CODEX ALIMENTARIUS COMMISSION

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Agenda Item 6 **CX/RVDF 13/21/6 Add.3**
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JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

Twenty-first Session

Minneapolis, Minnesota, United States of America, 26 – 30 August 2013

RISK MANAGEMENT RECOMMENDATIONS FOR RESIDUES OF VETERINARY DRUGS FOR WHICH NO ADI AND / OR MRL HAS BEEN RECOMMENDED BY JECFA DUE TO SPECIFIC HUMAN HEALTH (at Step 3)

PART 1 COMMENTS AT STEP 3 ON PROPOSED DRAFT RISK MANAGEMENT RECOMMENDATIONS FOR CHLORAMPHENICOL AND MALACHITE GREEN (CL 2012/23-RVDF, PART B)

Comments of Kenya, Nigeria, the Philippines and African Union (AU)

KENYA

Specific comments

a. In view of JECFA's conclusions on the available scientific information, that there is no safe level of residues of Chloramphenicol or its metabolites in food that represents an acceptable risk to consumers; we advise member states not to use Chloramphenicol in food producing animals. Kenya agrees with JECFA's conclusions that Chloramphenical should not be used in food producing animals and therefore we consider option A as an appropriate risk Management option

Justification/rationale

Kenya noted JECFA's evaluation that Chloramphenicol is a health related hazard because (a) it is carcinogenic with evidence of genotoxic mechanism and (b) epidemiological studies in humans showed that it is not possible to establish any dose-relationship or threshold dose for the induction of a potentially fatal aplastic anemia. JECFA concluded that it was not appropriate to establish an ADI or recommend MRLs; based on the available information, a concentration in food could not be established below which an exposure may be expected to be deemed safe.

Specific comments

b. In view of JECFA's conclusions based on the available scientific information, we recommend that member states should not use Malachite Green in food producing animals.

Information, a concentration in food could not be established below which an exposure may be expected to be deemed safe.

Kenya agrees with JECFA's conclusions that Malachite Green should not be used in food producing animals and therefore we consider option A as an appropriate risk Management option

RATIONALE

Kenya noted JECFA's evaluation of Malachite Green and its metabolites which showed that it is a health related hazard because (a) it is carcinogenic with the evidence of a genotoxic mechanism and (b) there is an inadequate margin of exposure to assure protection of public health based on its use in market size fish. JECFA concluded that it was not appropriate to establish an ADI or recommend MRLs for Malachite Green.

NIGERIA

Appendix I

PROPOSED DRAFT RISK MANAGEMENT RECOMMENDATIONS FOR CHLORAMPHENICOL

Nigeria supports JECFA recommendation that chloramphenicol should not be used in food producing animals, as there is no safe level of residues of chloramphenicol or its metabolites in food. There are alternative safer equivalents of chloramphenicol that do not pose as much risks. These alternative drugs are available in the market and affordable.

Appendix II

PROPOSED DRAFT RISK MANAGEMENT RECOMMENDATIONS FOR MALACHITE GREEN

Nigeria supports JECFA's recommendation of not using malachite green in food producing animals Nigeria wishes to suggest the identification and evaluation of alternative drugs that can be used against fungal and protozoan infections especially in aquaculture where the drug is commonly used.

Justification

The conclusions reached by JECFA on the health hazards of the parent drug and metabolites is in public health interest.

PHILIPPINES

Chloramphenicol

The Philippines reconfirms its position that competent authorities should prevent residues of chloramphenicol in food. This can be accomplished by not using chloramphenicol in food - producing animals. The following justifications are hereby enumerated:

1) The Philippine government's decision to ban a drug for use in food animals is reinforced by human health concern. It is based on genotoxicity, carcinogenicity and other significant health risks that the drug may cause to humans.

2) The Philippines believes that genotoxicity, carcinogenicity and other significant health risks cannot be compromised. The country does not support the use of alternative approaches like long withdrawal period and margin of exposure.

Hence, strongly recommend for its advancement to Step 5/8.

