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CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

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Agenda Item 9 **CX/RVDF 21/25/10**

September 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

DISCUSSION PAPER ON PARALLEL REVIEW OF A NEW VETERINARY DRUG BY JECFA AND NATIONAL REGULATORY AGENCIES

(Prepared by the Electronic Drafting Group
chaired by Canada[1] with the assistance of Australia, the United States of America,
the JECFA Secretariat and Health For Animals)

Introduction

1. At the 24th session of Codex Committee on Residues of Veterinary Drugs in Foods (CCRVDF24, 2018), the Committee agreed that a discussion paper should be drafted setting out the advantages, disadvantages and process, of review of a product by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) prior to approval of a marketing authorization by a national regulator. The concept of early engagement of the JECFA in global joint reviews has been raised as a tool to support the timelier establishment of Codex maximum residue limits (MRLs) for veterinary drugs while mitigating trade risks. A similar approach is being considered by the Codex Committee on Pesticide Residues (CCPR)[2]. Working document CX/RVDF 20/25/3 also complements the information provided in this paper about the JECFA88 (2019) evaluation of new compounds.[3]

2. This paper was drafted by Canada with input from the United States of America (USA), Australia, the JECFA Secretariat, and Health for Animals.

Context

3. Farmers in some countries – especially countries dependent on Codex for their regulatory needs – do not have access to Maximum Residue Limits (MRLs) for new products because they are set significantly later; in some cases, many years later. This delay limits farmers' ability to use new technologies in many countries – especially countries dependent on Codex MRLs. This is a result of the fact that JECFA may only review a veterinary pharmaceutical product after it has been reviewed and authorized by at least one national regulator and there is a defined usage condition (i.e., good veterinary practice (GVP) has been established).

4. Divergent methodologies/processes between reviews from JECFA and those of national authorities can result in calls for new data which must be generated and re-submitted, often causing further delays. These additional requirements and resulting delay can lead to the decision not to submit compounds to the Codex process.

Concept

5. The idea is to allow JECFA to review the human food safety dossier for a product (including both toxicology and residue data packages) during the same time frame as a national review of that product. The current process requires JECFA to wait until final approval of a product by a national authority prior to commencing its nomination and review process. Hence, the objective is to reduce time delays between the completion of a safety review by a national authority and the time a compound is placed on the CCRVDF priority list for review by JECFA.

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1 Please contact the focal point of the Member Country or Observer Organization for the details of the delegates.
The list of Codex contact points for members and observers are available from the Codex website at:
http://www.fao.org/fao-who-codexalimentarius/about-codex/members/en/
http://www.fao.org/fao-who-codexalimentarius/about-codex/observers/observers/obs-list/en/

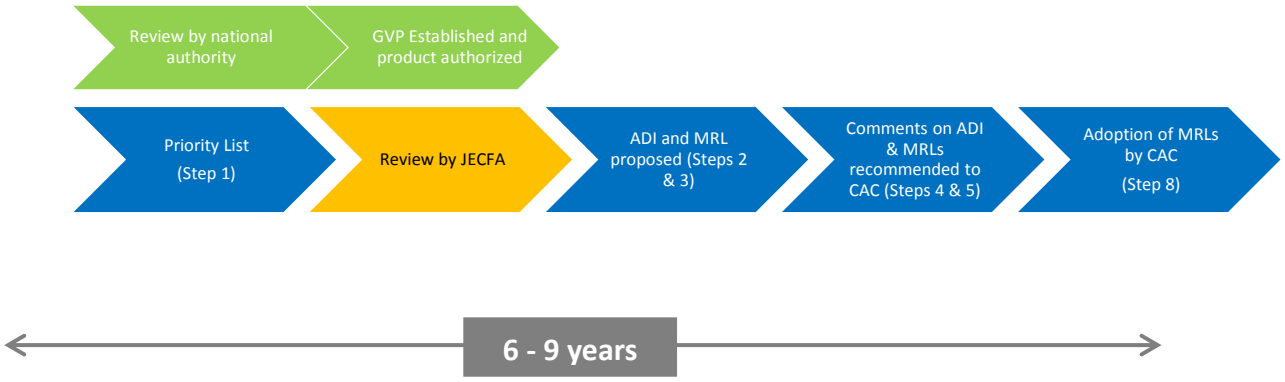
2 REP19/PR, paras. 198 – 202, CX/PR 20/52/16
Working documents including the report of the plenary session can be downloaded from the CCPR website:
http://www.fao.org/fao-who-codexalimentarius/committees/committee/related-meetings/en/?committee=CCPR

