

Codex Outreach Program - Preparation to CCRVDF26

ANALYSIS OF AGENDA ITEMS IN PREPARATION FOR THE 26th SESSION OF THE CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS (CCRVDF26)

Agenda items from 6 to 10

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Introduction

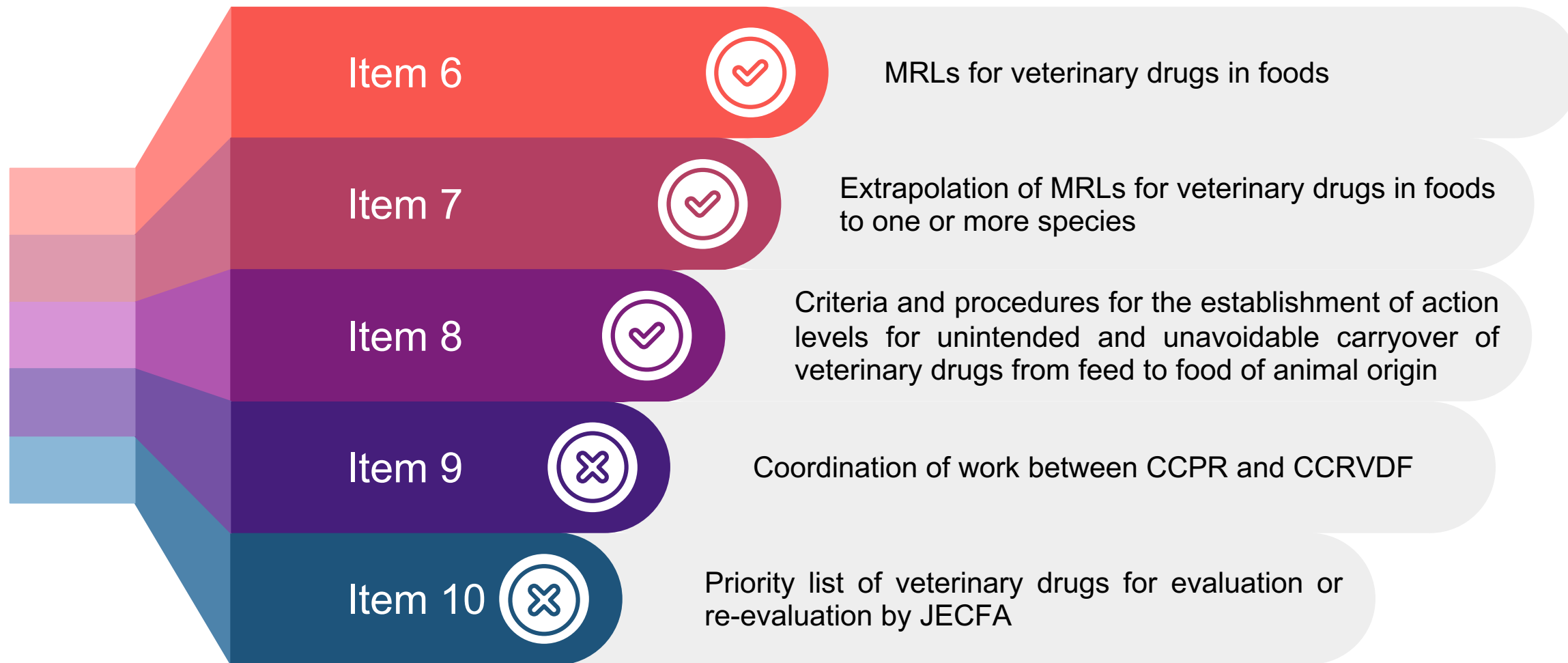
This presentation is part of the Codex outreach Program's contribution to enhancing awareness and supporting effective participation of delegations from Asia and the South-West Pacific in Codex meetings.

It aims to support the analysis of Agenda Items and Prepare positions for Select Meetings

This analysis is indicative in nature and does not represent an official position of the sponsors nor of the organizations with which experts are affiliated e.g., [GFoRSS](#)).



Most Relevant Agenda Items



Agenda item 6

Item 6



MRLs for veterinary drugs in foods

Item 6.1

MRLs for Ivermectin (sheep, pigs and goats – fat, kidney, liver and muscle)

Step 7

Item 6.2

MRLs for Ivermectin (pigs, sheep and goats) and Nicarbazin (chicken)

Step 4

Agenda item 6.1

Item 6



MRLs for veterinary drugs in foods

Item 6.1

MRLs for Ivermectin (sheep, pigs and goats
– fat, kidney, liver and muscle)

