



**JOINT FAO/WHO FOOD STANDARDS PROGRAMME
CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS**

Twenty-second Session

San José, Costa Rica, 27 April-1 May 2015

COMMENTS ON:

**THE PROPOSED DRAFT MRLS FOR DERQUANTEL, EMAMECTION BENZOATE, IVERMECTIN,
LASALOCID SODIUM AND MONEPANTEL, AT STEP 3**

**Comments of Brazil, Chile, Costa Rica, Gambia, India, Iran, Kenya, United States of America, Peru,
Philippines, African Union, IFAH**

BRAZIL

Brazil congratulates JECFA for its work and supports the recommendations of the 78th Meeting of the Joint FAO/WHO Expert Committee on Food Additives for the veterinary drugs derquantel, emamectin benzoate, lasalocid sodium and monepantel.

In relation to the recommended MRL for ivermectin of 4µg/kg in cattle muscle Brazil understands that there is a preliminary need for the revision of the established ADI, based on the recommendations of the 40th Meeting of JECFA, in 1992. For this to be accomplished, it is of utmost importance that new toxicological data are made available to JECFA. Therefore, Brazil suggests that the recommended MRL for ivermectin is held at Step 3 of the Procedure.

CHILE

It is important for Codex to move forward with the analysis and establishment of MRLs for active ingredients that are regularly used in animals, and for which Codex has not yet established an MRL. In accordance with the above, Chile supports advancing the proposed draft MRLs for derquantel, emamectin benzoate, ivermectin, sodium lasalocid and monepantel to the next step of the Codex procedure.

COSTA RICA

Costa Rica appreciates the opportunity to comment on the proposed draft MRLs for derquantel, emamectin benzoate, ivermectin, sodium lasalocid and monepantel. Our comments are included below:

1. Derquantel is an anthelmintic agent used in sheep that is not registered in Costa Rica. The re-evaluation of the MRLs was recommended by the 78th JECFA meeting and the following MRLs in sheep were recommended: muscle 0.3; liver 0.8; kidney 0.4 and fat 7.0 µg/kg. The MRLs are at Step 3 and our country agrees with continuing the procedure until they are subject to an accelerated procedure.
2. Monepantel is an anthelmintic agent used in sheep and, just as Derquantel, is not registered in Costa Rica. A re-evaluation of the MRLs for Monepantel was recommended by the 78th JECFA meeting and the following MRLs in sheep, which are higher than those established at Step 7, were recommended. The new MRLs in sheep are: muscle 500; liver 7000; kidney 1700 and fat 13000 µg/kg. The MRLs are at Step 3 and we agree with continuing the procedure until they are subject to an accelerated procedure.
3. Emamectin benzoate is an antiparasitic agent used in salmon and is not registered in Costa Rica. It was evaluated at the 78th JECFA meeting and an ADI of 0-0.5 µg/kg was recommended. The following MRLs in salmon were also recommended: muscle 100 and fillet* 100 µg/kg; these were also applied to trout (muscle 100 and fillet* 100 µg/kg) (*muscle and skin in normal proportions). They are at Step 3 and we agree with continuing the procedure.

4. Ivermectin is an external and internal antiparasitic agent that is registered in our country and which was evaluated in order to recommend an MRL in muscle. The 78th JECFA meeting recommended an MRL in bovine muscle of 4 µg/kg which is very important to meet the trade requirements between trading partners wherefore we agree with continuing the procedure.

5. Sodium lasolacid: antiparasitic agent registered in our country for use in poultry including, among others, chickens, replacement pullets and turkeys. The 78th JECFA meeting recommended an ADI of 0-5 µg/kg and, additionally, recommended the following MRLs in chickens, hens, turkeys, quails and pheasants: muscle 400; liver 1200; kidney 600 and skin + fat 600 µg/kg. Costa Rica agrees with continuing the procedure until they are subject to an accelerated procedure.