3 REP18/RVDF, paras. 98-103
Working documents including the report of the plenary session can be downloaded from the CCRVDF website:
http://www.fao.org/fao-who-codexalimentarius/committees/committee/related-meetings/en/?committee=CCRVDF

Pictorial representations of stages in current versus proposed:

Current Procedure

Proposed Procedure



Proposed Principles

6. The following principles, as is the case during any scientific review by JECFA, should be observed:

    1. **Transparency**. Nominating member country and drug sponsor should identify if a veterinary drug is intended for a parallel process and be open about dossier submission timeframes.
    2. **Confidentiality**. Much of the data submitted to JECFA or national regulator(s) is confidential and there is a good precedent to respect the confidentiality of the data.
    3. **Independence**. The national authorization process and JECFA process are two separate independent processes and subject to their own independent decisions and therefore are not contingent on one another.

Proposed Process

7. The proposed phases of the process are:

Phase 1: Identification of a candidate

8. A product is identified by a drug sponsor and during bilateral discussions with a member country(ies), the product is identified as a candidate. The current Priority List nomination requirements of a veterinary drug would also apply to a JECFA parallel review process. The Risk Analysis Principles Applied by the CCRVDF lists criteria required for a veterinary drug to appear on the Priority List. A proposed veterinary drug shall meet some or all of the following criteria:

    - "A Member has proposed the compound for evaluation (a template for information recommended for consideration in the priority list by Codex Committee on Residues of Veterinary Drugs in Foods has been completed and be available to the Committee);
    - "A Member has established good veterinary practices with regard to the compound;
    - "The compound has the potential to cause public health and/or international trade problems;
    - "The compound is available as a commercial product; and
    - "There is a commitment that a dossier will be made available."

Phase 2: Submission

9. A product is submitted (or is expected to be submitted) to a national regulatory authority, most likely in one of the larger markets (in practice, most veterinary products are first submitted for review in the U.S. or in Europe). At the following CCRVDF meeting, the product would be submitted (by the Codex Member who received the product application or is expected to receive the application by a certain date) for inclusion on the priority list at CCRVDF (Step 1).

Phase 3: Assessment

10. JECFA and the national assessor follow their normal processes of assessing the product. (Step 2).

Phase 4:

11. Draft ADI and MRLs proposed by JECFA and circulated for comment (step 3).

12. The remainder of the uniform procedures for the elaboration of Codex standards and related texts would be followed, consistent with the current process.

Advantages of the proposed process

13. Some of the benefits of engaging JECFA and National Regulator(s) in a parallel review include:

- **Earlier access to a new veterinary drug**

14. Some countries depend on Codex to first establish MRLs before they will consider authorizing the compounds for domestic use. Considering that many countries rely on Codex MRLs to support the domestic registration of veterinary drugs, narrowing the time gap between authorization of drugs in countries and MRL setting at Codex would allow for timelier access to new and safe veterinary drugs for food animal producers across the globe. Farmers in exporting countries will not need to delay using a new product until MRLs are established in foreign markets and/or at Codex.

