E

CODEX ALIMENTARIUS COMMISSION

Food and Agriculture Organization of the United Nations

World Health Organization

Viale delle Terme di Caracalla, 00153 Rome, Italy - Tel: (+39) 06 57051 - E-mail: codex@fao.org - www.codexalimentarius.org

Agenda Item 3 **CX/PR 19/51/2-Add.1**

March 2019

JOINT FAO/WHO FOOD STANDARDS PROGRAMME

CODEX COMMITTEE ON PESTICIDE RESIDUES

51st Session
Macao SAR, P.R. China, 8-13 April 2019

GUIDELINES FOR THE DETERMINATION OF PESTICIDES AS ENDOCRINE DISRUPTORS AND HARMONIZED RISK MANAGEMENT APPROACHES IN RESPECT OF THEIR PRESENCE IN FOODS

(Discussion Paper prepared by India)

Background

1. India had presented a proposal for new work on guidelines for "Uniform risk management guidelines to address endocrine disrupting chemicals (EDCs) as pesticides in food" in the 50th Session of Codex Committee on Pesticides Residues (CCPR50, 2018) as the issue had the potential to lead to major repercussions in international food trade, and accordingly requested the Committee to endorse this new work.

2. The Committee, while recognizing the importance of this issue in international food trade, noted that there was no evidence that trade disruption, arising from the presence or withdrawal of Codex maximum residue limits for pesticides (CXLs), had occurred. The Committee also pointed out that EDCs could arise from a wide range of sources and that the issue was broad and went beyond the mandate of CCPR. Therefore, the Committee could not recommend starting the proposed new work at that time. The Committee had also suggested that India, as a member of the Commission, could raise the concern to CAC on its own.[1]

3. In line with the observation of the CCPR50, India prepared a revised discussion paper as well as the project document[2] for the proposed new work and presented the same to the 41st Session of the Codex Alimentarius Commission (CAC41, 2018) for consideration and approval of the new work. The revised discussion paper and the project document focused essentially on pesticides having endocrine disrupting properties since many of the chemicals identified as endocrine disruptors are pesticides.

4. The Commission noted the issue raised by India in CRD4 relating to pesticides as endocrine disruptors; and further noted that India had revised its proposal based on the discussion at CCPR50 and could resubmit the proposal to CCPR as the relevant technical body.[3]

5. Based on the directions of the CAC41, India is re-presenting the proposal for new work (discussion paper and the project document), as under, for consideration of the Committee:

Purpose of the new work

6. The purpose of the proposed work is to provide guidelines which will promote internationally harmonized approach to address possible public health and trade issues arising from presence of pesticides having endocrine disrupting properties. It includes development of criteria for determination of pesticides as endocrine disruptors and harmonized approaches to risk management in respect of their presence in food based on the available scientific information, global best practices and risk analysis principles of Codex.

Endocrine Disruptors

7. Over the years, increasing reports of diseases like cancer, hormonal imbalance and fertility issues among humans has led to the identification of certain chemical substances interfering with the hormonal system and their linkage with these diseases. These chemicals which may affect endocrine system can be classified as Endocrine Disruptors (EDs). EDs encompasses a variety of chemicals including pesticides.

[1] REP18/PR, paras. 161-162
[2] CAC41/CRD4
[3] REP18/CAC, para. 153

8. As per World Health Organization/International Programme on Chemical Safety (WHO/IPCS, 2002) endocrine disruptor is defined as “an exogenous substance or mixture that alters function(s) of the endocrine system and consequently causes adverse health effects in an intact organism, or its progeny, or (sub) populations.” And, potential endocrine disruptor is defined as “an exogenous substance or mixture that possesses properties that might be expected to lead to endocrine disruption in an intact organism[4], or its progeny, or (sub) populations[5]”.

9. Endocrine disruption remains a field that deserves more research which requires involvement of various disciplines including ecotoxicology, toxicology, molecular biology, epidemiology, and clinical research. Although, studies showing the linkages between exposures to EDs and human diseases are much stronger now than in 2002, human studies can show associations only, not cause and effect. Hence, it is important to use both human and animal data to develop the evidence for a link between exposures to EDs and human disease. For risk assessment and informed risk management the actual exposure patterns and levels in humans[6]; the shape and slope of dose-response functions in humans (P.W. Stewart et al. 2008); the health impact (risk, or disease cases attributable to exposure to EDs) need to be evaluated. Over the past 10 years, there has been a dramatic shift in focus from investigating associations between adult exposures to EDs and disease outcomes to linking developmental exposures to disease outcomes later in life. This is now considered the most appropriate approach for most endocrine-related diseases and dysfunctions[7].

