 mg/kg bw per day. There was no evidence of teratogenicity. 100-fold UF used to set ARfD.



Typically, pyrethroid (type II) insecticides are neurotoxic (CNS), especially in humans. They interact with voltage-gated sodium channels in neurons, resulting in depolarization caused by the prolonged influx of sodium ions during excitation. The extended depolarization is what leads to repetitive nerve activity that can result in hyperexcitation and death. Type II pyrethroids also cause paresthesia, which is characterized by transient burning/tingling/itching sensation of the exposed skin. Although not described in the JECFA evaluation, this may be the basis for the skin lesions.

Intake: The global estimate of chronic dietary exposure (GECDE) is 0.008 µg/kg bw per day (general population) and 0.006 µg/kg bw per day (children).

The global estimate of acute dietary exposure (GEADE): 0.1 µg/kg bw per day (general population) and 0.1 µg/kg bw per day (children).

It is important to note that the Highest estimated dietary intakes would account for only 2% of the ARfD : very low contribution to the overall intake, leading to an excellent margin of safety.

Comments on the proposed MRL

The proposed MRL for honey is set at 6 µg/kg (6ppb), which is twice the limit of quantification of the most reliable analytical method (liquid chromatography coupled with tandem mass spectrometry; LC–MS/MS) used in the residue studies.

Of the studies reviewed by JECFA, **no quantifiable residues were found in honey** after treatment with the flumethrin products.

Conclusion

This MRLs appears to be both adequate for health protection and from the stand point of achievability and would benefit to move for Adoption at Step 8.

Recommendations of the Expert Working Group

There appears to be very limited data available documenting the occurrence of residues of veterinary substances and pesticides in honey. Honey being an importance food commodity consumed in the region, it is highly recommended that dedicated monitoring programs be devoted to this commodity.