CODEX ALIMENTARIUS COMMISSION

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World Health Organization

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Agenda Item 3.1 **CX/RVDF 21/25/3**

December 2020

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON RESIDUES OF VETERINARY DRUGS IN FOODS

25th Session
(Virtual)
12-16 and 20 July 2021

MATTERS OF INTEREST ARISING FROM FAO/WHO INCLUDING THE JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES (JECFA)

Information from the 88th Meeting of JECFA

1. Since the last session of CCRVDF (2018), five meetings of JECFA (i.e. JECFA 86th, 87th 88th, 89th and 90th) have been convened. These meetings addressed food additives (i.e. JECFA 86th, 87th and 89th), veterinary drug residues (i.e. JECFA88) and contaminants in food (i.e. JECFA90). The reports and detailed monographs from these meetings are available at the relevant FAO[1] and WHO[2] web sites:

2. JECFA88 was held in Rome, Italy, on 22–31 October 2019, to evaluate residues of certain veterinary drugs in food. The full report of the meeting is published in the WHO Technical Report Series (TRS 1023)[3].Toxicological monographs summarising the data that were considered by JECFA88 will be published in *WHO Food Additives Series No.79*[4]; residue monographs summarising the data that were considered by JECFA88 are published in *FAO JECFA Monographs No.24*[5].

3. JECFA88 recommended MRLs for the following veterinary drugs: diflubenzuron (salmon - muscle plus skin in natural proportion); halquinol (in swine - muscle, skin plus fat, liver and kidney); ivermectin (sheep, pigs and coats – fat, kidney, liver and muscle). These MRL proposals will be discussed under Agenda Item 6.1[6].

4. Furthermore, JECFA88 evaluated other compounds for which the assessment could not be finalized (due to incomplete data) and also provided some general considerations on issues related to the work of the committee, as summarized in this paper.

Ethion

5. During the evaluation of ethion at JECFA85 (2017), it was noted that the lack of qualitative or quantitative metabolite data was a major deficiency to be addressed before any MRLs can be determined for this substance. It was noted that at least one metabolite (ethion monoxon) retains significant anticholinesterase activity, and therefore must be accounted for in the residue assessment. In addition, the available data did not identify all the metabolites of concern that may lead to the identified reproductive toxicity.

6. One option identified by JECFA to address this issue was to identify and quantify all active ethion metabolites in tissue residues, and include these metabolites, along with parent ethion, as the MR. Alternatively, a single substance could be selected as the MR. However, to estimate the toxicological activity of the total ethion residues (including metabolites), knowledge of the MR:TR ratio over time would be required. Because such data were not available, an accurate assessment of the total toxicological activity of ethion residues (and subsequent residue exposure assessment) could not be performed.

7. No relevant data were submitted to JECFA88, but the Committee nonetheless conducted a thorough review of the literature that had been published since the time of JECFA85. There were no additional data available that would fill the identified gaps.

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[1] http://www.fao.org/food-safety/resources/publications/en/
[2] www.who.int/foodsafety/publications/jecfa/en/
[3] https://apps.who.int/iris/bitstream/handle/10665/330821/9789241210324-eng.pdf
[4] http://www.who.int/foodsafety/publications/monographs/en/
[5] http://www.fao.org/documents/card/en/c/ca9167en
[6] CL 2020/17-RVDF
http://www.fao.org/fao-who-codexalimentarius/committees/committee/related-circular-letters/en/?committee=CCRVDF
CX/RVDF 20/25/6 http://www.fao.org/fao-who-codexalimentarius/meetings/detail/en/?meeting=CCRVDF&session=25

8. JECFA88 reiterated that the following information, identified at JECFA85, would be needed to complete the assessment:

- A metabolism study, using radiolabelled ethion in cattle, that identifies the metabolites and measures the depletion of total residues. Suitable MRs should be identified, and their relative distribution in edible tissues and the ratio of marker to total residues should be determined. A way to address this would be to provide a study conducted in line with the VICH GL46.
- Depending on the outcome of the metabolism and MR determination, if the MR is different to parent ethion, a non-radiolabelled residues study, in line with good practice in the use of veterinary drugs.
- A comparison between metabolites in cattle and metabolites in laboratory species, to ensure that all residues of toxicological concern produced in cattle are covered by the available toxicology studies.
- Analytical method(s) that can measure suitable MRs in all edible tissues, validated in accordance with established guidance, if it is found to be necessary to change the proposed MR.