10. New approaches are also being explored whereby large batteries of high-throughput in vitro tests are being investigated for their ability to predict toxicity, the results of which may be used in hazard identification and potentially risk assessment. A challenge to moving forward is that EDs research over the past decade has revealed the complex interactions of some chemicals with endocrine systems, which may escape detection in current validated test systems[4].

Pesticides as endocrine disruptors

11. As per in vitro studies, many chemicals that have been identified as endocrine disruptors are pesticides (Wissem Mnif et al. 2011). The legislators should take guidance on toxicity of a pesticide based on evaluation by epidemiologists and toxicologists rather than merely on its classification as endocrine disruptors. Toxic effects have not been always proven to be due to hormonal disruption (J.P. Myers et al. 2016). Hence, all EDs are not potential carcinogens; some are innocuous or protective at low doses as in the case of soy phytoestrogens. Legislators should refrain from legislating on the basis of in vitro ED classification tests when the in vivo toxicity mechanism is unknown. Each molecule should be considered separately in terms of mechanism and toxicity.

12. As for all other forms of toxicity, the important information to consider is potency and exposure of endocrine disruptors since the risk is dependent on both exposure and potency. Therefore, for risk assessment and informed risk management it is important to consider both the potential hazard and exposure of all suspected molecules as thoroughly as possible in order to evaluate the risk for human and/or wildlife populations. In this prospect, it is important to consider (1) the exposure of populations to the chemical under study, (2) the dose responses of its effects, (3) the cocktail effect, and (4) the health impact (risk, or disease cases attributable to exposure to EDs).

Regulatory approaches toward pesticides as endocrine disruptors

13. Globally, regulations of pesticides are being carried out largely based on risk based approaches. However, regulations of some countries include a combination of hazard and risk based approaches for decision-making to be applied in different ways.

14. A risk-based approach takes into account the exposure assessment. However, a hazard-based approach considers only intrinsic properties, without taking account of the exposure to the substance. As per ‘Hazard criteria’, even a minimal presence of side effects would be treated as unsafe to human health, plant, and wildlife. This approach discards ‘tolerable daily intake’ of substances. In other words, any inherent presence of risks in the chemical substances would be considered as hazardous. It does not consider the conditions of coming into contact, dosage level, duration of exposure, time of occurrence, in risk management.

[4] The term “intact organism” is understood to mean that the effect would occur in vivo, either observable in a test animal system, epidemiologically or clinically. However, it does not necessarily mean that the adverse effect has to be demonstrated in an intact test animal, but may be shown in adequately validated alternative test systems predictive of adverse effects in humans and/or wildlife.

[5] State of the Science of Endocrine Disrupting Chemicals (WHO, 2002)

[6] http://www.cdc.gov/exposurereport/

[7] State of science of endocrine disrupting chemicals 2012; summary of decision makers (WHO, 2013)

15. US- Environmental Protection Agency has developed Endocrine Disruptor Screening Program (EDSP) which uses a two tiered approach for screening chemicals. Tier 1 screening data is used to identify substances that have the potential to interact with the endocrine system and chemicals which are found to exhibit the potential to interact with the hormone systems will proceed to Tier 2. The Tier 2 testing identifies any adverse endocrine-related effects caused by the substance, and establishes a quantitative relationship between the dose and that adverse effect. The results of Tier 2 will be combined with other hazard information and exposure assessment on a given chemical resulting in the risk assessment. Risk assessments are used to inform risk mitigation measures, as necessary and regulatory decisions concerning chemicals[8].

16. Japan has recognized that it is important to identify the exact harmful effects induced by suspected endocrine disrupters by accumulating the results and data of scientific researches and assessments on the issue in cooperation with relevant authorities, so as to deal with the adverse effects (toxicity) on the basis of appropriate risk assessment[9].

17. Very recently, European Commission has also notified the criteria for determination of endocrine disrupting properties in plant protection products as part of its regulation EC No. 1107/2009 based on the WHO/IPCS definition[10].Therefore, any chemical which is identified as Endocrine Disruptor against the above criteria will not be allowed approval as Plant Protection Product. In other words, any inherent hazardous nature of chemical substances would be considered as a risk without going through the process of risk assessment based on exposure.

