

CODEX ALIMENTARIUS COMMISSION



Food and Agriculture
Organization of the
United Nations



World Health
Organization

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Agenda Items 8

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REPORT OF THE VIRTUAL PRE-MEETING

GUIDELINES FOR COMPOUNDS OF LOW PUBLIC HEALTH CONCERN THAT MAY BE EXEMPTED FROM THE ESTABLISHMENT OF CODEX MAXIMUM RESIDUE LIMITS OR DO NOT GIVE RISE TO RESIDUES

(Prepared by the Electronic Working Group chaired by Chile and co-chaired by India and the United States of America)

This CRD should be read in conjunction with CX/PR 21/52/12; CX/PR 21/52/12-Add.1 and CRD¹ presented by Codex Members and observers

INTRODUCTION

1. On 23 July 2021 the pre-meeting of the Electronic Working Group (EWG) on the Guidelines for compounds of low public health concern that may be exempted from the establishment of Codex maximum residue limits or do not give rise to residues took place virtually. The meeting was held in English, French and Spanish and the program was published on the Codex website.²
2. The objective was to provide Members and Observers with an opportunity to make progress on the development of these Guidelines based on the information provided in the working document³ and comments received in reply to CL 2021/38-PR in order to facilitate the consideration of this item by CCPR. The conclusions and recommendations of this meeting will be presented to the consideration of the CCPR52.

METHODOLOGY

3. In order to facilitate the discussion, Chile, as the Chair of the EWG, presented⁴ a summary of the work carried out. Subsequently, the draft of the Guidelines was presented (Appendix I of CX / PR 21/52/12) where Members and observers had the opportunity to make general and specific comments on the structure and its content.

SUMMARY OF DISCUSSION

4. Members and observers expressed their support for the work done by the EWG.
5. Specific comments and suggestions were received on:
 - The scope of the Guidelines;
 - Definitions
 - Criteria

¹ CRDs 4; 5; 6; 13; 14; 15; 16; 17; 18

² [Pre-meeting program](#)

³ Reference documents: CL 2021/38-PR; CX/PR 21/52/12; CX/PR 21/52/12-Add.1 (Comments in reply to CL 2021/38-PR)

⁴ [Chair presentation](#)

- Examples of compounds.

6. Regarding the examples, the WG chair clarified that according to the EWG terms of reference, they will not be an integral part of the guideline.
7. There was agreement to reestablish the EWG to continue to work on the guidelines based on comments submitted. Chile expressed interest in continuing to chair the group.
8. The Chair thanked the comments and indicated that they will be included in a revised document when the EWG is reestablished.

CONCLUSIONS

9. It was agreed to continue working on the guidelines and to recommend advancement to Step 5 of the Codex Procedure.

RECOMMENDATIONS FOR THE CCPR52

10. Codex members and observers are invited
 - To consider advancement of the Guidelines for compounds of low public health concern that may be exempted from the establishment of codex maximum residue limits or do not give rise to residues (see Appendix I) for adoption of CAC at step 5 of the Codex procedure
 - Reestablish the eWG working in English and Spanish to further develop the guidelines based on the written comments provided to this Session, and those provide in plenary and in the pre-meeting, with a view to finalizing the Guidelines for consideration by CCPR53(2022).
 - Note that Guidelines should provide harmonized definitions and criteria as agreed by CCPR51. Examples of compounds could be provided to facilitate the development of the guideline, however, they will not remain in the final document but could be made available to Codex members, for instance, on the Codex website.