Malachite Green

Considering the finding of JECFA that malachite green is health-related hazard because of a) carcinogenicity with the evidence of a genotoxic mechanism and b) an inadequate margin of exposure to assure protection of public health based on the use of malachite green in marketable fish. JECFA concluded that it is not appropriate to establish an ADI or recommend MRLs; based on the available information, a concentration in food could not be established below which an exposure may be expected to be deemed safe. The Philippines position is for competent authorities to prevent residues of Malachite Green in food. This can be accomplished by not using Malachite Green in food producing animals.

Hence, strongly recommend for its advancement to Step 5/8.

AFRICAN UNION (AU)

Chloramphenicol

African Experts noted JECFA's evaluation that Chloramphenicol is a health related hazard because (a) it is carcinogenic with evidence of genotoxic mechanism and (b) epidemiological studies in humans showed that it is not possible to establish any dose-relationship or threshold dose for the induction of a potentially fatal aplastic anemia. JECFA concluded that it was not appropriate to establish an ADI or recommend MRLs; based on the available information, a concentration in food could not be established below which an exposure may be expected to be deemed safe.

African Experts *agreed with JECFA's conclusions that Chloramphenical should not be used in food producing animals.*

In view of JECFA's conclusions on the available scientific information, that there is no safe level of residues of **Chloramphenicol** or its metabolites in food that represents an acceptable risk to consumers; The AU advices that **Chloramphenicol** should not be used in food producing animals.

Malachite Green

African Experts noted JECFA's evaluation of **Malachite Green** and its metabolites which showed that it is a health related hazard because (a) it is carcinogenic with the evidence of a genotoxic mechanism and (b) there is an inadequate margin of exposure to assure protection of public health based on its use in market size fish. JECFA concluded that it was not appropriate to establish an ADI or recommend MRLs for **Malachite Green.** Based on the available information, a concentration in food could not be established below which an exposure may be expected to be deemed safe.

African Experts *agreed with JECFA's conclusion that Malachite Green should not be used in food producing animals.*

In view of JECFA's conclusions based on the available scientific information, the AU recommends that **Malachite Green** should not be used in food producing animals.

PART 2 COMMENTS AT STEP 3 ON PROPOSED DRAFT RISK MANAGEMENT RECOMMENDATIONS FOR CARBADOX, THE TWO NITROFURANS (FURAZOLIDONE AND NITROFURAL), CHLORPROMAZINE, STILBENES, OLAQUINDOX AND THE FOUR NITROIMIDAZOLES (DIMETRIDAZOLE, IPRONIDAZOLE, METRONIDAZOLE AND RONIDAZOLE) (CX/RVDF 13/21/6)

Comments of Kenya, Nigeria, the Philippines and African Union (AU)

KENYA

General comments

Kenya appreciates the work done lead by the EU in developing the report of the electronic Working Group to develop risk management recommendations for certain veterinary drugs for which JECFA has been unable to establish an acceptable daily intake (ADI) or recommend maximum residue limits (MRLs) due to specific human health concerns. Kenya has carefully considered the report, comments by other members of the electronic Working Group and come up with the following comments and recommendations as indicated below:

Specific comments

In view of the health risks identified by JECFA, the experts opted for risk management recommendation option A for Carbadox, Dimetridazole, Furazolidone, Nitrofural, Chlorpromazine, Stillbenes, Olaquindox, , Ipronidazole and Ronidazole.

Kenya consider risk management recommendation option B for Metronidazole because there is little or no information on toxicity, total residues depletion studies and metabolism of Metronidazole in food producing animal.

NIGERIA

Based upon the fact that there are (available) alternative veterinary drugs that has data on ADI and MRLs, Nigeria wishes to support Option A as the risk management measures for each of the substances (i.e. carbadox, furazolidone and nitrofural, chlorpromazine, stilbenes, olaquindox and the four nitroimidazoles (dimetridazole, ipronidazole, metronidazole and ronidazole).

PHILIPPINES

Specific comments

The Philippines appreciates the effort of the Electronic Working Group (e-WG) in charge of developing risk management recommendations for which no ADI and/or MRL has been recommended by JECFA due to specific human health concerns.