GAMBIA

Emamectin benzoate,

- *JECFA recommended the following MRLs for emamectin B1a*
- *salmon :100 µg/kg in muscle and fillet,*

And **extended these MRLs** (100 µg/kg in muscle and fillet) to trout.

- The EDI is 11 µg/person per day, which represents 37% of the upper bound of the ADI
- The Gambia recommended advancement of the MRL.

Ivermectin, draft MRL at step 3

- The Committee recommended an MRL of 4 µg/kg for cattle muscle
- The MRL was determined as ivermectin B1a and based on 2 × LOQ of the analytical method.
- The Gambia recommended advancement of the MRL.
- **lasalocid sodium draft MRL at step 3**
- *The 78th JECFA extended the MRLs in chicken to turkey and quail and extrapolated the MRLs in chicken to pheasant.*
- *No information was available for duck, including on approved uses.*
- *As the compound is not registered for use in laying hens, according to the sponsor, it is not appropriate to recommend MRLs for eggs*
- The Gambia recommended advancement of the MRL.

INDIA

India supports the residue level prescribed by JECFA on deraquantel, emamectin benzoate, lasalocid sodium and monepental at Step 3.

However, MRL for ivermectin in cattle muscle as recommended by 78th JECFA at the level of 4 microgram/kg is too stringent. It is lower than that of the MRLs established by EU which is 30 microgram/kg (Commission Regulation No. 418/2014 of 24th April, 2014) and Canada 10 microgram/kg (marketing authorization for MRLs for veterinary drugs in foods dated 13th February, 2015). Since no assessment on the dietary exposure is undertaken, further study may be required for the same before fixing the MRL.

IRAN

Iran is in agreement with the proposed MRLs.

KENYA**DERQUANTEL** (anthelmintic agent)**Acceptable Daily Intake (ADI):**

Residue Definition:		Derquantel.					
Species	Tissue	MRLs(µg/kg) recommended by the 75 th JECFA	Step	JECFA	MRLs (µg/kg) recommended by the 78 th JECFA	Step	JECFA
Sheep	Muscle	0.2	4	75	0.3	3	78
Sheep	Liver	2.0	4	75	0.8	3	78
Sheep	Kidney	0.2	4	75	0.4	3	78
Sheep	Fat	0.7	4	75	7.0	3	78

In shaded font are the MRLs held at Step 4 by CCRVDF21.

COMMENT ON THE DERQUANTEL IN THE TABLE ABOVE:

Kenya appreciate the evaluation by JECFA the results at the 78th session meeting here in the table

1. We have noted that increase of MRLs of sheep fat from 0.7 microgram/kg in JECFA evaluation of 75th session to 7.0 microgram/kg recommendation so we would like to request JECFA on clarification on this .

2. Kenya has no objection with the results of Emamectin benzoate and Ivermectin and recommend for the advancement of the two to the next step.

3. Lasalocid sodium

Kenya took note that the 78th JECFA extended the MRLs for Lasalocid in chicken to turkey and quail and extrapolated the MRLs in chicken to pheasant. No information was available for duck, including on approved uses.

COMMENT:

As the compound is not registered for use in laying hens, according to the sponsor, it is not appropriate to recommend MRLs for eggs

UNITES STATES OF AMERICA

The United States supports advancing the proposed draft MRLs at Step 3 for dequantel, emamectin benzoate, lasalocid sodium, and monepantel to Step 5/8.

The United States recognizes that new data are available for ivermectin that may change the current JECFA recommendation for an MRL for residues of ivermectin in cattle muscle. While the United States notes that the new data are not anticipated to call into question the safety of the current recommendation, the new data are likely to support higher tissue MRLs, including in cattle muscle, when good practice of veterinary drugs is followed. Consequently the United States supports holding the draft MRLs for ivermectin in cattle muscle at Step 4.