APPENDIX I

**GUIDELINES FOR COMPOUNDS OF LOW PUBLIC HEALTH CONCERN
THAT MAY BE EXEMPTED FROM THE ESTABLISHMENT OF CODEX MAXIMUM RESIDUE LIMITS
OR DO NOT GIVE RISE TO RESIDUES**

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PREFACE

1. Pesticides are substances used in agriculture to achieve health, quality and performance in crops through preventive and control of biotic factors that affect them. They include, inter alia, insecticides, fungicides, herbicides, acaricides, growth regulators, semiochemicals, and repellents.
2. Pesticides contain active substances that can be of chemical or biological origin.
3. Among pesticides of chemical origin there are synthetic and natural mineral substances and other natural substances.
4. Among pesticides of biological origin, a.k.a. Biopesticides, for the purpose of this Guidance Document, make reference to active substances based on microorganisms (Microbial pesticides), compounds made from plants like plant extracts (Botanical pesticides), pheromones (Semiochemicals) and substances of animal origin. Therefore, substances referred to as biofertilizers, bioregulators or biostimulants as well as invertebrates such as insects and nematodes or other macroorganisms are not covered by this Guidance Document.
5. Sometimes authorized uses of the pesticides on food crops result in residues. Codex Alimentarius has set Maximum Residue Limits (MRLs) for pesticides on specific foodstuffs or food groups traded internationally to protect the health of consumers in accordance with the recommendations of the Joint FAO/WHO Meeting on Pesticide Residues (JMPR). Some countries establish their own MRLs as a result of the evaluations carried out by national or regional agencies on risk assessment.
6. Codex MRLs (CXLs) have been adopted based on the recommendations of the JMPR evaluations and in accordance with Good Agricultural Practices (GAP) data. Food resulting from commodities that comply with the MRLs will be toxicologically acceptable (are considered to be safe for consumers). The question whether an active substance fulfills one or more criteria with the aim to exempt the substance from the setting of Codex Maximum Residue Limits is the result of an evaluation of toxicology and residue behavior.
7. When authorized uses of pesticides do not produce residues or are identical and indistinguishable from certain natural components of the food commodities either considered to be of low or no toxicological significance, some regulations explicitly grant an exemption from the requirement to establish an MRL or state that an MRL is not required for the respective active substance or its authorized uses. However, there are no harmonized or internationally recognized criteria for MRL exemptions; further, there is not a harmonized list of active substances for which exemptions have been deemed appropriate.
8. These guidelines represent a first step toward harmonisation or international recognition of criteria for exempting active substances or their authorized uses of low public health concern from the requirement to establish MRLs.

SECTION 1. SCOPE

9. These guidelines apply without prejudice to any other provisions of the Codex Alimentarius Commission (CAC) establishing MRLs for pesticides on foodstuffs.
10. These guidelines aim to make use of the different criteria used by some countries and international organizations regarding the establishment of pesticides MRL exemption for active substances or their authorized uses, considered of low risk or low public health concern
11. These criteria are presented in an attempt to provide a consistent and harmonized approach for determining when an active substance or its authorized uses could be considered exempt from the establishment of CODEX MRLs.
12. These guidelines are intended to be used by the countries' competent authorities that do not have established criteria for the MRLs exemption for active substances or its authorized uses in their respective legislation.

SECTION 2. DEFINITIONS

13. **Acceptable daily intake (ADI):** It is the daily intake which, during an entire lifetime, appears to be without appreciable health risks to the consumer on the basis of all the known facts at the time of the evaluation. It is expressed in milligrams of the chemical per kilogram of body-weight.
14. **Acute Reference Dose (ARfD):** It is the estimate of the amount of a substance in food or drinking water, expressed on a body weight basis that can be ingested in a period of 24 h or less without appreciable health risk to the consumer. It is derived on the basis of all the known facts at the time of evaluation. The ARfD is expressed in milligrams of the chemical per kilogram of body weight.