The Philippines considers Option A (competent authorities should prevent residues of these veterinary drugs in food. This can be accomplished by not using these veterinary drugs in food producing animals.) for the following veterinary drugs with no ADI and/or MRLs recommended by JECFA due to Specific Human Health Concerns: Carbadox Furazolidone, Nitrofural, Chlorpromazine, Stilbenes, Olaquindox, Dimetridazole, Ipronidazole, Metronidazole and Ronidazole.

Justification:

The Philippine government's decision of not using these veterinary drugs in food-producing animals is reinforced by human health concern based on genotoxicity, carcinogenecity and other significant health risks that may cause to humans, as human safety is always a top priority.

AFRICAN UNION (AU)

In view of the health risks identified by JECFA, AU recommends that countries should opt for risk management recommendation **option A** for Carbadox, Dimetridazole, Furazolidone, Nitrofural, Chlorpromazine, Stillbenes, Olaquindox, Dimetridazole, Ipronidazole, Ronidazole and risk management recommendation **option B** for Metronidazole.

Carbadox

African Experts noted JECFA's evaluation of **Carbadox** and its metabolites which showed that they are hazardous to health because they are carcinogenic. JECFA also could not determine the amount of residues of **Carbadox** and its metabolites in food that represented an acceptable risk to consumers.

African Experts *agreed with the electronic working group's (eWG) conclusion that Carbadox should not be used in food producing animals.*

In view of the JECFA conclusions on the available scientific information, there is no safe level of residues of ***Carbadox*** *or its metabolites in food that represents an acceptable risk to consumers. For this reason, AU recommends that competent authorities should prevent residues of* ***Carbadox*** *in food under* ***Option A****. This can be accomplished by not using* ***Carbadox*** *in food producing animals.*

Furazolidone

African Experts noted JECFA's evaluation of **Furazolidone** which showed that it is a genotoxic carcinogen. JECFA also could not determine the amounts of residues of furazolidone in food that represented an acceptable risk to consumers.

African Experts *agreed with recommendation 'A' of the electronic working group.*

*In view of the JECFA conclusions on the available scientific information, there is no safe level of residues of F****urazolidone*** *or its metabolites in food that represents an acceptable risk to consumers. For this reason, AU also recommends that competent authorities should prevent residues of* ***Furazolidone*** *in food as shown under* ***Option A****. This can be accomplished by not using* ***Furazolidone*** *in food producing animals*".

Nitrofural

African Experts noted JECFA's evaluation of **Nitrofura**l which showed that it is fetotoxic at maternally toxic doses, genotoxic *in vitro*, but not *in vivo*, tumorigenic but not carcinogenic in rats and mice, with the conclusion that it may be a secondary carcinogen, producing effects in endocrine-responsive organs by a mechanism that remains to be elucidated. JECFA also could not determine the amounts of residues of **Nitrofural** and its metabolites in food that represented an acceptable risk to consumers.

African Experts *supported option A of the eWG's recommendation that Nitrofural should not be used in food producing animals.*

In view of the JECFA conclusions on the available scientific information, there is no safe level of residues of ***Nitrofural*** *or its metabolites in food that represents an acceptable risk to consumers. For this reason, AU advises competent authorities should prevent residues of* ***Nitrofural*** *in food as stated under* ***Option A****. This can be accomplished by not using* ***Nitrofural*** *in food producing animals.*

Chlorpromazine

African Experts noted JECFA's information of chlorpromazine *ie*; the lack of relevant toxicological data; the long-term persistence of **Chlorpromazine** in humans; the spectrum of additional effects of the drug; and the probability that even small doses can cause behavioural change. JECFA also could not determine the amounts of residues of chlorpromazine and its metabolites in food that represented an acceptable risk to consumers.

African Experts *agreed with JECFA's suggestion that* ***Chlorpromazine*** *should not be used in food producing animals.*

In view of the JECFA conclusions on the available scientific information, there is no safe level of residues of ***Chlorpromazine*** *or its metabolites in food that represents an acceptable risk to consumers. For this reason,*

*AU encourages competent authorities to prevent residues of **Chlorpromazine** in food as stated under **Option A**. This can be accomplished by not using **Chlorpromazine** in food producing animals.*

Diethyl Stilbestrol (DES) or Stilbenes

African Experts noted JECFA's evaluation of **Diethyl Stilbestrol (DES) or Stilbenes** and its metabolites which showed that they are carcinogenic. JECFA also could not determine the amounts of residues of DES and its metabolites in food that represented an acceptable risk to consumers.