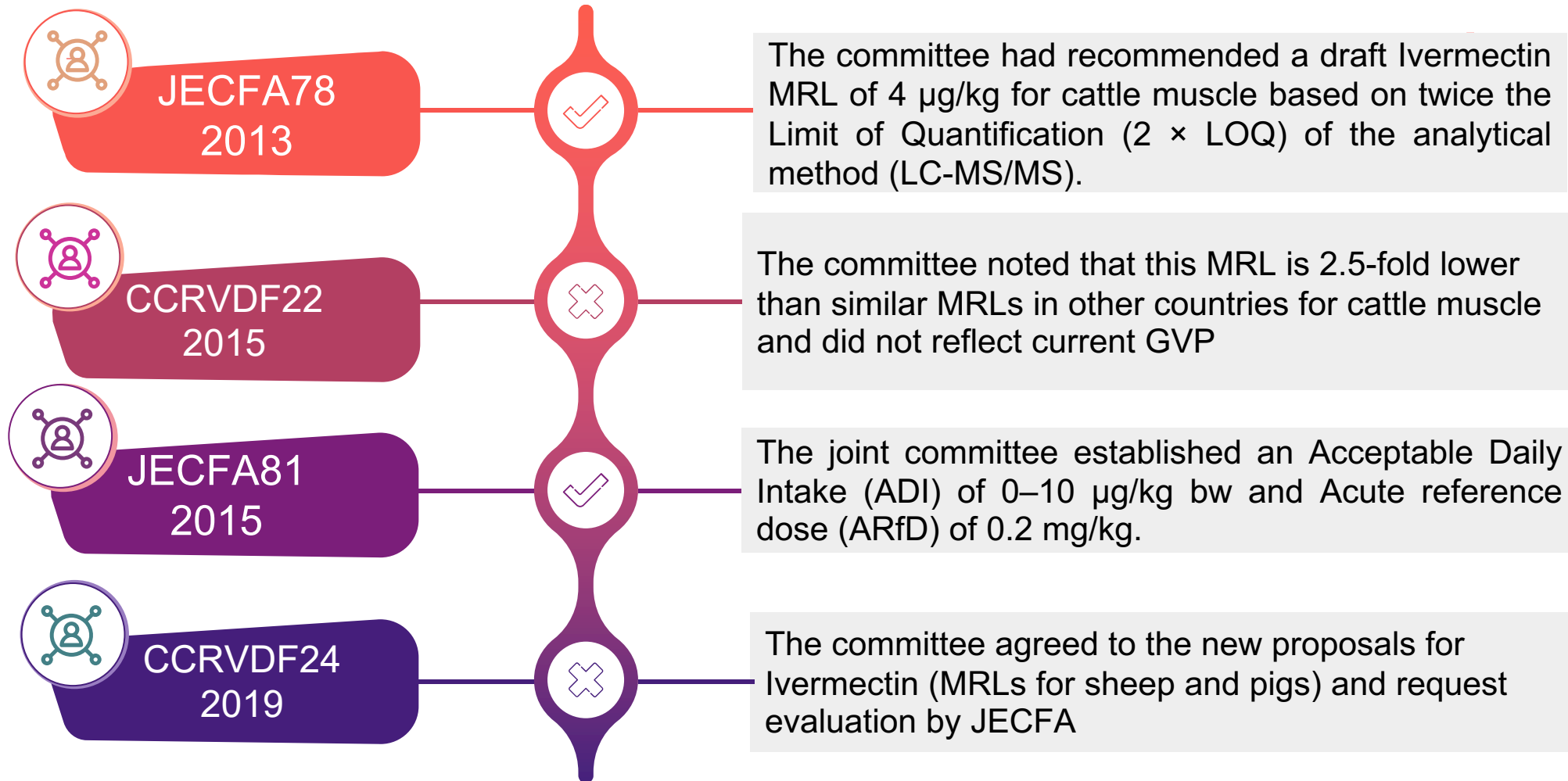
Step 7

Item 6.2

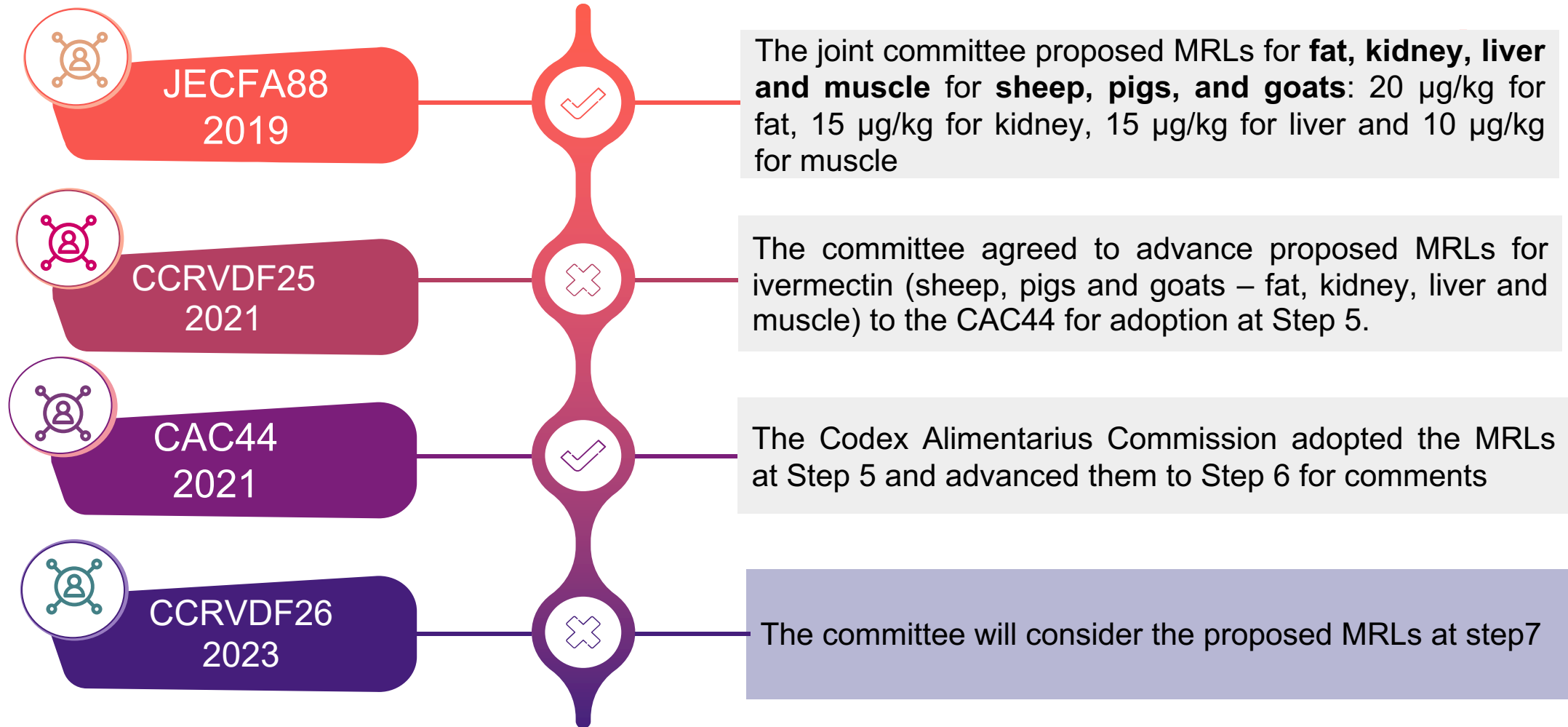
MRLs for Ivermectin (pigs, sheep and goats)
and Nicarbazin (chicken)

Step 4

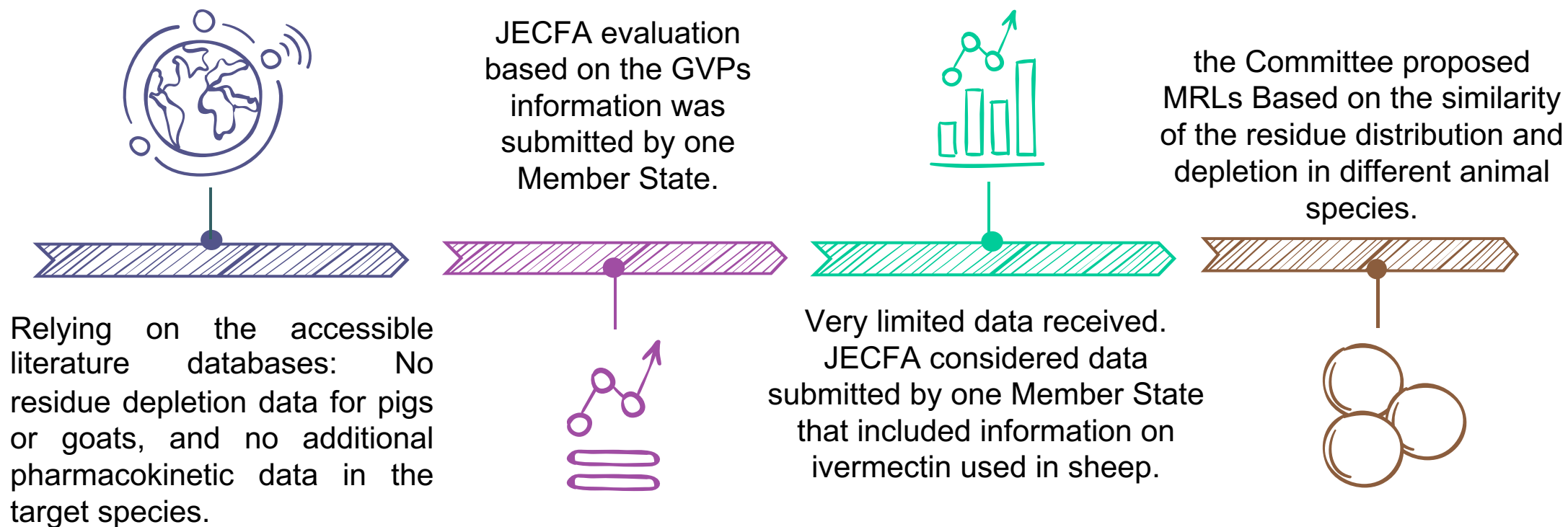
Background-1



Background-2

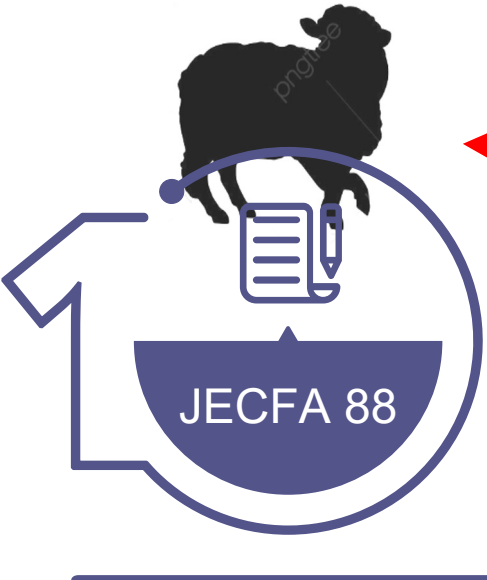


Analysis of the agenda item 6.1

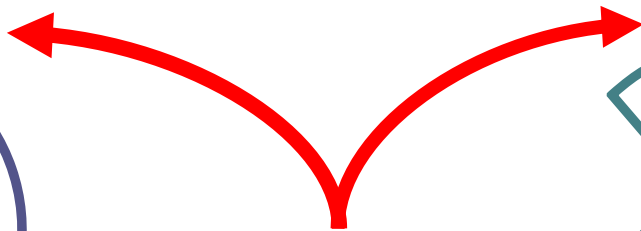


Analysis of the agenda item 6.1

Recommended MRLs by JECFA 88	Muscle (µg/kg)	Kidney (µg/kg)	Liver (µg/kg)	Fat (µg/kg)
Sheep, Pigs and goats	10	15	15	20



JECFA recommended 15 µg/kg for kidney and 10 µg/kg for muscle



JECFA88 re-confirmed the existing MRLs for fat of 20 µg/kg and liver of 15 µg/k (pig and sheep) that were previously recommended (JECFA 36).