15. **Active substance/ingredient:** The component(s) of the product that directly or indirectly (metabolites) provides the pesticide action.
16. **Authorized use:** Authorized use refers to the safe use of a pesticide based upon a use pattern determined at national level. It includes domestically approved, registered or recommended uses, which take into account public and occupational health and environmental safety considerations.
17. **Basic Substance:** Active substance which is not a substance of concern; and does not have an inherent capacity to cause endocrine disrupting, neurotoxic or immunotoxic effects; and is not predominantly used for plant protection purposes but nevertheless is useful in plant protection either directly or in a product consisting of the substance and a simple diluent; and is not placed on the market as a pesticide (For example Calcium hydroxide, Lecithins).
18. **Biological pesticide (Biopesticide):** Active substances made from living or dead microorganisms such as bacteria, algae, protozoa, viruses and fungi (See Microbial pesticides), pheromones and other semiochemicals (See Semiochemicals pesticides), and plants or parts of plants (See botanical pesticides), designed to repel, destroy or control any pest or regulate the growth of plants (For example *Bacillus amyloliquefaciens* strain FZB24, *Trichoderma atroviride* strain).
19. **Botanical pesticide:** Active substances that consists of one or more components found in plants and obtained by subjecting plants or parts of plants of the same species to a process such as pressing, milling, crushing, distillation and/or extractions. The process may include further concentration, purification and/or blending, provided that the chemical nature of the components is not intentionally modified/alterd by chemical and/or microbial processes (For example *Annona* spp. (Annonins, Squamocin), neem (*Azadirachta indica*)).
20. **Feed:** Any single or multiple materials, whether processed, semi-processed or raw, which is intended to be fed directly to food producing animals
21. **Food Group/Crop Group:** A collection of foods/crops subject to MRLs that have similar characteristics (for example Stone fruits) and similar potential for residue for which a common group MRL can be set. Representative commodities can be used to establish MRLs on an entire crop group or subgroup. The Codex classification of food and animal feed commodities describe the various food groups moving in trade and lists commodities included in each group.
22. **Good Agricultural Practice:** Good agricultural practice in the use of pesticides (GAP) includes the nationally authorized safe uses of pesticides under actual conditions necessary for effective and reliable pest control. It encompasses a range of levels of pesticide applications up to the highest authorized use, applied in a manner which leaves a residue which is the smallest amount practicable. Authorized safe uses are determined at the national level and include nationally registered or recommended uses, which take into account public and occupational health and environmental safety considerations. Actual conditions include any stage in the production, storage, transport, distribution of food commodities and animal feed.
23. **Joint FAO/WHO meeting on pesticide residues (JMPR):** The "Joint Meeting on Pesticide Residues" (JMPR) is an expert *ad hoc* body administered jointly by Food and Agriculture Organisation and World Health Organisation. The JMPR has met annually since 1963 to conduct scientific evaluations of pesticide residues in food. It provides advice on the acceptable levels of pesticide residues in internationally traded food. The JMPR consists of experts who attend as independent internationally recognized specialists acting in a personal capacity and not as representatives of national governments.
24. **Maximum residue limit (MRL):** A Maximum Residue Limit (MRL) is the maximum concentration of a pesticide residue (expressed as mg/kg), recommended by the Codex Alimentarius Commission to be legally permitted in or on food commodities and animal feeds. MRLs are based on good agricultural practice (GAP) data and foods derived from commodities that comply with the respective MRLs are intended to be toxicologically acceptable.

Codex MRLs which are primarily intended to apply in international trade, are derived from estimations made by the JMPR following:

- (a) Toxicological assessment of the pesticide and its relevant metabolites; and
- (b) Review of residue data from supervised trials and supervised uses including those reflecting national good agricultural practices. Data from supervised trials conducted at the highest nationally recommended, authorized or registered uses are included in the review. In order to accommodate variations in national pest control requirements, Codex MRLs take into account the higher levels shown to arise in such supervised trials, which are considered to represent effective pest control practices.

Consideration of the various dietary residue estimates and determinations both at the national and international level in comparison with the ADI and the ARfD, should indicate that foods complying with Codex MRLs are safe for human consumption.