Need for harmonized guidelines to determine pesticides as endocrine disruptors

18. Over the years, there has been growing concerns over the potential adverse effects that may occur from exposure to pesticides having endocrine disrupting properties. Such pesticides may have the potential to alter the functioning of endocrine system in humans. These concerns have driven the member countries to develop regulatory approaches for pesticides exhibiting endocrine disrupting properties, with the limited scientific information available. Different Risk Management approaches by countries in regulating pesticides having endocrine disrupting properties may not lead to any gains objectively in respect of food safety but could only lead to trade difficulties.

19. Therefore, evidence based assessment of actual risk associated with such pesticides is very important in regulatory decisions otherwise there is every possibility that some of the pesticides (still one of the important component of Pest Management System) will be removed despite of their safe usage. Such approach may do little or nothing to protect public health but has the potential to significantly impact the sustainable agricultural production, food security and disruption of international food trade. Accordingly, it is the need of the hour to have guidelines for determination of pesticides as endocrine disruptors and harmonized Risk Management Approaches in terms of their presence in food which can be uniformly followed by member countries.

20. One of the strategic objectives of the Codex Alimentarius Commission (CAC) is to proactively identify emerging issues and members' needs and consider such emerging issues which could lead to repercussions in international trade, and develop harmonized guidelines to ensure health protection and fair practices in the international food trade. Further, CCPR is the relevant technical bodyto deal with pesticides having endocrine disrupting properties. Accordingly, the Committee needs to take cognizance of the issue and initiate new work on the pesticides as endocrine disruptors.

21. A similar work on development of risk management guidelines to address chemicals inadvertently present in food at very low levels- is already approved by the Commission and currently undertaken by CCCF. Recently, another similar new work proposal on harmonized guidelines for bio-pesticides has been endorsed by CCPR (REP18/PR, Paragraphs 158-160).

Recommendation

22. It is recommended that the CCPR:

    a. endorses new work on the guidelines for determination of pesticides as endocrine disruptors and risk management approaches in terms of their presence in food; and

    b. Forward the attached Project Document (Annex) to the CAC for approval.

[8] https://www.epa.gov/endocrine-disruption/endocrine-disruptor-screening-program-edsp-tier-1-assessments
[9] http://www.meti.go.jp/english/report/data/g020205be.pdf
[10] http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:52016DC0350&from=EN

APPENDIX

PROJECT DOCUMENT

Guidelines for determination of pesticides as endocrine disruptors and harmonized risk management approaches in respect of their presence in food

(Prepared by India)

1. Purpose

The purpose of the proposed work is to provide guidelines which will promote internationally harmonized approach to address possible public health and trade issues arising from presence of pesticides having endocrine disrupting properties.

It includes development of criteria for determination of pesticides as endocrine disruptors and harmonized approaches to Risk Management in respect of their presence in food based on the available scientific information, global best practices and risk analysis principles of Codex.

2. Scope

This document would cover the pesticides having endocrine disrupting properties present in the food of interest.

3. Its relevance and timeliness

Over the years, there has been growing concerns over the potential adverse effects that may occur from exposure to pesticides having endocrine disrupting properties. Such pesticides may have the potential to alter the functioning of endocrine system in humans. These concerns have driven the member countries to develop regulatory approaches for pesticides exhibiting endocrine disrupting properties, with the limited scientific information available. Therefore, evidence based assessment of actual risk associated with such pesticides is very important in regulatory decisions otherwise there is every possibility that some of the pesticides (still one of the important component of Pest Management System) will be removed despite of their safe usage. Such approach may do little or nothing to protect public health but has the potential to significantly impact the sustainable agricultural production, food security and disruption of international food trade. Accordingly, it is the need of the hour to have criteria for determination of pesticides as endocrine disruptors and harmonized risk management approaches in terms of their presence in food which can be uniformly followed by member countries.

The Codex Alimentarius Commission (CAC) is ideally placed under its mandate to consider such emerging issues which could lead repercussions in international trade and develop harmonized guidelines to ensure health protection & fair practices in food trade.

4. The main aspects to be covered

The proposed work will review the existing scientific information on endocrine disrupting properties of pesticides, possible concerns to public health and current regulatory approaches to deal with pesticides having endocrine disrupting properties. Based on information available, evidence based criteria for determination of pesticides as potential endocrine disruptors and harmonized risk management approaches in terms of presences of these pesticides in food, would be developed.