African Experts *agreed with option A of the eWG's recommendation that DES should not be used in food producing animals.*

*In view of the JECFA conclusions on the available scientific information, there is no safe level of residues of **Stilbenes** or its metabolites in food that represents an acceptable risk to consumers. For this reason, AU recommends that competent authorities should prevent residues of **Stilbenes** in food as stated under **Option A**. This can be accomplished by not using **Stilbenes** in food producing animals.*

Olaquindox

African Experts noted JECFA's evaluation of **Olaquindox** and its metabolites which showed that they are genotoxic, potential germ cell mutagen and tumorigenic. JECFA also could not determine the amounts of residues of **Olaquindox** and its metabolites in food that represented an acceptable risk to consumers.

African Experts *agreed with option A of the eWG's recommendation that **Olaquindox** should not be used in food producing animals.*

*In view of the JECFA conclusions on the available scientific information, there is no safe level of residues of **Olaquindox** or its metabolites in food that represents an acceptable risk to consumers. For this reason, competent authorities should prevent residues of **Olaquindox** in food. This can be accomplished by not using **Olaquindox** in food producing animals.*

Dimetridazole

African Experts noted that JECFA considered **Dimetridazole** to be a health related hazard because it was tumorigenic in rodents and information on carcinogenicity or tumorigenicity in a non-rodent mammalian bioassay was not available. JECFA also could not determine the amounts of residues of **Dimetridazole** in food that represented an acceptable risk to consumers.

African Experts *agreed with option A of the eWG's recommendation that **Dimetridazole** should not be used in food producing animals.*

*In view of the JECFA conclusions on the available scientific information, there is no safe level of residues of **Dimetridazole** or its metabolites in food that represents an acceptable risk to consumers. For this reason, AU advises competent authorities to prevent residues of **Dimetridazole** in food as stated under **Option A**. This can be accomplished by not using **Dimetridazole** in food producing animals*".

Ipronidazole

African Experts noted that JECFA considered **Ipronidazole** to be a health related hazard. It is tumorigenic in rodents although the mode of action could not be identified.

JECFA also could not determine the amounts of residues of Ipronidazole in food that represented an acceptable risk to consumers.

African Experts *agreed with option A of the eWG's recommendation that Ipronidazole should not be used in food producing animals*.

*In view of the JECFA conclusions on the available scientific information, there is no safe level of residues of **Ipronidazole** or its metabolites in food that represents an acceptable risk to consumers. For this reason, AU advises that competent authorities prevent residues of **Ipronidazole** in food as stated under **Option A**. This can be accomplished by not using **Ipronidazole** in food producing animals*".

Metronidazole

African Experts noted that there is little or no information on the toxicity, total residue depletion and metabolism of **Metronidazole** in food producing animals. Besides, there are no analytical procedures to measure and identify its residues.

African Experts *agreed with eWG's recomendation 'B' that no specific risk management measures can be recommended for **Metronidazole**.*

AU recommends that; i*n absence of a JECFA evaluation, no specific risk management measures can be recommended for* ***Metronidazole. AU supports Option B.***

Ronidazole

African Experts noted that JECFA considered **Ronidazole** to be genotoxic *in vitro*, carcinogenic in rats and tumorigenic in mice. JECFA also could not determine the amounts of residues of **Ronidazole** in food that represented an acceptable risk to consumers.

African Experts *agreed with option A of the eWG's recommendation that* ***Ronidazole*** *should not be used in food producing animals.*

In view of the JECFA conclusions on the available scientific information, there is no safe level of residues of ***Ronidazole*** *or its metabolites in food that represents an acceptable risk to consumers. For this reason, AU recommends that competent authorities should prevent residues of* ***Ronidazole*** *in food, as stated under* ***Option A****. This can be accomplished by not using* ***Ronidazole*** *in food producing animals*".