25. **Microbial pesticide:** Active substances used for the control or management of pests such as invertebrates, weeds or microbial pathogens of crops, made from microorganisms such as bacteria, protozoa, fungi and viruses. They include complete organisms (either viable or non-viable), organelles of the organism, metabolites produced by the organism, spores of the organism or occlusion bodies.
26. **Background exposure:** Natural levels of substances and levels arising from past human activities present in the environment (e.g. agriculture), in situations relevant for the respective environmental compartment.
27. **Natural Substances:** Natural substances consist of one or more components that originate from nature, including but not limited to: plants, algae/microalgae, animals, minerals, bacteria, fungi, protozoans, viruses, viroids and mycoplasmas. They can either be sourced from nature or are nature identical synthesized or produced by microorganisms. This definition excludes semiochemicals and microbials.
28. **Pest:** means any species, strain or biotype of plant, animal or pathogenic agent injurious to plants and plant products, materials or environments and includes vectors of parasites or pathogens of human and animal disease and animals causing public health nuisance.
29. **Pesticide:** Pesticide means any substance intended for preventing, destroying, attracting, repelling, or controlling any pest including unwanted species of plants or animal during the production, storage, transport, distribution and processing of food, agricultural commodities, or animal feeds or which may be administered to animals for the control of ectoparasites. The term includes substances intended for use as a plant growth regulator, defoliant, desiccant, fruit thinning agent, or sprouting inhibitor and substances applied to crops either before or after harvest to protect the commodity from deterioration during storage and transport. In these guidelines, the term excludes fertilizers, plant and animal nutrients, food additives, and animal drugs.
30. **Pesticide residue:** Pesticide Residue means any specified substance in food, agricultural commodities, or animal feed resulting from the use of a pesticide. The term includes any derivatives of a pesticide, such as conversion products, metabolites, reaction products, and impurities considered to be of toxicological or ecotoxicological significance. The term "pesticide residue" includes residues from unknown or unavoidable sources (e.g. environmental contamination) as well as known, authorized uses of the chemical.
31. **Semiochemicals:** Active substances or mixtures of substances emitted by plants, animals, and other organisms that evoke a behavioural or physiological response in individuals of the same or other species. Different types of semiochemicals include:
 - Allelochemicals produced by individuals of one species that modify the behaviour of individuals of a different species (i.e., an interspecific or interspecies effect). They include allomones (emitting species benefits), kairomones (receptor species benefits) and synomones (both species benefit).
 - Pheromones produced by individuals of a species that modify the behaviour of other individuals of the same species (i.e. an intraspecific or intraspecies effect).
 - Straight-chained lepidopteran pheromones (SCLPs) are a group of pheromones consisting of unbranched aliphatics having a chain of nine to eighteen carbons, containing up to three double bonds and ending in an alcohol, acetate or aldehyde functional group. This structural definition encompasses the majority of known pheromones produced by insects in the order Lepidoptera, which includes butterflies and moths.

SECTION 3. CRITERIA FOR THE RECOGNITION OF ACTIVE SUBSTANCES OR AUTHORIZED USES OF ACTIVE SUBSTANCES OF LOW PUBLIC HEALTH CONCERN THAT ARE CONSIDERED EXEMPTED FROM THE ESTABLISHMENT OF CODEX MAXIMUM RESIDUE LIMITS (CXLs)

32. To grant the exemption from the establishment of MRLs to an active substance and / or its authorized uses, active substances mandatorily must meet the requirements indicated in Criterion 1 and must also meet the requirements indicated at least for one of the other criteria as appropriate.
33. Special consideration must be taken for those situations where the MRL exemption is linked to a certain pesticide GAP use.
34. It can be GAP dependent whether or not residues are expected; in case residues are expected or will occur according to GAP expected/measured residue levels have to be assessed in comparison with possible background levels.