PERU**GENERAL OBSERVATIONS:**

The collegial decision of the Technical Committee on Residues of Veterinary Drugs in Foods was to support the regional position agreed by the Codex Alimentarius Coordinating Committee for Latin America and the Caribbean -CCLAC-, concerning Derquantel, Emamectin Benzoate, Ivermectin, Sodium Lasalocid and Monepantel, specifically for each substance or in general.

<p>the analytical method.</p> <p>Lasalocid sodium</p> <p>AU took note that the 78th JECFA <u>extended</u> the MRLs for Lasalocid A in chicken to turkey and quail and <u>extrapolated</u> the MRLs in chicken to pheasant. No information was available for duck, including on approved uses.</p> <p>As the compound is not registered for use in laying hens, according to the sponsor, it is not appropriate to recommend MRLs for eggs</p>	<p>AU recommended advancement of the MRLs.</p>
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IFAH

IFAH, the International Federation for Animal Health, is pleased to provide the following thoughts for consideration.

DERQUANTEL

IFAH supports the derquantel MRLs as recommended by the 78th JECFA for advancement to Step 5. Furthermore, as MRLs have now been secured in all major markets where the product is sold, IFAH further supports the advancement of the derquantel MRLs to Step 5/8 so as to secure final Codex MRLs, which are both protective of public health and which facilitate international trade, at the earliest opportunity,

LASALOCID

At the request of Zoetis, the United States Delegation nominated lasalocid for inclusion on the priority list to be discussed at the 20th CCRVDF in San Juan Puerto Rico. The specific request was as in Table 1 (excerpted from the final report of the 20th CCRVDF).

Table 1. Priority List Request for Lasalocid

Lasalocid	Request to establish ADI and recommend MRLs in poultry (tissues and eggs) use patterns in all regions where it is registered. Chickens, turkey, duck, quail, pheasant.
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Report of the 20th Session of the CCRVDF (San Juan, PR May 2012)

REP12/RVDF Appendix IX (page 52)

The Priority List clearly indicated a request for MRLs in poultry tissues and eggs. The 78th JECFA evaluated lasalocid and recommended the following ADI and MRLs for poultry tissues only. JECFA did not consider it appropriate to recommend MRLs for eggs as the compound is not registered for use in laying hens.

Table 2 summarizes the JECFA recommendations.

Table 2. Current Recommendations by the 78th JECFA for Lasalocid MRLs in Poultry

NOEL =	0.5 mg/kg		Safety Factor (SF) =	100		
ADI =	5 µg/kg		(NOEL/SF x 1000 µg/mg)			
(or) ADI =	300 µg/day		(ADI x 60 kg bw)			
Tissue	MRL (µg/kg)	Median Residues (1-Day Withdrawal)	Marker/Total Ratio	Total Residues (µg/kg)	Cons. Factor (kg)	Intake (µg)
Liver	1200	124	0.22	564	0.1	56.4
Kidney	600	50.0	0.41	122	0.01	6.10
Muscle	400	25.1	0.55	45.5	0.3	13.7
Skin / Fat	600	41.8	0.52	80.3	0.09	4.01
				Total Intake (µg) =		80.1
				% of ADI =		27%

IFAH supports the tissue MRLs as recommended by JECFA.

However, IFAH deems it unfortunate that JECFA did not recommend MRLs for eggs as clearly requested by the 20th CCRVDF. The Sponsor was clearly aware that no approvals exist for use of lasalocid in layers and this MRL was not sought to provide a basis for such an approval. The Sponsor included the following rationale with respect to the importance of an egg MRL for lasalocid in the dossier so that JECFA was fully informed of the need for this MRL.

Avatec® (lasalocid) is not approved (or recommended) for use in laying birds producing eggs for human consumption as lasalocid partitions into fat (egg yolks) at high concentrations. It is only authorised for use in layer replacement chickens up to an age of 16 weeks, ca 3 weeks before birds start laying eggs. Nevertheless, it is critically important that an MRL be established for lasalocid in eggs. It has been recognized over the past several years that cross-contamination of feed can lead to exposure of non-target species to lasalocid as well as other veterinary medicinal products. Many producer feed-mixing facilities do not have sufficient equipment or procedures to allow for complete flushing of their systems between medicated and subsequent non-medicated batches. So cross-contamination can occur.