Extended MRLs for sheep muscle and kidney to pig muscle and kidney considering the similarity of the overall tissue distribution and residue depletion in both species



Based on the similarity of the residue distribution and depletion in different animal species, JECFA recommended **extrapolation of the MRLs** for sheep and pig tissues to goat tissues



General comments on the proposed MRLs



Recommendation

Considering the new evaluation from JECFA94, Codex may suggest **suspending work** on this agenda item as it was based on an **outdated JECFA evaluation (JECFA88)**.

Agenda item 6.2

Item 6



MRLs for veterinary drugs in foods

Item 6.1

MRLs for Ivermectin (sheep, pigs and goats
– fat, kidney, liver and muscle)

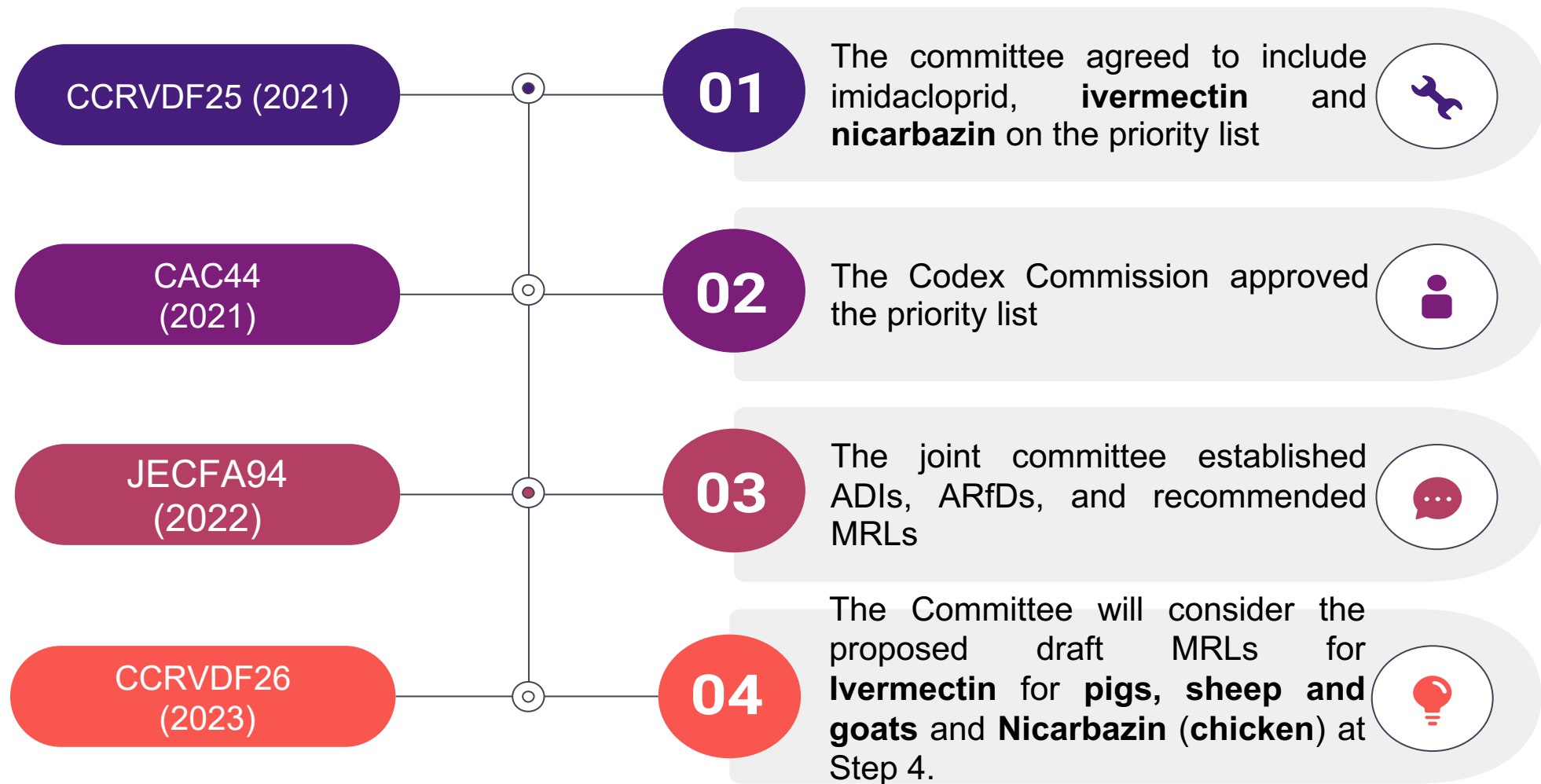
Step 7

Item 6.2

MRLs for Ivermectin (pigs, sheep and goats)
and Nicarbazin (chicken)

Step 4

Background



NICARBAZIN



Reviewed data from radiolabelled and non-radiolabelled studies on residue depletion and pharmacokinetics of nicarbazin in chicken.



Considered data from metabolism studies and. **The analytical method** used to analyze tissue samples was assessed

Data provided to support the assessment by the sponsor studies as well as data from published literature studies



JECFA94 established an ADI (0–0.9) mg/kg.bw based on toxicological effects and concluded that it was not necessary to establish an ARfD

IVERMECTIN



Considered data submitted by three sponsors that included information on residue depletion studies in pigs, sheep and goats



Reviewed metabolism studies in pigs (one study) and sheep (one study). No metabolism studies were available for ivermectin in goats.




Results analysis of liver and muscle samples (2015-2021) provided from one competent national authority for residues control


Considering the ADI and the ARfD previously established JECFA81(2015)

- ADI : (0-10) µg/kg. bw
- ARfD :0.2 mg/kg

The Proposed MRLs for consideration


Proposed MRLs for IVERMECTIN

	Muscle (µg/kg)	Liver (µg/kg)	Kidney (µg/kg)	Fat (µg/kg)
JECFA88	10	15	15	20
JECFA94	30	60	20	100

	Muscle (µg/kg)	Liver (µg/kg)	Kidney (µg/kg)	Fat (µg/kg)
JECFA88	10	15	15	20
JECFA94	15	30	20	20

The The global estimated chronic dietary exposure (GECDE) for adults increased from 4% to 7.2% of the upper bound of the ADI

Proposed MRLs for NICARBAZIN

	Liver (µg/kg)	Kidney (µg/kg)	Fat (µg/kg)	Muscle (µg/kg)
JECFA94	4000	15000	8000	4000

The GECDE for adults represents 13% of the upper bound of the ADI



Saudi Arabia, Brazil, Chile, Costa Rica, Cuba and Panama support advancing the proposed draft MRL for the **Ivermectin and Nicarbazine** to the next steps

Recommendation

Considering the new evaluation from JECFA94, taking into account the additional data and GVPs, Codex delegations may support the adoption of MRLs for Ivermectin and Nicarbazin proposed by JECFA94 at step 5/8. The application of these MRLs are achievable and in line with Good Veterinary Practice (GVP)

Agenda item 7

Item 7



Extrapolation of MRLs for veterinary drugs in foods to one or more species

Item 7.1	Extrapolated MRLs for different combinations of compounds/commodities	Step 4
Item 7.2	Approach for the extrapolation of MRLs for residues of veterinary drugs for offal tissues	

Agenda item 7



CCRVDF26
(2023)

- ◆ Agenda item 7.1: Extrapolated MRLs for different combinations of compounds/commodities at Step 4
- ◆ Agenda Item 7.2: Extrapolation of MRLs for residues of veterinary drugs in edible tissues.