Flumethrin

9. Flumethrin was previously assessed at JECFA85 in order to recommend an MRL for honey. JECFA88 evaluated flumethrin at the request of CCRVDF24[7], with a view to recommend MRLs for cattle edible tissues and milk.

10. JECFA88 concluded that it would not be possible to recommend MRLs with the available data.

11. The first major issue was the incomplete determination of the metabolic profile in cattle. The identity of the metabolites in cattle could not be confirmed by the Committee. It is also not known what contribution the various metabolites make to the toxicity profile of flumethrin. Additionally, there was no radiolabelled residue depletion study that may have allowed a calculation of the MR:TRR ratio at relevant time points.

12. The second major issue was that of the unknown metabolite in milk which made up 11.5% of the TRRs. This metabolite has not been identified, and it is not known whether it is one of the metabolites seen in the rat metabolism studies. Therefore, it is also not known whether it is formed in the laboratory animals used in the toxicity testing, and therefore whether it has been toxicologically assessed.

13. Another issue is that of the identification of the worst-case dosing regimen according to authorized GVP, in terms of residue levels in fat. It is highly likely that flumethrin will accumulate in fat after repeated treatments; however, not all of the dosing regimens that would likely lead to the highest residues in fat have been studied. It is considered necessary to know what the highest concentration of residues are under approved conditions of use when setting MRLs.

14. In order for JECFA to be able to recommend MRLs for flumethrin in cattle tissues and milk, these data will be required:

- Data to confirm the metabolites formed in cattle after treatment with flumethrin.
- Data to confirm the MR, and to determine the MR:TRR ratio at suitable timepoints.
- Data to identify the unidentified metabolite in milk and determine whether this metabolite is formed in laboratory species, and then, if not, to determine its toxicological profile.
- Residue depletion data from studies conducted according to GVP, using the dosing regimen leading to the highest and most persistent residues, in both edible tissues and milk.

Fosfomycin

15. Fosfomycin has not previously been evaluated by JECFA. JECFA88 evaluated fosfomycin at the request of CCRVDF24[7] with a view to establishing an ADI and recommending MRLs in the edible tissues of chickens and pigs.

16. Taking into account the information submitted by the sponsor and the remaining data gaps notwithstanding the extensive and detailed literature searches carried out by JECFA88, the Committee decided that no MRLs could be recommended for fosfomycin for edible tissues of chickens and pigs.

17. The end-point of microbial resistance could not be assessed, and as such it was not possible to determine an overall mADI. JECFA88 was therefore unable to establish an ADI for fosfomycin.

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[7] REP18/RVDF, para. 112, App.VI
http://www.fao.org/fao-who-codexalimentarius/meetings/detail/en/?meeting=CCRVDF&session=24
REP18/CAC, App. VI http://www.fao.org/fao-who-codexalimentarius/meetings/detail/en/?meeting=CAC&session=41

18. Only limited information on approved oral uses of fosfomycin in the target species, including intended dosage regimens and withdrawal periods, was available. No information on approved uses via other routes of administration was available.

19. The sponsor did not provide any results of original studies. The data for fosfomycin residues in chickens and pigs available from the literature were not sufficient to assess the residue depletion. The articles contain inconsistent information on residue depletion in the target species. Studies in chickens using lower doses led to higher initial residue concentrations. Only mean residue concentrations were available and limited information on variation around the mean was provided. It was not known whether this might be related to inadequate method validation, animal husbandry or other factors. Therefore, the inconsistencies could not be further assessed.

20. No residue depletion studies in chickens using the highest intended treatment duration and no studies in pigs using the highest intended dose and duration were available.

21. No analytical method, validated according to the requirements published in the Codex *Guidelines for the Design and Implementation of National Regulatory Food Safety Assurance Programs Associated with the Use of Veterinary Drugs in Food Producing Animals* (CXG 71-2009)[8], is available.