The European Union and other regulatory agencies have thus established an MRL in eggs for lasalocid to help avoid the unnecessary discard of food commodities (eggs) when small amounts of lasalocid are detected. While prevention is the best precaution, it is recognized that this is extremely difficult to achieve (i.e. zero residues) commercially and the elaboration of a minimal MRL for eggs has proven to be a more practical safeguard. In the European Union, an MRL for eggs of 150 µg/kg has been elaborated. This MRL does not permit use of lasalocid in layer feed as residues (in eggs) would be far in excess of the MRL and the withdrawal time for residue depletion would be impractical from a commercial viewpoint.

It is important to note that a sufficient amount of residue data to set an MRL for eggs was submitted to JECFA for review. JECFA failed to set an MRL based on a policy decision and not due to any safety concern.

As the 22nd CCRVDF has the authority to accept, reject or modify the JECFA recommendations for MRLs, IFAH requests that CCRVDF use this authority to modify the JECFA recommendations to include eggs with an MRL = 150 µg/kg, consistent with the value elaborated by the European Union. IFAH makes the following additional points to support its proposal:

1. The purpose of CCRVDF is to protect public health but also to facilitate international trade. There is a clear need for an MRL for lasalocid in eggs with respect to this second mandate.
2. Without an MRL, eggs that might contain small quantities of lasalocid due to cross-contamination from feed mixing operations would need to be discarded even if safe for human consumption. IFAH sees no benefit in discarding wholesome food commodities unnecessarily, and negatively (and randomly) impacting producers who are unaware that trace contamination may be present in commercially obtained non-medicated feed.
3. The European Union was of the opinion that the issue of cross-contamination was of sufficient importance to establish legislation addressing the issue.
4. CCRVDF has used its authority to modify MRLs recommended by JECFA at previous meetings (e.g. milk MRL for pirlimycin) so this action has precedent at CCRVDF.

The specific recommendations by IFAH for consideration by the 22nd CCRVDF are as follows:

5. Accept the tissue MRLs as recommended by the 78th JECFA
6. Include an MRL for eggs equivalent to 150 µg/kg in agreement with that established by the European Union (the EU has completed a safety assessment for eggs based on the same dossier submitted to JECFA).
7. To demonstrate safety, update the % ADI utilization for eggs using the TMDI approach. JECFA used the EDI approach for the edible tissues so inclusion of the TMDI calculation for eggs reflects a more conservative approach. The maximum intake is still well below the recommended ADI confirming there is no safety concern for eggs.

The updated proposal by IFAH is summarized in

Table 3.

Table 3. IFAH Recommendation for Modification of the Lasalocid MRLs for Poultry

NOEL =	0.5 mg/kg		Safety Factor (SF) =		100	
ADI =	5 µg/kg		(NOEL/SF x 1000 µg/mg)			
(or) ADI =	300 µg/day		(ADI x 60 kg bw)			
Tissue	MRL (µg/kg)	Median Residues (1-Day Withdrawal)	Marker/Total Ratio	Total Residues (µg/kg)	Cons. Factor (kg)	Intake (µg)
Liver	1200	124	0.22	564	0.1	56.4
Kidney	600	50.0	0.41	122	0.01	6.10
Muscle	400	25.1	0.55	45.5	0.3	13.7
Skin / Fat	600	41.8	0.52	80.3	0.09	4.01
Eggs	150	150	0.38	395	0.10	39.5
				Total Intake (µg) =		120
				% of ADI =		40%

This decision rests with the CCRVDF. There is no reason to return this to JECFA for further review as JECFA is unable to provide further guidance as a result of its internal policies.

IFAH requests that CCRVDF make this modification to the lasalocid MRLs as recommended by JECFA and thereby make a firm statement about its commitment to the facilitation of international trade.