Adoption of the MRL extrapolation approach in several sessions of CCRVDF

Make the MRLs of veterinary drug residues more available
Overcome the lack of scientific data needed for risk assessment



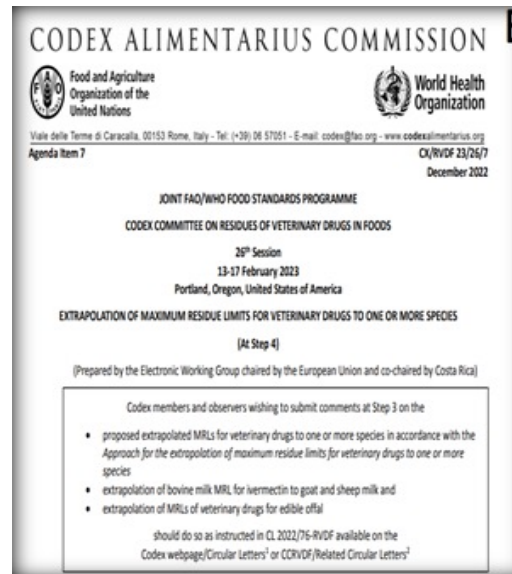
CCRVDF24

Establishment of an EWG

Develop a pragmatic approaches to extrapolate MRLs to one or more species

Compare these approaches with the revised Option C for aquatic species

Conduct a pilot study on the extrapolation of some compounds



Establishment of principles/practical modalities of application

Extension of the approach to all animal species (beyond aquatic species)

Modification of the Risk Analysis Principles applied by the CCRVDF to provide more autonomy to risk managers to propose extrapolation of MRLs to one or more species

CCRVDF25

Adoption by CAC44 (2021) and its inclusion as Annex C of the Risk Analysis Principles



Establishment of an EWG

Prepare revised proposals for consideration by the Twenty-sixth Session of the CCRVDF

Consider the extrapolation of MRLs for Ivermectin in milk from goats and sheep

Develop an adapted approach for offal tissues



CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations | World Health Organization

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Agenda Item 7 | CX/RVDF 23/26/7 | December 2022

JOINT FAO/WHO FOOD STANDARDS PROGRAMME
CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS
26th Session
13-17 February 2023
Portland, Oregon, United States of America

EXTRAPOLATION OF MAXIMUM RESIDUE LIMITS FOR VETERINARY DRUGS TO ONE OR MORE SPECIES
(At Step 4)

(Prepared by the Electronic Working Group chaired by the European Union and co-chaired by Costa Rica)

Codex members and observers wishing to submit comments at Step 3 on the

- proposed extrapolated MRLs for veterinary drugs to one or more species in accordance with the Approach for the extrapolation of maximum residue limits for veterinary drugs to one or more species
- extrapolation of bovine milk MRL for ivermectin to goat and sheep milk and
- extrapolation of MRLs of veterinary drugs for edible offal

should do so as instructed in CL 2022/76-RVDF available on the Codex webpage/Circular Letters¹ or CCRVDF/Related Circular Letters²

CCRVDF26

Discussion of the EWG's proposals

Proposed MRLs under the application of the approach extrapolation



Possibility to Extrapolate of bovine milk MRL for ivermectin to goat and sheep milk



Point of view on the possibility to apply Extrapolation of MRLs for edible tissues

Agenda item 7

Proposed MRL for vet drugs under the application of MRL extrapolation Approach for ruminants

Vet drug	Recommended MRL
Tétracyclines	Muscle 200 µg/kg Liver 600 µg/kg Kidney 1200 µg/kg Milk 100 µg/kg
Deltaméthrine	Muscle 30 µg/kg Fat 500 µg/kg Liver 50 µg/kg Kidney 50 µg/kg
Moxidectine	Muscle* 20 µg/kg Fat 500 µg/kg Liver 100 µg/kg Kidney 50 µg/kg
Spectinomycine	Muscle 500 µg/kg Fat 2 000 µg/kg Liver 2 000 µg/kg Kidney 5 000 µg/kg Milk 200 µg/kg
Tilmicosine	Muscle 100 µg/kg Fat 100 µg/kg Liver 1000 µg/kg Kidney* 300 µg/kg

Vet drug	Recommended MRL
Amoxicillin	Muscle 50 µg/kg Fat* 50 µg/kg Liver 50 µg/kg Kidney 50 µg/kg Milk 4 µg/kg
Benzylpenicillin	Muscle 50 µg/kg Liver 50 µg/kg Kidney 50 µg/kg Milk 4 µg/kg
Cyhalothrine	Muscle 20 µg/kg Fat 400 µg/kg Liver 20 µg/kg Kidney 20 µg/kg Milk 30 µg/kg
Cyperméthrine	Muscle 50 µg/kg Fat 1 000 µg/kg Liver 50 µg/kg Kidney 50 µg/kg
Levamisole	Muscle 10 µg/kg Fat 10 µg/kg Liver 100 µg/kg Kidney 10 µg/kg

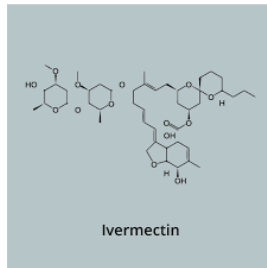
Agenda item 7

Extrapolation of bovine milk MRL for ivermectin to goat and sheep milk

The extrapolation of MRLs to goat and sheep milk is not possible



The approach does not allow the extrapolation for this compound/commodity and species.



Proposed MRL for Finfish

Vet drug	Recommended MRL
Deltamethrine	Muscle 30 µg/kg
Flumequine	Muscle 500 µg/kg



Agenda item 7

Extrapolation of MRLs for residues of veterinary drugs in edible tissues



The EWG was unable to develop a suitable approach to extrapolate MRLs for veterinary drug residues in edible offal tissue

The extrapolation of an MRL does not consider the additional source of dietary exposure from the consumption of edible offal tissue with the newly extrapolated MRL

There is no evidence that the M:T ratio determined in liver or kidney is applicable to other edible organ meats

There is no evidence that the elimination (e.g., kinetics, binding, etc.) of a marker residue in kidney or liver is similar to its elimination in other edible offal tissues



Further discussions at the CCRVDF26 level are needed on how to generate MRLs in edible offal tissues other than kidney and liver

General Comment and recommendations



The Committee may wish to continue the discussion on the MRL extrapolation approach for edible tissues given the limitations and concerns identified by the EWG

The intent is to find practical yet scientifically robust approaches for MRL development, supported by the relevant data
Codex Outreach Program supported submission of studies on feasibility of extrapolation

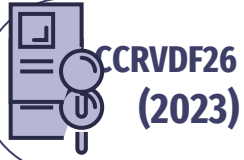
Agenda item 8

Item 8



Criteria and procedures for the establishment of action levels for unintended and unavoidable carryover of veterinary drugs from feed to food of animal origin

Agenda item 8



Criteria or requirements for the establishment of action levels for unintended or unavoidable carryover of veterinary drugs from feed to food of animal origin



CAC requested to revise and update the Codex Code of Practice on Good Animal Feeding to address emerging hazards

CCRVDF initiate work and discussions on the possibility of defining criteria/requirements for the establishment of action levels for residues of veterinary drugs in foods of animal origin resulting from such transfer.

CCRVDF23

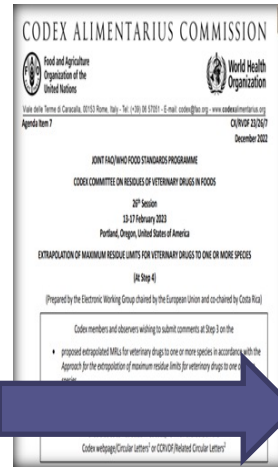
CCRVDF22

EWG: Key recommendations

The Code of Practice on Good Animal Feeding includes the management of unavoidable and unintended residues of approved vet drugs in food

Development of risk management recommendations to minimize the unavoidable and unintentional presence of residues of approved veterinary drugs in food as a result of the transfer of veterinary drugs into animal feed

Identification of relevant issues for scientific evaluation by FAO and WHO (case study Lasalocid sodium in eggs).