- **Trade facilitation**

15. With population growth and changing food preferences, international trade has played an important role in meeting global demands for safe, abundant, diverse, and affordable food choices. Trade has also been critical in improving global food security, particularly in net-importing countries where agronomic conditions limit the potential for increases in agricultural productivity. Food animal producers rely on safe and effective veterinary drug products to address animal health challenges. Given the importance of international trade of agricultural products and the need to have exported foods of animal origin meet the requirements of importing markets, food animal producers must ensure that MRLs for the veterinary drugs they use are set in foreign markets, including at Codex. While some countries may have a regulatory framework that allows the registration of new veterinary drugs and the establishment of MRLs, food animal producers from these countries are often unable to export their products to countries until the Codex MRLs are established.

- **Optimization of resource management**

16. The involvement of the JECFA in parallel reviews is expected to accelerate the establishment of Codex MRLs for a new veterinary drug by giving the JECFA evaluators access to the relevant full data packages for evaluation prior to a national registration. In particular, technical issues identified by the JECFA evaluators may be resolved while the new veterinary drug is still undergoing review leading to better resource utilization.

- **Availability of the same data package supporting alignment of MRLs**

17. The submission of the same data package to national authorities and to JECFA at the same time, is expected to contribute to a more global scientific assessment by allowing the review of the same data in parallel. Involving Codex in the global review process up front provides the additional benefit of having all of the globally available scientific expertise applied at the beginning—reducing rework and providing the final link in ensuring that results are globally harmonized to the fullest extent possible.

Challenges with the proposed process

- **Project management**
    - The Codex MRL-setting process typically follows a set cycle. It is based on a strict schedule that starts with the submission of the data package, and incorporates fixed milestones. Careful consideration should be given by the drug sponsor(s) and nominating country (ies) to support the narrowest interval between national product registration and setting of the Codex MRLs.

- **Parallel review timelines**
    - There is a concern that engagement in parallel review will have to consider timeliness of the work tasked to JECFA experts. It will be important to identify critical milestones for participation of JECFA reviewers, with a distinction between WHO and FAO reviewers, and to determine how to minimize multi-year engagement on JECFA resources to ensure they are not over utilized.
    - Concerns relate to the impact late changes to the critical good veterinary practice (e.g. dosage, duration etc.) may have on JECFA resources, should changes occur after the completion of the JECFA assessment which may invalidate the review or require that it be redone. Building on some countries product registration experience, it is generally observed that the GVP on the final label remains the same as the one on the proposed label.
- **Candidate selection and outcome**
    - Selection criteria should be established to ensure that the candidates for a JECFA parallel review support consideration for including minimum number of participating countries and harmonization of use patterns (similar GVP).
    - Different outcomes may occur when data packages are provided to the individual authorities and JECFA (e.g. different MRLs based on different number and location of residue trials and corresponding critical GVPs, etc.). JECFA remains an independent scientific body following its governing requirements and meeting its responsibilities. There would never be any requirement that the expected outcome of any process that is developed has harmonized endpoints/MRLs.
- **Independence of the process**
    - To ensure international and public trust in Codex MRLs, it will be important to maintain the independence of JECFA reviewers involved in parallel reviews to ensure they are not the same experts as the ones involved in the national authorization process.
- **Product labelling**
    - For a parallel review, a draft label will need to be available, but no officially approved label will be available at the time of the initial JECFA evaluation. Therefore, only limited/proposed GVP conditions, in particular only a proposal for suitable withdrawal times, will be available. While an evaluation regarding the proposed withdrawal times is possible, the final approved (by the national authority) withdrawal times may differ in turn.

Other Considerations

- **Appropriate protection of intellectual property**

18. The main IP falls under the realm of Confidential Business Information which is protected in the national authorities by strict rules. The Risk Analysis Principles Applied by the CCRVDF references the WHO/FAO requirements for maintaining confidentiality. Submission of a dossier prior to marketing authorization in a country should be treated in the same manner in which WHO/FAO protects confidential information during a normal JECFA evaluation.

Recommendation

19. Codex members and observers are invited to consider the proposed process as described in paragraphs 7 – 12 while taking into account the advantages and challenges of the proposed process including other considerations raised in paragraph 18.