22. JECFA88 noted that the following data will be required to complete the assessment:

- Information on the selection for and emergence of resistance in the microbiota in the gastrointestinal tract.
- Results from non-radiolabelled studies in both target species, using the highest intended dose and duration of treatment, as well as the administration route leading to the highest residue concentrations in edible tissues derived from treated animals.
- Full study reports, including individual sample residue concentrations.
- Full validation data according to the requirements published in CXG71 for the liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) method, to allow for assessment of the usability of LC-MS/MS in routine residue control.

Selamectin

23. JECFA88 evaluated Selamectin as part of a pilot program in which it conducts a parallel review of the information at the same time as the sponsor pursues approval in the proposed species with national authorities, as discussed at CCRVDF24[9].

24. JECFA88 established an ADI of 0–0.01 mg/kg bw, and an ARfD of 0.4 mg/kg bw; however, MRLs could not be recommended for selamectin due to incomplete characterization of residues, lack of data necessary to establish reliable MR:TRR ratios over time, and lack of an analytical method for monitoring.

25. JECFA88 noted that the following data will be needed to complete the residue assessment:

- Characterization of the residues in tissues in order to establish an MR:TRR.
- An MR depletion study under conditions of use.
- Information on an analytical method suitable for monitoring purposes.
- Information on the proposed withdrawal period.
- Confirmation of the stability of the radiolabel in tissues.

General Considerations

26. Some of the general considerations from JECFA88 are summarized and reported here below. The full considerations are available and published in TRS 1023.

JECFA's comments on the parallel review process

27. Based on the experience with the evaluation of selamectin, JECFA88 offered several considerations regarding the parallel review process, as outlined below.

[8] http://www.fao.org/fao-who-codexalimentarius/meetings/detail/en/?meeting=CCRVDF&session=25
[9] REP18/RVDF, paras. 98-103
http://www.fao.org/fao-who-codexalimentarius/meetings/detail/en/?meeting=CCRVDF&session=24

28. JECFA concluded that the process and requirements for this parallel review approach should be essentially the same as those for a compound that has already received registration in a Member State. This includes providing all necessary information required to establish a HBGV and recommend MRLs in the tissue(s) of interest, as is the mandate of JECFA. The Committee noted that only limited information on the fate of residues in the target animal was provided, and emphasized that a parallel review requires that all relevant information be submitted. The Committee stressed that a complete dossier is needed, including both the data necessary to characterize the toxicity of the compound leading to establishment of an HBGV such as an ADI or ARfD, and information on residue uptake, metabolism, disposition, and depletion and monitoring with a suitable analytical method in order to recommend MRLs.

29. JECFA acknowledged that a finalized GVP may not be available for a product not yet formally approved or registered; however, proposed dosing regimen(s) and withdrawal period(s) should be provided in order to facilitate a JECFA review. This information is necessary for recommending appropriate MRLs; it will also be important to have information on the status of the evaluation that is ongoing in parallel at the level of a national authority.

30. JECFA noted that CCRVDF agreed to develop a discussion paper to examine the advantages and disadvantages of a parallel approach to compound evaluation. Although JECFA is generally supportive of the approach, it would welcome additional discussion on this process. This matter will be discussed under Agenda Item 9[10].

Report on the JECFA/JMPR Residue Definition Working Group

31. Previous JECFA and JMPR working groups (i.e. those on estimation of less-than-lifetime exposure, and dietary exposure to residues of drug/pesticide substances) have recommended that JECFA and JMPR pursue harmonization of their residue definitions to facilitate exposure assessment of dual-use compounds (i.e. those used both as a veterinary drug and as a pesticide) and harmonization of enforcement strategies.

32. Based on this recommendation, a joint Working Group of JECFA and JMPR experts met in conjunction with an OECD Working Group in Geneva on 3–7 December 2018.

33. The conclusions and recommendations of the JECFA/JMPR Working Group on residue definition included those outlined below.