Establishment of Criteria and approach

EWG (co-chaired by United States and Canada to prepare discussion paper

Online forum to provide answers related to the scope of the project, the relevant data required and the need to establish a specific standard considering existing policies/guidelines/codes of practice..



request for scientific advice JECFA to test the criteria for requesting risk management measures/recommendations and general considerations and to use Lasalocid sodium in eggs as a case study.

Agenda item 8



CCRVDF26
(2023)

Criteria or requirements for the establishment of action levels for unintended or unavoidable carryover of veterinary drugs from feed to food of animal origin



Presentation of JECFA's scientific recommendations

The experts raised the importance of efforts to reduce and avoid hazards associated with the transfer of veterinary drugs for the safety of food for human consumption.

They pointed out the recent revision of the manual of Good Practices for the Animal Feed Industry - Implementation of the Codex Alimentarius Code of Practice on Good Animal Feeding published by FAO and IFIF in 2020, which includes guidance on transfer.

Establishment of EWG

- prepare a discussion paper on criteria or requirements for the development of action levels for foods derived from non-target animals to address the unavoidable and adventitious transfer of veterinary drugs from animal feed;
- conduct a pilot study on the establishment of action levels for Nicarbazine in chicken eggs derived from non-target animals resulting from the unavoidable and adventitious transfer of Nicarbazine in non-target animal feed.

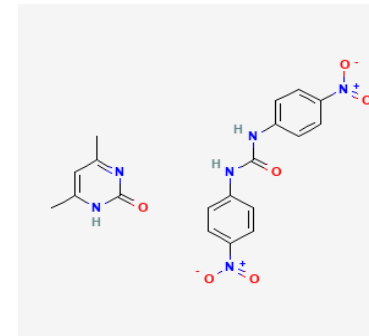
AT CCRVDF26

Discussion of the EWG's proposals noticed in the working document which include:

Proposed approach for the establishment of action levels for veterinary drugs in food from non-target animals, resulting from the unavoidable and accidental transfer of veterinary drugs in food intended for non-target animals

Outcome of the pilot study estimating action levels for the unavoidable and accidental transfer of Nicarbazine in chicken eggs

- Step 1** Animal Dietary Exposure Assessment (to be conducted by CCRVDF as part of an EWG);
- Step 2** Estimates of anticipated residue levels in food products of animal origin (to be conducted by CCRVDF under an EWG);
- Step 3** Action Levels (to be completed by CCRVDF as part of an EWG);
- Step 4** Human dietary exposure assessment (to be performed by JECFA upon request from CCRVDF, based on the evidence established in the previous steps including the proposed action levels from Step 3).



General Comment and Possible Recommendation



The pilot study on Nicarbazin residues in chicken eggs illustrates the proposed approach to estimate action levels and provides support for the observations on the proposed approach.

The example studied confirms that unavoidable or accidental transfer of veterinary drugs from medicated feed to non-medicated feed can occur and result in detectable residues in commodities requiring the establishment of MRLs.

The Guidance is meant to offer additional support (Science-based approach) to competent authorities to enable taking risk management measures that are not based on a Zero Tolerance with possible negative impacts on Trade

Agenda item 9

Item 9



Coordination of work between CCPR and CCRVDF



Item 9.1	Matters of interest arising from the Joint CCPR/CCRVDF Working Group	
Item 9.2	Work in parallel on issues pertaining to harmonization of edible offal i.e. <ul style="list-style-type: none">□ Classification of Food and Feed (CXA 4-1989)□ Food descriptors – Coordination between JECFA/JMPR	