5. An assessment against the criteria for the establishment of work priorities Criteria applicable to general subjects

a. Diversification of national legislations and apparent or potential impediments to international trade

Globally, regulations of pesticides are being carried out largely on risk based approaches. The pesticides having endocrine disrupting properties should also need to be dealt in same manner and evidence based risk assessment is very important for any regulatory decision toward use of such products in agricultural production.

In absence of any uniform guidelines, there is every possibility of diversification in regulatory approaches followed by nations while dealing with pesticides having endocrine disrupting properties which will pose unnecessary international trade barriers. Therefore, criteria for determination of pesticides as potential endocrine disruptors and harmonized guidelines shall facilitate member countries to base their regulatory decisions toward use of pesticides exhibiting endocrine disrupting properties in terms of actual risk assessment which in turn would lead to sustainable agricultural production without creating unnecessary trade barriers.

b. Scope of work and establishment of priorities between the various sections of work

See 1 and 2 above

c. Work already undertaken by other international organizations in this field and/or suggested by the relevant international intergovernmental body (ies)

WHO International Programme on Chemical Safety (IPCS) published a document in 2002 titled ***"Global Assessment of the State-of-the-Science of Endocrine Disruptors"*** which discussed about potential adverse effects that may result from exposure to a group of chemicals that have the potential to alter the normal functioning of the endocrine system and the available scientific information. The study also indicated that Worldwide, despite large efforts, comparable data sets for assessing exposures to Endocrine Disrupting Chemical (EDCs) for humans or wildlife are not available and such information is essential to adequately evaluate exposure–response relationships in field and epidemiology studies to produce credible risk assessments. These concerns in relation to EDCs stimulated many national governments, international organizations, scientific bodies, and public interest groups to establish research programs, organize conferences/workshops, and form expert groups/committees to address and evaluate EDC-related issues including PPPs having endocrine disrupting properties.

d. Amenability of the subject of the proposal to standardization

The proposed work would draw on the experience gained from scientific work done so far on the subject as well as current regulatory approaches. Members would benefit with the availability of uniform risk based management decision guidelines to deal with the pesticides having endocrine disrupting properties without any compromise with consumer safety.

e. Consideration of the global magnitude of the problem or issue

The pesticides are essential component of Pest Management System to achieve global targets of food production. The worldwide consumption of pesticides is about 2-3 million tonnes per year and global market size of pesticides was more than 60 Billion USD in 2016. On other hand, export of agricultural products is increasing at an average of 5% per year and global trade of Agricultural Products was more than 15 trillion USD in 2016 (World Trade Statistical Review 2017). As noted in this paper, the issue of pesticides having endocrine disrupting properties is of significant interest to the wider membership of Codex and an internationally harmonised approach to deal with such products will be helpful to:

- Promote scientific and risk based approach in regulatory decision making
- Promote efficient use of limited resources to address public health concerns associated with such pesticides by avoiding duplication of research and assessment activities;
- Minimise any potential impediments to international trade of food and agricultural products;
- Enhance risk communication to consumers and promote confidence in regulatory decisions.

6. Relevance to the Codex Strategic Objectives

The proposed work would contribute to the Commission's Strategic Goal 1 to establish international food standards that address current and emerging food issues by promoting a harmonized approach to risk analysis.

i. Goal 1, Objective 1.1: *Establish new and review existing Codex standards, based on priorities of the CAC- Activity 1.1.1*

ii. Goal 1, Objective 1.2: *Proactively identify emerging issues and Member needs and, where appropriate, develop relevant food standards- Activity 1.2.2*

7. Information on the relation between the proposal and other existing Codex documents

The proposed work will be strongly linked to and guided by, but not limited to the:

- Working Principles for Risk Analysis for Application in the Framework of the Codex Alimentarius;
- Risk Analysis Principles Applied by the Codex Committee on Pesticide Residues
- Working Principles for Risk Analysis for Food Safety for Application by Governments

8. Identification of any requirement for and availability of expert scientific advice

Relevant scientific advice from JMPR specifically on gaps and uncertainties in the risk associated with pesticides having endocrine disrupting properties may be appropriate.

9. Identification of any need for technical input to the standard from external bodies so that this can be planned for the proposed timeline for completion of the new work

Not seen at this stage.

10. Proposed timeline for completion of work

Subject to approval as new work by CAC41, a first draft of the guidelines will be considered by CCPR52 (2020). Final adoption by CAC is expected in 2022 or earlier.