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 6.1:
MRLs for halquinol (in swine - muscle, skin plus fat, liver and kidney) at Step 4

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 6.1: Maximum residue limits for halquinol (in swine - muscle, skin plus fat, liver and kidney) at Step 4

Documents: CL 2020/17-RVDF and CX/RVDF 21/25/6

MRLs for Halquinol in swine – muscle (40 µg/kg), skin plus fat (350 µg/kg), liver (500 ug/kg) and kidney (9000 ug/kg).

The proposed draft MRLs are available for comment at Step 3 and will be discussed by CRVDF25 (2021) at Step 4. The Committee may consider recommending adoption by the next Codex Alimentarius Commission at Step 5 (allowing for another round of comment and consideration by the Committee) or Step 5/8 (final adoption).

Background

Haliquinol: a mixture of chlorinated products of quinoline-8-ol comprising 5,7-dichloroquinolin-8-ol (5,7-DCL or DCHQ; 57–74% weight per weight [w/w]), 5-chloroquinolin-8-ol (5-CL or CHQ; 23–40% w/w) and 7-chloroquinolin-8-ol (7-CL; 0–4% w/w). CAS No. 8067-69-4. Halquinol (trade name Quixalud®) is an antimicrobial used as a feed additive for poultry and as a growth promotant in pigs. Halquinol also is used in swine for the control, treatment and prevention of scours (diarrhoea) caused or complicated by E. coli and Salmonella spp. Halquinol is administered to swine orally in the feed at a dose of approximately 2.4 to 24 mg halquinol/kg bw/day for up to 10 consecutive days with feed concentrates range from 12-60 % halquinol, and varying dose regimens and withdrawal periods. Halquinol was added to the JECFA priority list in 2016 at the request of the USA, supported by the Philippines (CCRVDF23).

85th JECFA (2017): the sponsor reported that halquinol has been approved for over a decade in Thailand, Vietnam, Indonesia and Taiwan and 6 years in the Philippines. During the initial registration of halquinol in these countries, human food safety data (including ADME, residue depletion, etc.) were not required.

Australia completed a special review of halquinol in 1996 but the Australian Pesticides and Veterinary Medicines Authority (APVMA) concluded that there were insufficient toxicological data to support the continued registration of halquinol or its associated MRLs. There are no veterinary products containing halquinol currently registered in Australia for the treatment of food-producing animals.

MRLs could not be recommended by JECFA at the 85th meeting for halquinol due to the lack of an established HBGV and incomplete characterization of residues in tissues (particularly liver and kidney). CCRVDF24 supported the continuing evaluation of halquinol by JECFA.

88th JECFA (2019): ADI of 0–0.2 mg/kg bw, based on histopathological changes in the kidney, accompanied by increases in absolute and relative renal weight in a 1-year chronic toxicity study in rats (NOAEL 15 mg/kg bw/day, 100-fold UF).

Acute reference dose (ARfD) of 0.3 mg/kg bw, based on clinical signs in dams observed in a developmental toxicity study in mice (NOAEL 30 mg/kg bw/day, 100-fold UF).

GECDE (general population): 5.9 µg/kg bw per day (3% of the ADI).

GECDE (children): 6.9 µg/kg bw per day (3.4% of the ADI).

GEADE (children and adults): 2-224 µg/kg bw per day (0.5–75% of the ARfD). The highest GEADE were from consumption of kidney in adults, with all estimates for other tissues being less than 15% of the ARfD.

JECFA affirmed the suitability of the LC-MS/MS method evaluated by the 85th JECFA for determining residues, with the LOQ of the method in all tissues being 10 µg/kg. MRLs were calculated on the basis of 95/95 UTLs (95% confidence interval over the 95th percentile of residue concentrations from non-radiolabelled residue depletion study upper tolerance limits) in swine liver, kidney, muscle and skin + fat at an 8-hour withdrawal period (shortest withdrawal period for an approved product).

Issues

The EU noted that halquinol is an antimicrobial agent, which is indicated for use in pigs and poultry as a growth promoter and for controlling diarrhea. The EU emphasised that the use of antimicrobial agents, including halquinol, is not authorised in the EU for growth promotion and as a result voiced strong concerns as to the establishment of MRLs for halquinol. Halquinol is not authorised as a veterinary medicinal product nor as a feed additive in the EU, therefore no MRLs are established for halquinol in the EU. EFSA has been requested to provide an opinion on the use of halquinol as an antimicrobial feed additive but has yet to complete its evaluation.

Conclusion

There will likely be divergent of opinion by delegates, with all EU member states not supporting advancement of this work due to the EC prohibition on the use of antimicrobials in food-producing animals. Countries where halquinol is already in use, will support the advancement of the JECFA proposed MRLs likely to step 5 in the Codex process. At a minimum, CCRVDF25 should provide an opinion on the updated JECFA evaluation for halquinol and the proposed MRLs, similar to zilpaterol.