- For dual-use compounds, when determining the relevant residue of toxicological or microbiological concern, the working group continues to recommend using the most refined approach; that is, a toxicological evaluation of all metabolites and degradates identified (above a defined percentage of the TR) based on data submitted by the sponsors.
    - Although this approach is used routinely by JMPR, JECFA has only infrequently had the relevant data available to use such an approach in its assessment.
    - Where the relevant toxicological data are not available in the veterinary drug dossier, JECFA encourages the compound sponsor to access such data if possible. This could include, for example, buying such data or right of reference from the pesticide sponsor dossier.
    - Simply using the JMPR report or monograph is typically not a feasible option for the JECFA experts, because the JMPR documents only provide a summary of the data (not the original data). JECFA will continue to use the TRR method where it is not possible to use a more refined approach. It was noted that the TRR approach is less accurate and may be significantly (and unnecessarily) more conservative than the JMPR approach, but it may be the only viable strategy for compounds in which the relevant data are unavailable.
- With respect to metabolite identification and evaluation for animal commodities:
    - As described in the VICH GL46, a threshold for identifying metabolites of potential concern would be:
        - ≥100 µg/kg; or
        - ≥10% of the TRR, in a sample collected at the earliest euthanasia interval (or following attainment of steady state, or at or near the end of treatment for continuous-use drug products).

[10] CL 2021/5/OCS-RVDF
http://www.fao.org/fao-who-codexalimentarius/committees/committee/related-circular-letters/en/?committee=CCRVDF
CX/RVDF 20/25/10 http://www.fao.org/fao-who-codexalimentarius/meetings/detail/en/?meeting=CCRVDF&session=25

- The Working Group recommends that JMPR follows a similar approach for identifying metabolites of concern in animal commodities, in parallel with existing JMPR methods for deriving thresholds of metabolite identification.
- JECFA and JMPR confirmed the expectation that a majority of the TR be structurally identified. If this is not feasible, the sponsor is expected to provide a scientific explanation of why this was not possible.
- The Working Group recommends that a TR approach such as TRR be added to the OECD guidelines, to cover cases where data are insufficient to enable individual metabolite assessment.

- For bound residue assessment, JMPR and JECFA should compare the analytical extraction methods used in order to sufficiently demonstrate that the residue is actually "bound". Specific details regarding the extraction protocols are not necessary, but the general extraction procedure performed should be described (e.g. acid, base or enzymatic digestion).
- The definition of "muscle" and "fat" should be harmonized between CCRVDF and CCPR. This issue was considered [11] at CCPR51 (2019) and will be further discussed [12] at CCPR52 (2021). CCRVDF25 would consider this matter under Agenda Item 8[13].
- When defining residues for monitoring purposes, both JECFA and JMPR should include relevant instructions necessary for their analysis (e.g. hydrolysis of conjugates).
- JECFA81 (2015) concluded that information regarding potential food processing effects on residues, when available, should be considered in the assessment. For dual-use substances, JECFA should consider relevant information on the effects of processing from JMPR monographs.
- Guidance documents for JECFA monographers should be updated regarding approaches for metabolite assessment, including TTC.
- JECFA and JMPR should explore what minimum values or levels (on a percentage or µg/kg basis) are necessary in order to consider a metabolite to have a significant toxicological impact on the exposure assessment.

34. Since the meeting in 2018, the OECD Working Group has continued electronic discussions on issues of concern for determining a common residue definition. Case study assessments using data for specific compounds are ongoing.

35. JECFA88 agreed with the above conclusions and recommendations, and supports further work on this subject.

General considerations about the use of scientific literature in risk assessment

36. JECFA88 considered that the ideal source for data used in a scientific risk assessment is from studies conducted and presented to internationally agreed guidelines, and conducted in accordance with the principles of GLP, if applicable. Ideally, study reports should contain individual data, rather than just summary statistics. However, JECFA acknowledged that published scientific literature may provide evidence that supports the evaluation, and affirmed that it considers all relevant evidence (e.g. peer-reviewed publications and theses) in support of a risk assessment. Such literature should be in English; if the original language of a publication is not English, the sponsor should provide a suitable translation.

37. For the toxicological evaluation, published reports of toxicity studies should contain a clear description of the study details, including the following, as appropriate: characteristics of treated animals (age, weight, sex, species, and strain or breed), experimental design (number of dose groups, doses administered, number of animals per group, duration and schedule of treatment, and route and method of administration), substance administered (identity, source, purity and formulation used), end-points measured (with sufficient information to assess the methods used; e.g. a published reference) and summarized results with appropriate statistical information (e.g. mean and standard deviation).