Agenda item 9.1

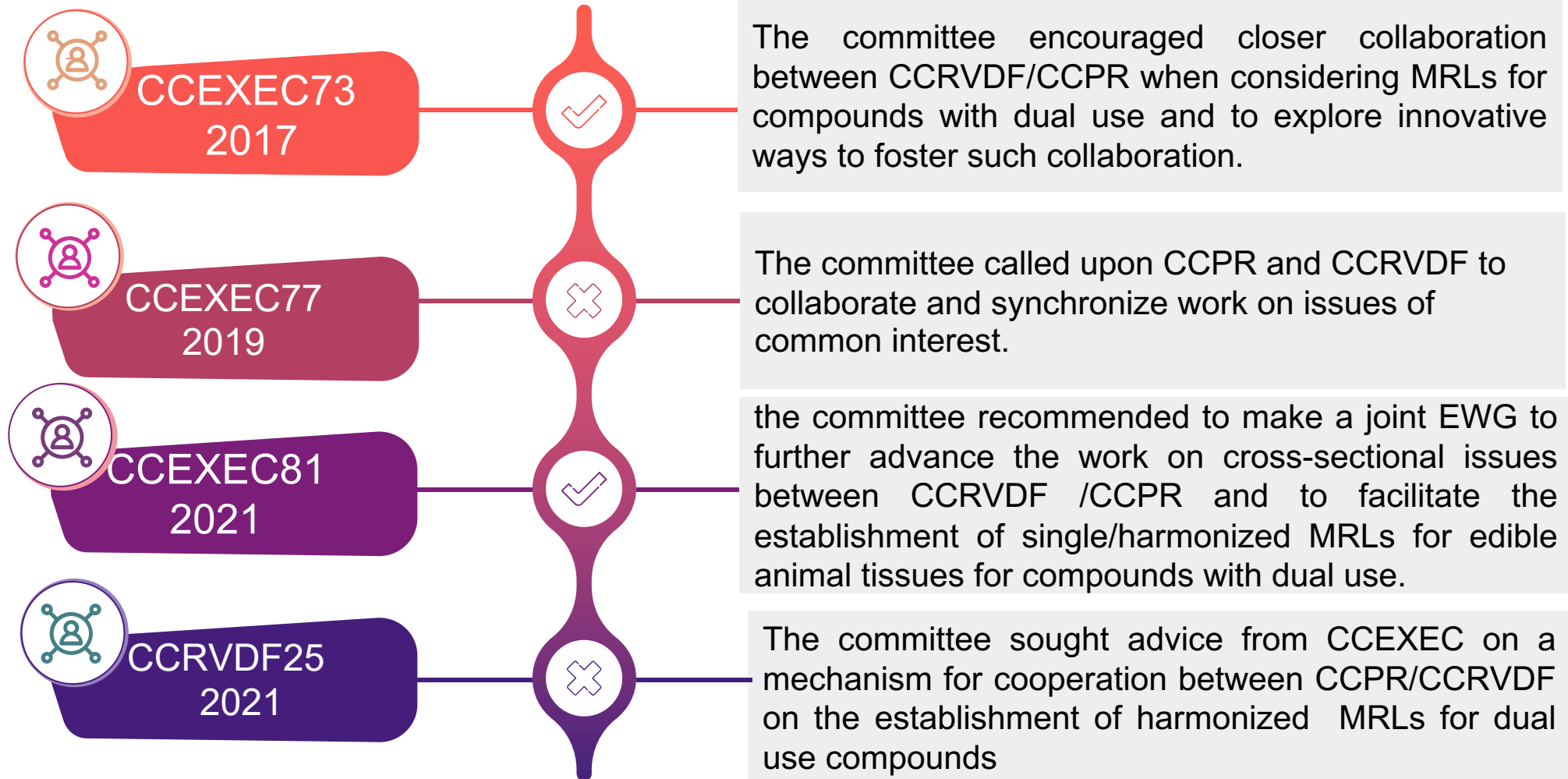
Item 9



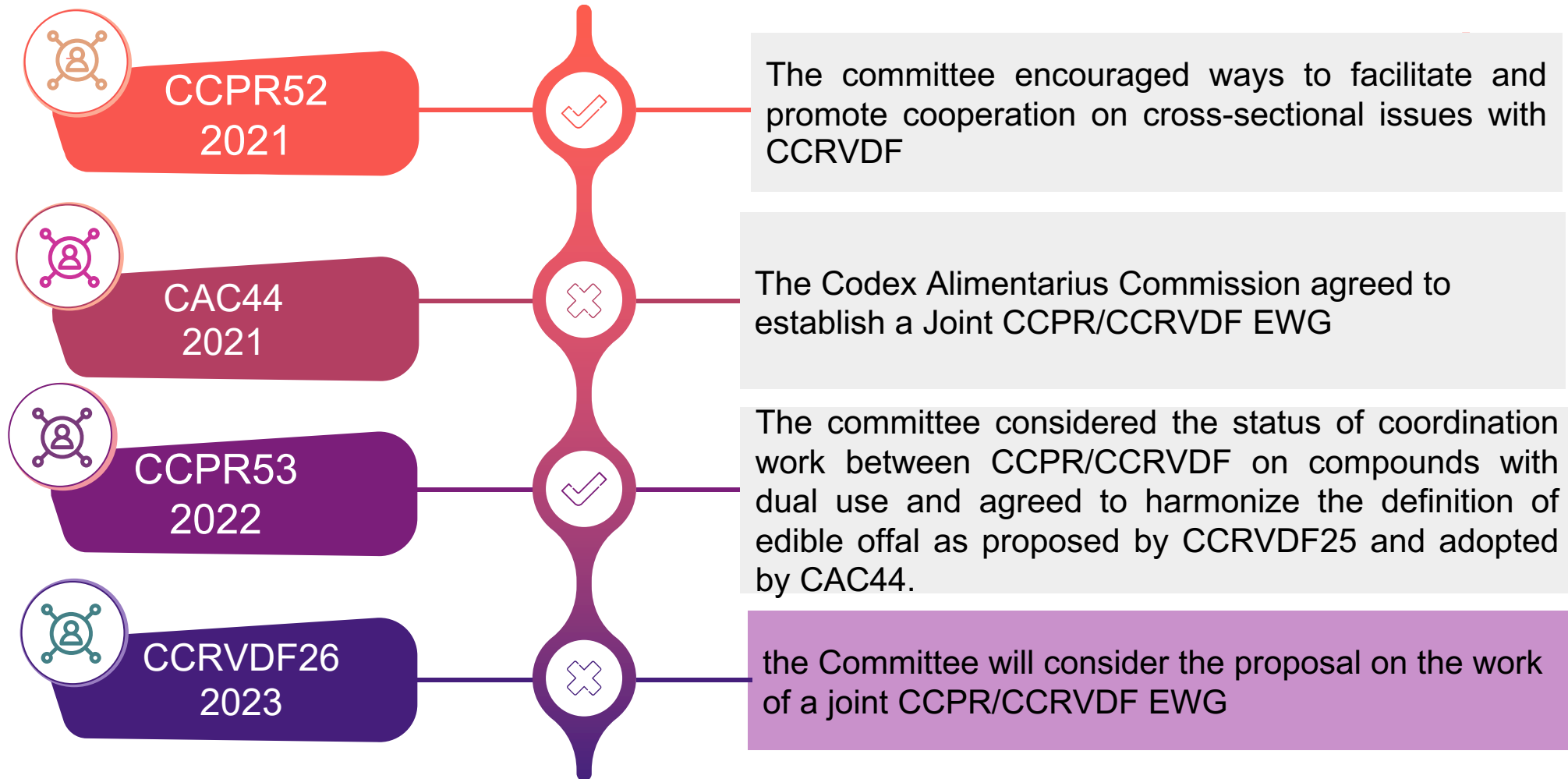
Coordination of work between CCPR and CCRVDF

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Background-1



Background-2



Analysis of agenda item 9.1

The discussion paper provides a summary of Member responses on Matters of common interest and cooperative mechanisms between CCPR/CCRVDF



work has been done cooperatively between CCRVDF and CCPR

1

2

Areas where CCRVDF and CCPR could collaborate in the future



Mechanisms could be used to collaborate between CCRVDF and CCPR

3

4

Mechanisms could be recommended to JMPR and JECFA to facilitate data sharing between the two risk assessments groups.



Ways to harmonize MRLs for dual-use compounds that have different MRLs for the same edible commodity

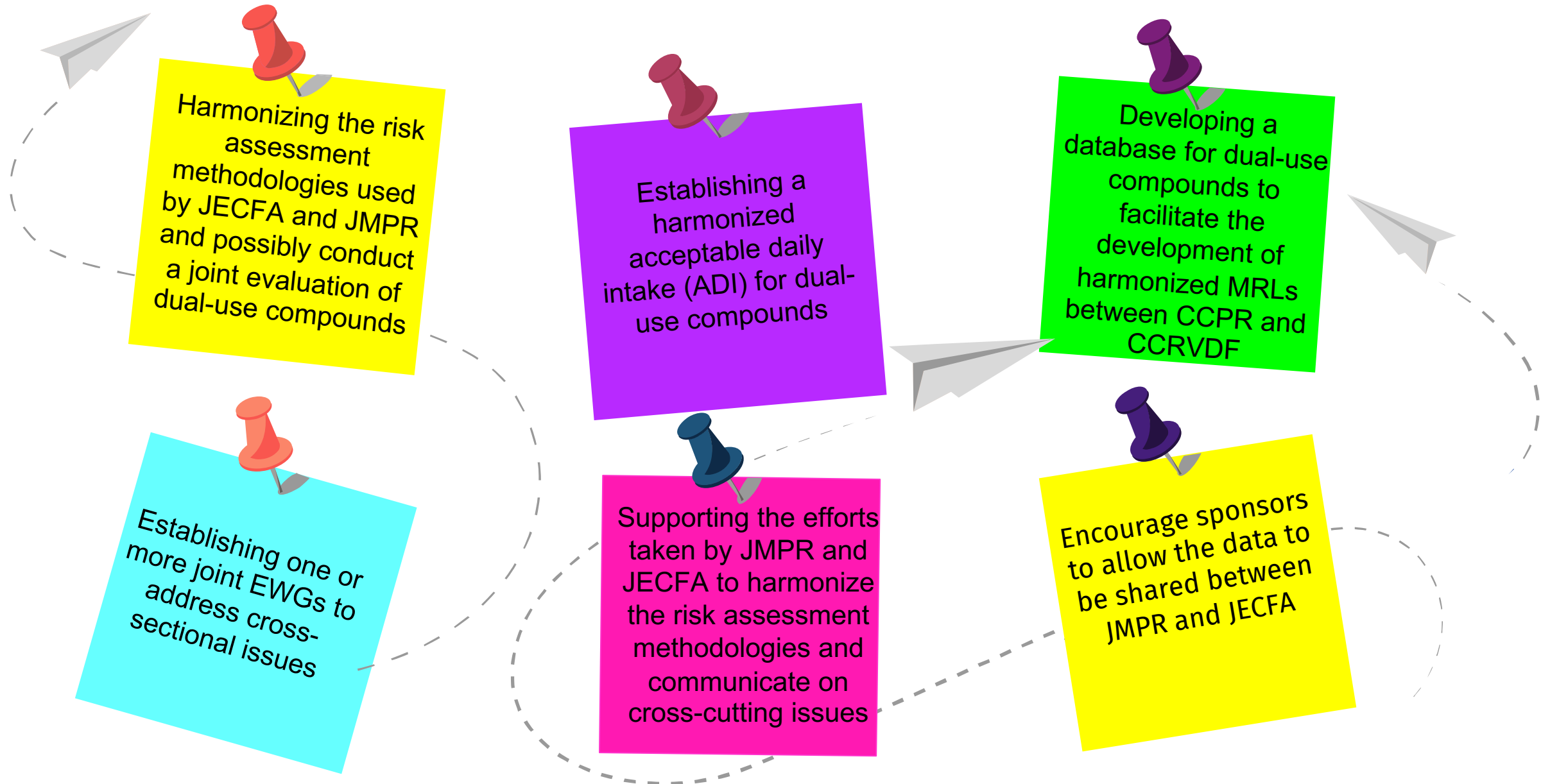
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Other additional topics affecting both CCPR and CCRVDF that have not been considered by either the draft discussion paper or questions



Main Comments from Codex Delegations



Possible Recommendation

Codex delegations may wish to offer support to all proposed recommendations that enable better cooperation between CCPR and CCRVDF.

