Implementation of the proposed systematic approach – working examples

The scope of this exercise is to explore the usefulness and the practical aspects of implementing a systematic approach for the priorization of emerging issues CCRVDF has to tackle, as described in the document CX/RVDF 16/23/8. In that view, during this side-event, the device proposed from the work of the EWG chaired by France is to be tested through three issues CCRVDF has already faced:

- The policy for the establishment of MRLs or other limits in honey – referred to as "honey" within this document;
- The establishment of MRLs for colistin;
- The establishment of MRLs for clenbuterol.

Therefore, participants of this side-events are kindly invited to provide their inputs and their comments in order to find an agreement on how those three issues should be examined using the proposed priorization device. Because some background related to those past works undertaken by CCRVDF might be necessary, participants of the side-event should consider *inter alia* the following information:

1. Policy for the establishment of MRLs or other limits in honey – "honey"

Short description of the issue:

While many countries authorize the use of veterinary drugs in honey producing bees, most of the time, no MRLs have been established to ensure the safety of honey. As a result, consumers might be overexposed to certain compounds, especially because of the combination of several foodborne and non-foodborne sources of chemical residues.

The evaluation of that prospective risk is particularly challenging, given the intrinsic characteristics of honey production:

- Honey is a non-homogenous product of animal origin. When considering a honey bulk, concentration of residues may be highly variable depending of the position considered within the hive.
- There is no real pharmacokinetic depletion of residues following treatment of bees as is found, for example, after treatment of mammals. When present in honey, residues deplete only by dilution as more honey is produced and possibly by thermal degradation or acidic hydrolysis.
- It's very difficult to apply a withdrawal period considering the real honey production conditions. Therefore, most of the time, a "zero" withdrawal period is recommended.

Also, the breeding and collecting of honey may vary a lot between countries or in relation with climate conditions.

Context which led to raise the issue in CCRVDF:

The issue regarding MRLs or other limits in honey has to do with two important issues that took place in Codex from the late 2000s (2008 onward):

- The extrapolation of MRLs from one species to another and from one tissue from another;
- The appropriateness of revising the approach implemented by JECFA and CCRVDF to assess the consumption of products from animal origin.

In 2011, JECFA noted that CCRVDF haven't provided any guidelines regarding the establishment of MRLs in honey and requested the committee to do so. An EWG was set up to that purpose.

Public health aspects related to the issue:

Possible overexposure, especially for high consumers of honey, as multiple sources or residues may exist.

Trade aspects related to the issue:

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Availability of data:

Very few data regarding worldwide consumption of honey, depletion aspects of veterinary drugs in hives, and the possibility to extrapolate scientific knowledge from mammal food production to honey bee production.

Low probability of new data to be provided.

Other aspects to be considered:

VICH have been requested data related to honey production if available.

2. Establishment of MRLs for colistin

Short description of the issue:

Colistin is a peptidic antimicrobial agent that have been used in food-producing animals since the mid-1950's against gastrointestinal bacterial infection. Determination of an ADI and relative MRLs were needed as residues from veterinary treatments may be ingested by human consumers.

Context which led to raise the issue in CCRVDF:

In 2004, a delegation proposed to put colistin on the priority list for evaluation by JECFA and provided scientific data. JECFA evaluated colistin in 2006 and proposed an ADI and MRLs.

Public health aspects related to the issue:

The oral absorption of colistin or its metabolites is very low. Therefore, the main hazards the foodborne absorption of colistin (meat, milk or eggs that might contain residues of veterinary treatments) can cause to consumers are related to its effects on the commensal gastrointestinal flora (diarrhea, vomiting, opportunist infections, etc.)

Recently, the interest of colistin have been recognized in some human infections. This raised some concerns about the effects its use as a veterinary drug could have on the development of antimicrobioresistance.

Trade aspects related to the issue:

International trade benefits from Codex MRLs in general.

Availability of data:

At the time where colistin was added to the JECFA priority list, the requesting delegation ensured that it was willing to submit data.

Scientific data were sufficient for JECFA to proposed an ADI on the basis of an EDI (Estimated Daily Intake) approach and to recommend MRLs in a wide variety of species and tissues.

Other aspects to be considered:

The international commitment against antimicrobioresistance (?)

3. <u>Establishment of MRLs for clenbuterol</u>

Short description of the issue:

Clenbuterol is a beta-agonist drug that have been used in food-producing animals from the 1970's onward. Given its affinity for the beta-2-adrenergic receptor, clenbuterol has an activity on both respiratory tracks and cardiac and smooth muscles. As such, it is used in the cure of respiratory affections and to induce tocolysis.

In human overdose of clenbuterol can cause severe cardiorespiratory failures and might be lethal. Clenbuterol has also been described as having an history of illegal abuses. For instance, it has been involved in food frauds and in doping affairs.

Context which led to raise the issue in CCRVDF:

Clenbuterol has been added to the JECFA priority list in 1994. However, it has not been evaluated before 1998. In the absence of internationally recognized guidelines related to the authorization of veterinary drugs at that time, MRLs were needed to ensure the safety of the consumer.

Public health aspects related to the issue:

Overdose of clenbuterol can cause severe health troubles in human. The foodborne intake of clenbuterol, especially in the case that illegal use of the drug as a growth promoting agent occurs, can participate to the human exposure.

Trade aspects related to the issue:

The main issue raised by clenbuterol in international food exchanges is related to its illegal use as a growth promoter.

As a beta agonist growth promoting agent, use of clenbuterol is restricted in several countries, which may have created barriers to trade.

Its control in dairy cows seems to be less challenging as it is less likely to find illegal uses in dairy production farms.

Availability of data:

Clenbuterol was put in the JECFA priority list in 1995, but its first evaluation by this committee was only performed in 1998. Though it was commercialized several decades ago, the general knowledge about beta-agonized allowed JECFA to recommend MRLs in horse and cattle tissues and in milk.

Other aspects to be considered:

Risk management issues regarding its potential illegal use in meat-producing cattle.