[11] REP19/PR, paragraphs 157-177, 179(v); CX/PR CX/PR 19/51/3-Add.1 and CX/PR 19/51/12
http://www.fao.org/fao-who-codexalimentarius/meetings/detail/en/?meeting=CCPR&session=51
[12] CL 2020/13-PR
http://www.fao.org/fao-who-codexalimentarius/committees/committee/related-circular-letters/jp/?committee=CCPR
http://www.fao.org/fao-who-codexalimentarius/meetings/detail/jp/?meeting=CCPR&session=52
[13] CX/RVDF 20/25/9 http://www.fao.org/fao-who-codexalimentarius/meetings/detail/en/?meeting=CCRVDF&session=25

38. For the residue evaluation, published reports should contain, at least, a clear description of the study details, including the following, as appropriate: characteristics of treated animals (age and weight), experimental design, conditions of use (drug formulation, route and method of administration, the dose(s) used, the number of administrations and interval between doses), the analytical method (description, range, validation results, LOD and LOQ), sampling schedules, pharmacokinetic parameters and summarized residue depletion data (i.e. mean or median data with SDs). If the publication concerns radiolabel studies, sufficient detail on the radiolabel position, activity and assays performed must be given to allo w the assessment of the extent of metabolism, the metabolic pathways, the excretion via urine and faeces, or the depletion of the MR and total tissue residue with their ratios, depending on the type of study. Ideally, all individual data and parameters would be reported.

39. JECFA will *not* be able to use reports that are missing critical information. Sponsors are therefore encouraged to take account of these points when submitting a data package for evaluation by JECFA.

Microbiological effects on the safety evaluation of veterinary drug residues in food

40. JECFA assesses chronic risk of residues in food of veterinary drugs for food-producing animals by determining an ADI, based on toxicological or pharmacological effects. In the case of veterinary drugs with antibacterial activity, effects on the human intestinal microbiota are also assessed, to determine a mADI.

41. JECFA follows VICH GL36, which provides a step-by-step approach to determine whether drug residues with antimicrobial activity reaching the human colon remain microbiologically active, and whether determination of an mADI is necessary. Two end-points of concern for human health are considered in this assessment: disruption of the colonization of the human intestinal microbiome and increases in the population(s) of resistant bacteria in the human intestinal microbiome. Resistance is defined in the guideline as the increase of the population(s) of bacteria in the intestinal tract that is (are) insensitive to the test drug or other antimicrobial drugs. Methods suitable for such assessments were indicated by JECFA85, reflecting VICH GL36.

42. JECFA88 noted that although sponsors typically provide adequate data on disruption of the colonization barrier, they often do not provide data to address the antimicrobial resistance end-point of concern. Without such information, JECFA may not be able to complete its assessment, resulting in the inability to establish an ADI for the compound, as was the case with fosfomycin at JECFA88. The Committee therefore emphasizes the need for sponsors to take into account the potential for veterinary drugs at residue levels in food to select for the development of resistance in the microbiota in the gastrointestinal tract when submitting a data package for evaluation by JECFA. Suitable in vivo and in vitro test systems and methods for determining NOAECs and NOAELs for the end-point of antimicrobial resistance are provided in VICH GL36.

Updated chapters of the Environmental Health Criteria 240[14] - Principles and methods for the risk assessment of chemicals in food

43. Since the publication of the EHC 240 in 2009 science has further evolved as well as risk assessment practices. FAO and WHO have recently finalized several projects to update (sub) chapters as follows:

- **Section 4.5 - Genotoxicity**[15]: The updated section 4.5 on genotoxicity published in November 2020 will be incorporated in the online version of the EHC 240 in the coming months.
- **Chapter 5 - Dose-Response Assessment and Derivation of Health-Based Guidance Values**[16]: The updated chapter 5 on dose-response assessment and derivation of health-based guidance published in December 2020 will be incorporated in the online version of the EHC 240 in the coming months.
- **Chapter 6: Dietary Exposure Assessment of Chemicals in Food**[17]: The updated chapter 6 on Dietary Exposure Assessment of Chemicals in Food published in November 2020 will be incorporated in the online version of the Environmental health criteria 240 in the coming months.
- **Section 9.1.4.2 Enzymes**[18]: The updated section 9.1.4.2 on enzymes published in November 2020 will be incorporated in the online version of the EHC 240 in the coming months.