Agenda item 9.2

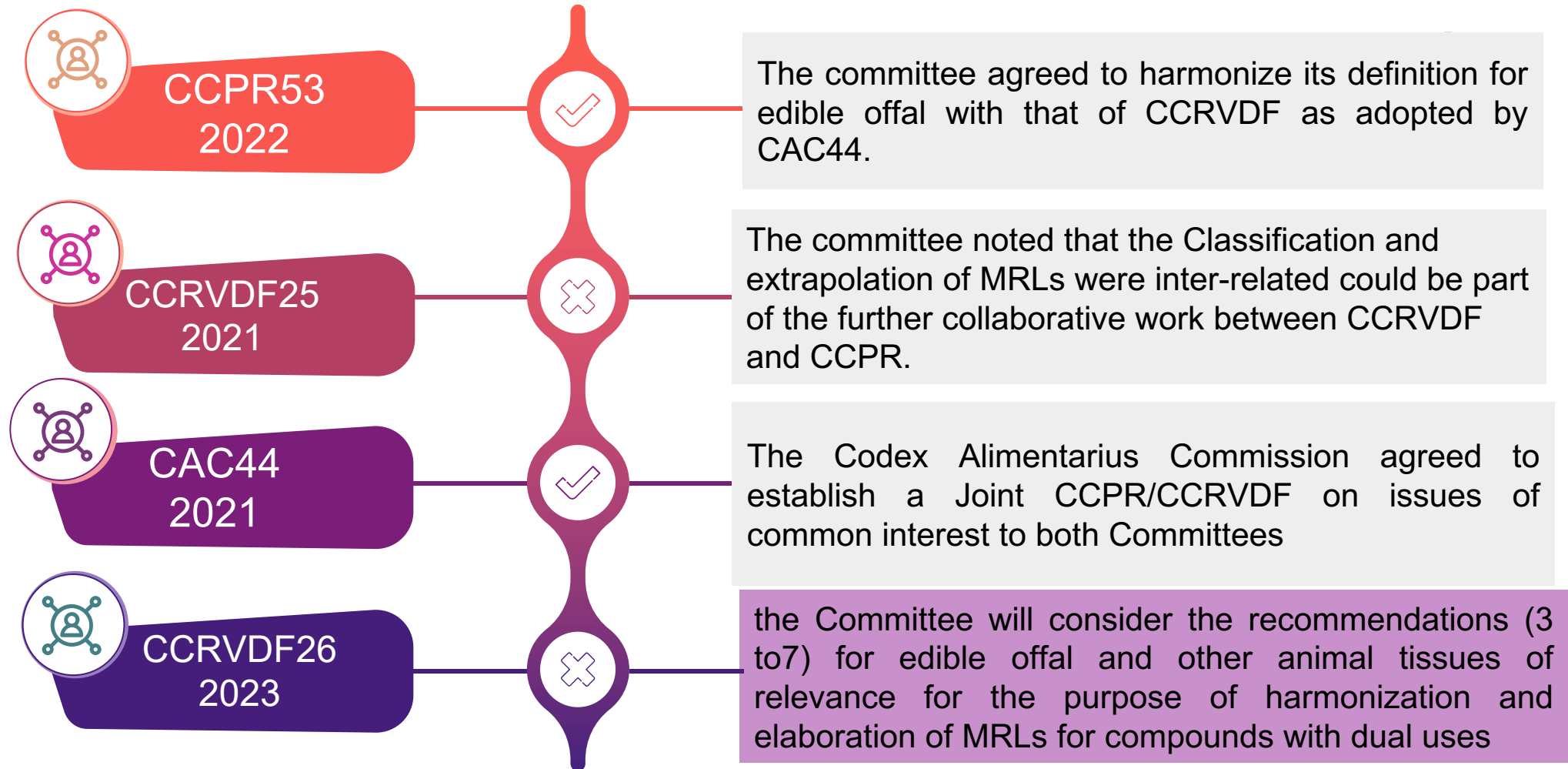
Item 9



Coordination of work between CCPR and CCRVDF

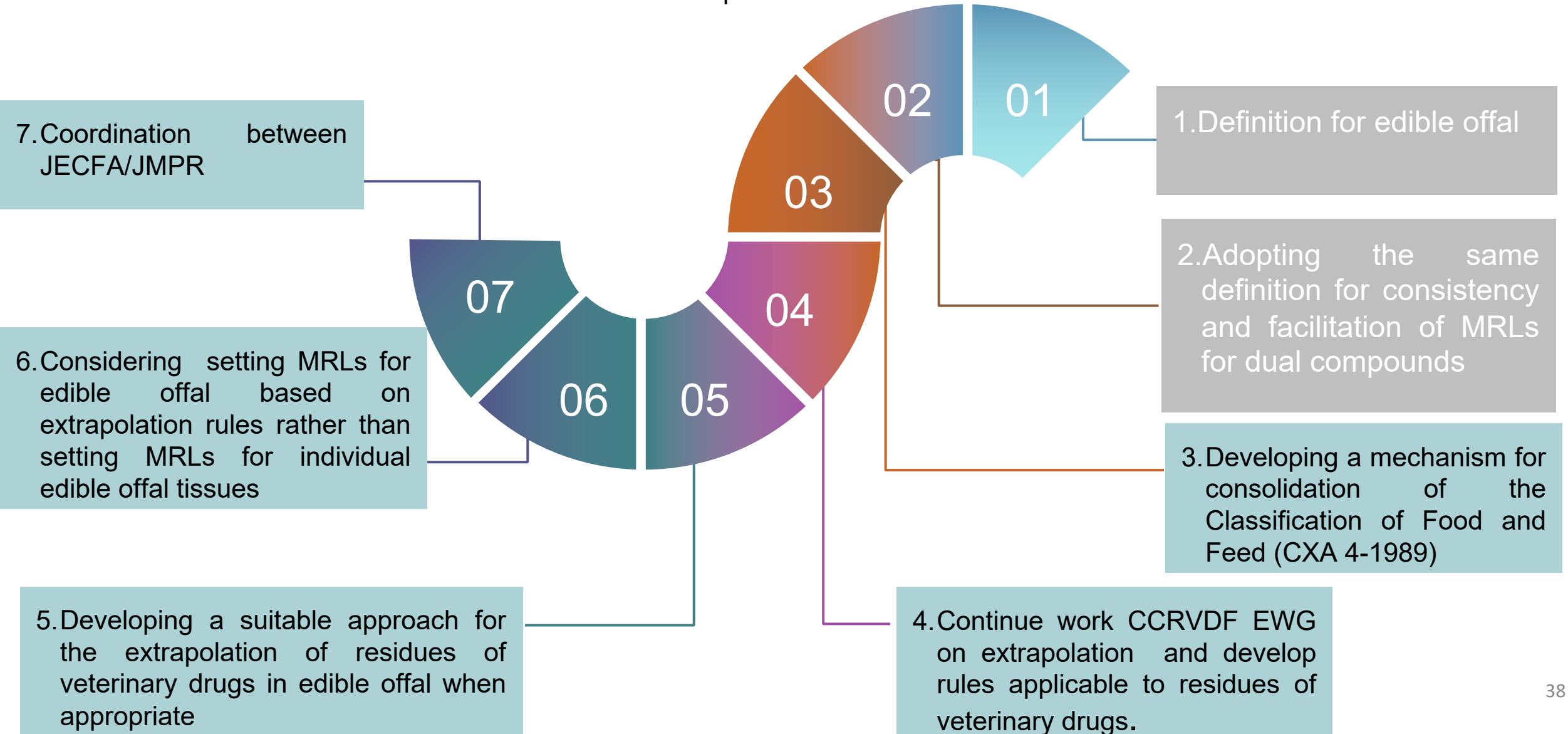
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Background