[14] https://www.who.int/publications/i/item/9789241572408
[15] https://www.who.int/docs/default-source/food-safety/publications/section4-5-genotoxicity.pdf?sfvrsn=8ec3434_2
[16] https://www.who.int/docs/default-source/food-safety/publications/chapter5-dose-response.pdf?sfvrsn=32edc2c6_5
[17] https://www.who.int/docs/default-source/food-safety/publications/chapter6-dietary-exposure.pdf?sfvrsn=26d37b15_6
[18] https://www.who.int/docs/default-source/food-safety/publications/section9-1-4-2-enzymes.pdf?sfvrsn=e238e86e_2

Assessment of veterinary drug residues in food: Considerations when dealing with sub-optimal data

44. While the process of veterinary drug residue risk assessment continues to evolve as new data emerge, a recurring challenge for JECFA is when sub-optimal or incomplete data are provided with the expectation of supporting a robust risk assessment. Recent developments in veterinary drug residue risk assessment are described in a new publication, including specific consequences of sub-optimal data during the risk assessment process. When feasible, practical solutions to such challenges are also highlighted. Case examples from recent JECFA veterinary drug evaluations are provided to clearly quantify and illustrate the concepts described. The information provided is intended to facilitate the generation of improved quality data, enabling more timely and robust veterinary drug residue risk assessments.

45. The paper[19] has been published in "Regulatory Toxicology and Pharmacology" (Volume 118, December 2020).

Harmonized methodology to assess chronic dietary exposure to residues from compounds used as pesticide and veterinary drug

46. The risk assessment of residues of pesticides and veterinary drugs in food is a field that continues to evolve. In recent years, JECFA and JMPR have undertaken a number of activities to ensure, to the extent possible, harmonization of the approaches used in order to ensure the most scientifically sound basis for the risk assessment.

47. The paper[20] has been published last year in Critical Review in Toxicology (Crit Rev Toxicol. 2019; 49(1):1-10), and describes the models used by the two Committees to assess chronic dietary exposure and further illustrates the results of combined chronic dietary exposure assessments for eight compounds that are used both as pesticide and veterinary drugs. The work compares the results from models in use by JMPR and JECFA with those from national estimates performed by 17 countries.

Activities on feed safety relevant to food safety and the work of CCRVDF

48. Information on these activities will be provided under CX/RVDF 20/25/3-Add.1[21].

Activities on antimicrobial resistance

49. This section provides a summary update on activities on AMR that have been carried out since the last session of CCRVDF.

50. JEMRA, in collaboration with OIE, published a Meeting Report, on *Foodborne AMR: Role of the Environment, Crops and Biocides (MRA 34)*[22].

51. The UN IACG on AMR was convened by the UN Secretary-General after the UN High-Level Meeting on AMR. The IACG brought together partners across the UN, international organizations and individuals with expertise across human, animal and plant health, as well as the food, animal feed, trade, development and environment sectors, to formulate a blueprint for the fight against AMR. The IACG Secretariat was provided by WHO, with contributions from FAO and OIE. The IACG completed its mandate on 29 April 2019 upon the handover of its report[23] to the UN Secretary-General.

52. Further to a two-year consultation, the Tripartite has developed a monitoring and evaluation framework[24] for the GAP with a harmonized list of indicators for monitoring at the national and global levels. The Tripartite is currently developing guidance to countries on developing national monitoring frameworks for NAPs through in country and country desk assessments.

53. TFAMR is working to develop a new Codex Guidelines on Integrated Monitoring and Surveillance of Foodborne AMR and update the Codex *Code of Practice to Minimize and Contain Foodborne AMR* (CXC 61-2005). The Task Force met in Pyeongchang, Republic of Korea, in December 2019 (REP20/AMR)[25].