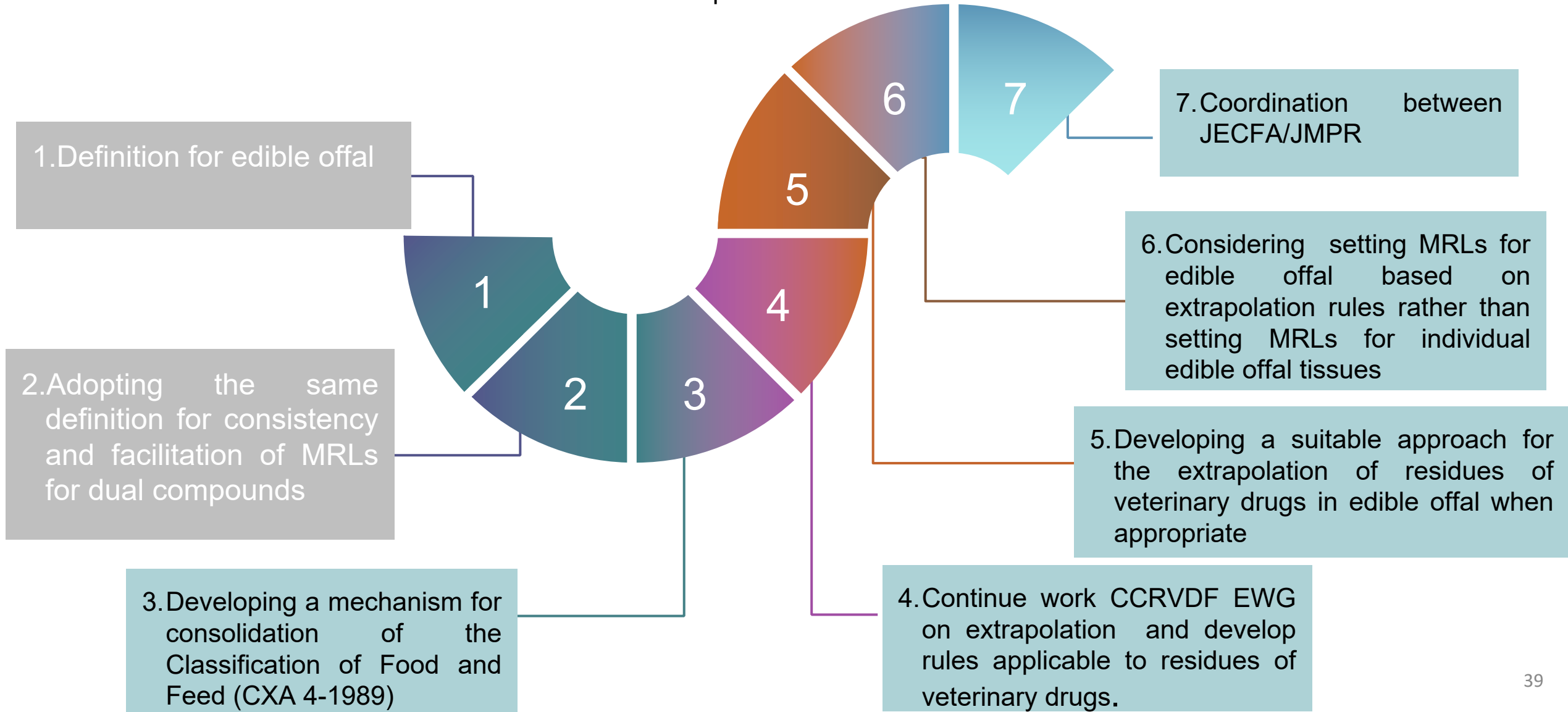
Analysis of agenda item 9.1

Recommendations for edible offal and other animal tissues of relevance for the purpose of harmonization and elaboration of MRLs for compounds with dual uses.



Analysis of agenda item 9.1

Recommendations for edible offal and other animal tissues of relevance for the purpose of harmonization and elaboration of MRLs for compounds with dual uses.



Possible Recommendation

Codex delegations may wish to support all proposed recommendations for edible offal and other animal tissues of relevance for the purpose of harmonization and elaboration of maximum residue limits for compounds with dual uses.

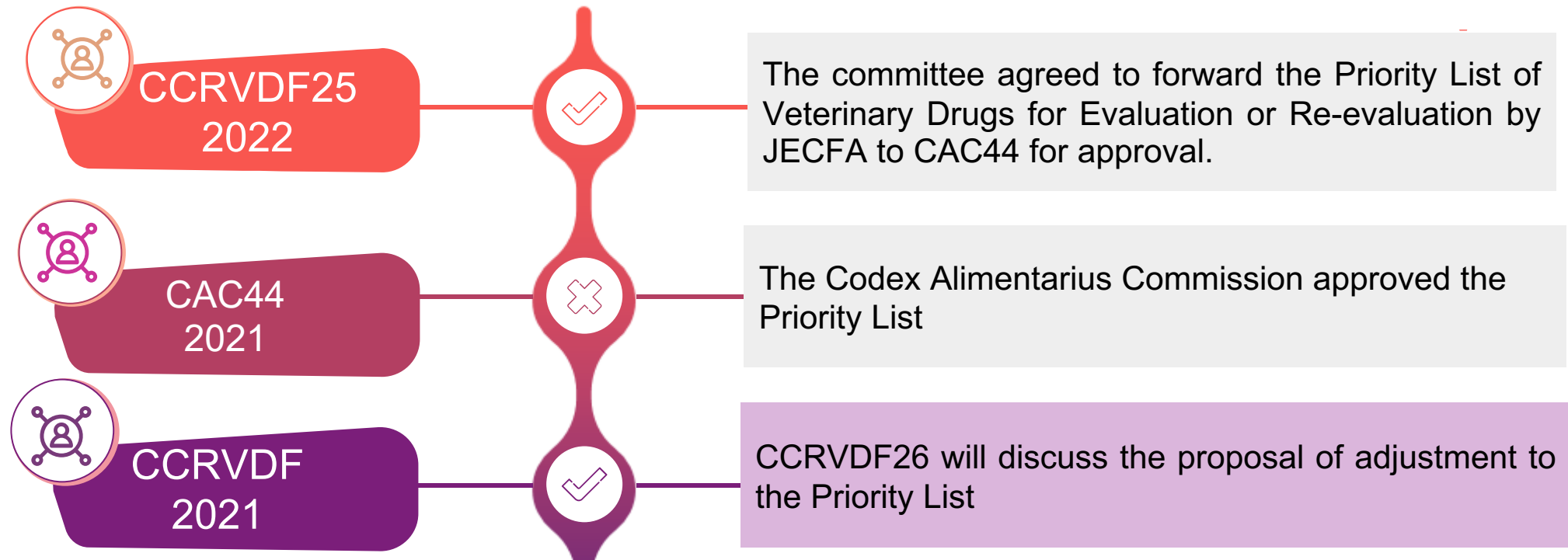
Agenda item 10

Item 10



Priority list of veterinary drugs for evaluation or re-evaluation by JECFA

Background



Criteria for inclusion in the Priority List

The veterinary drug shall meet some or all the following criteria for inclusion in the Priority List



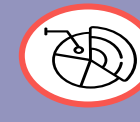
A Member has proposed the compound for evaluation

A Member has established good veterinary practices regarding the compound.



The compound has the potential to cause public health and/or international trade problems

The compound is available as a commercial product.



There is a commitment that a dossier will be made available

Analysis of agenda item 10

Discussion paper of Priorities with considering the proposals of Codex Alimentarius members and observers

✓

Veterinary drugs for inclusion in the Priority List

Chile proposes a reevaluation of Amoxicillin 50% to develop MRLs for in broiler chicken tissues

Korea requests to include Clopidol and Fumagillin

Part I

✓

Veterinary drugs for which data availability should be confirmed

Peru inform that toxicological data has been processed to support the evaluation of norfloxacin

Part II

✓

Veterinary drugs for which additional data / information is necessary

JECFA88 could not recommend MRLs for Ethion, Flumethrin and Fosfomycin with the available data

JECFA94 (2022) could not recommend MRLs for Imidacloprid and Selamectin

Part III

✓

Parallel review - Evaluation of a new compound

JECFA94 evaluated 4 veterinary drugs i.e., Imidacloprid, Ivermectin, Nicarbazin and Selamectin

Part IV