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[19] https://www.sciencedirect.com/science/article/pii/S0273230020302324?via%3Dihub
[20] https://www.tandfonline.com/doi/full/10.1080/10408444.2019.1578729
[21] http://www.fao.org/fao-who-codexalimentarius/meetings/detail/jp/?meeting=CCRVDF&session=25
[22] http://www.fao.org/3/ca6724en/ca6724en.pdf
[23] https://www.who.int/antimicrobial-resistance/interagency-coordination-group/final-report/en/
[24] https://www.who.int/antimicrobial-resistance/global-action-plan/monitoring-evaluation/tripartite-framework/en
[25] http://www.fao.org/fao-who-codexalimentarius/meetings/detail/en/?meeting=TFAMR&session=7

54. Given the transnational and multisectoral nature of AMR and the support requested from countries and other stakeholders, the Tripartite organizations are scaling up existing efforts to support countries to urgently counter this immediate threat through a One Health Approach and has launched the AMR-Multi-Partner Trust Fund. The AMR-MPTF is a strategic, inter-sectoral, multi-stakeholder initiative inviting partnership and financing to leverage the Tripartite convening and coordinating power as well as mandates and technical expertise to mitigate the risk of AMR and contribute to the achievement of the SDGs by catalyzing the implementation of One Health NAPs on AMR.

55. The FAO/OIE/WHO Tripartite organizations are establishing a standing Tripartite Joint Secretariat to lead and coordinate the global response to AMR in close collaboration across and beyond the UN organizations. The TJS consolidates cooperation between FAO, OIE, and WHO drawing on their respective core mandates and comparative advantages to address needs of the global response across the One Health spectrum.

56. After consensus on the vision of a shared AMR data portal, the vison of the Tripartite Integrated Surveillance System has been reached at all levels by the Tripartite organizations and approved by Tripartite Executive meetings in 2017 and 2018, a feasibility study has been developed with technical details discussed and agreed by the Tripartite staff from the 3 organizations working on AMR surveillance-related issues on 30 April 2019. The TISSA platform represents an initial step towards an integrated system for surveillance on AMR and AMU, but there is flexibility in the current proposed IT structure to be broader and host other types of data, links and documents. The TISSA platform represents an opportunity to showcase the success of Tripartite collaboration. It can be achieved in a short time and will likely have great impact globally but also at country level by stimulating efforts to build up national databases on AMR/AMU.

57. The WHO AGISAR has been dissolved. A new Tripartite AGISAR is expected to provide additional technical support to the Tripartite on AMR issues.

ACRONYMS USED IN THIS DOCUMENT

ADI	Acceptable Daily Intake
AGISAR	WHO Advisory Group on Integrated Surveillance of AMR
T-AGISAR	Tripartite Advisory Group on Intersectoral Support of AMR
AMR	Antimicrobial Resistance
AMR-MPTF	AMR-Multi-Partner Trust Fund
AMU	Antimicrobial Use
ARfD	Acute Reference Dose
CCPR	Codex Committee on Pesticide Residues
CCRVDF	Codex Committee on Residues of Veterinary Drugs in Foods
CXG	Codex Guidelines
EHC	Environmental Health Criteria
FAO	Food and Agriculture Organization
GAP	Global Action Plan for AMR
GL	Guideline(s)
GLP	Good Laboratory Practice
GVP	Good Veterinary Practice
HBGV	Health-Based Guidance Value
IACG	The United Nations Interagency Coordination Group on AMR
JECFA	Joint FAO/WHO Expert Committee on Food Additives
JEMRA	Joint FAO/WHO Expert Meeting on Microbiological Risk Assessment
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
LC	Liquid Chromatography
LOD	Limit of Detection
LOQ	Limit of Quantification
NAP	National Action Plan for AMR
mADI	Microbiological ADI
MR	Marker Residue
MRA	Microbiological Risk Assessment
MRL	Maximum Residue Limit
MS	Mass Spectrometry
NOAEC	No-Observed-Adverse-Effect Concentration
NOAEL	No-Observed-Adverse-Effect Level
OECD	Organization for Economic Cooperation and Development
OIE	World Organization for Animal Health
SD	Standard Deviation
SDG	Sustainable Development Goals
TFAMR	Ad Hoc Codex Intergovernmental Task Force on Antimicrobial Resistance
TISSA	Tripartite Integrated Surveillance System
TJS	Tripartite Joint Secretariat
TR	Total Residue
TRR	Total Radioactive Residue
TRS	Technical Report Series
TTC	Threshold of Toxicological Concern
UN	United Nations
VICH	International Cooperation on Harmonization of Technical Requirements for Registration of Veterinary Medicinal Products
WHO	World Health Organization