35. Therefore, everytime a new use is requested, this new use should be assessed with regard to its exemption from MRLs (whether or not the active substance has already been exempted from MRL setting).
36. According to the criteria proposed below, active substances or their authorized uses that after a risk assessment process are concluded that they do not have an immediate or delayed harmful effect on human or animal health, directly or through drinking water, foods, or through aggregate effects, may be exempted from setting MRLs.

Criterion 1. Basic substances and active substances without hazardous properties identified

37. Active substances and their relevant metabolites for which, according to risk assessments, it has been considered that it is not necessary to establish Guidance Values for Human Health (ADI/ARfD). It should be taken into account that there are active substances that do not have ADI / ARfD established because they are genotoxic substances or due to lack of data to define these values.
38. Active substances and relevant metabolites that do not bioaccumulate or do not have the capacity to cause significantly toxic effects such as, corrosive, sensitizing, neurotoxic, immunotoxin, carcinogenic, mutagenic, reproductive, developmental or endocrine disrupting effects, among others at environmental background levels.

Criterion 2. Active substances for which it is not possible to differentiate between the exposure associated with its use as pesticide with its background exposure levels or its other uses in the food chain

39. Basic substances, and other substances which, by themselves, are food components or have low-toxicity of no public health concern (no tox-endpoint needs to be set).
40. Active substances for which background exposure associated with the food substance cannot be differentiated from the one linked to the use as a pesticide (Botanical pesticides, natural chemical substances)
41. Food and/or feed items which are known allergens should be considered carefully.
42. Measurable background levels should be assessed carefully and taken into consideration when deciding on the use of this criteria.

Criterion 3. Active substances for which no consumer exposure linked to the mode of application is foreseen

43. This criterion includes substances such as pheromones and other semiochemicals dispersed through dispensers for mating disruption purposes where the consumer's exposure from the application level is similar to the background exposure level of the substance.

Criterion 4. Microorganisms which are not pathogenic and do not produce mammalian toxins or other potentially toxic secondary metabolites of human health concern.

44. This criterion includes microbial active substances. For microorganisms that are closely related to known toxigenic human pathogens, it must be demonstrated that toxins/metabolites toxic to humans, animals are not likely to be produced by the microorganism, and should they be present in the products, these toxins/metabolites should not be present on edible parts of the treated crops, following application, at levels on or in the treated crop that will either exceed natural background levels or potentially cause harm to public health. Attention should be given to any mammalian toxins or other potentially toxic secondary metabolites of human health concern produced by microorganisms.
45. This criterion excludes microorganisms that are either primary mammalian pathogens or are taxonomically close relatives to microbes that are primary mammalian pathogens.

ANNEX

EXAMPLES OF SUBSTANCES

The list of examples are not exhaustive nor indicative of any agreed list recommended for international harmonization. They are presented to support better understanding of the provisions in the Guidelines and may not remain in the Guidelines once adopted by the Codex Alimentarius Commission

Criterion	Examples of substances/microorganisms
Criterion 1. Basic substances and Active substances without hazardous properties identified (very low or no toxicological concern)	1. Calcium hydroxide
	2. Fructose
	3. Hydrogen peroxide
	4. Sodium chloride
	5. Sodium hydrogen carbonate
	6. Sucrose
	7. Vinegar
	8. L-ascorbic acid (Vitamin C)
Criterion 2. Substances for which it is not possible to differentiate between the exposure associated with its use as pesticide and its other uses in the food chain	9. <u>Plant oils/ Vegetable oils</u> Rapeseed oil, Castor oil, corn oil, rice bran oil, cotton seed oil, Sesame oil, linseed oil, olive oil, peanut oil, Tea tree oil, Neem oil, Karanj oil, Mahua (Madhuca) oil
	10. <u>Plant essential oils</u> Clove oil, citronella oil orange oil, spearmint oil, citrus oil, fennel oil, cedarwood oil, lemongrass and, rosemary oil, turmeric oil, thyme oil, vetiver oil, catnip oil. eucalyptus leaf oil and extract
	11. <u>Essential oil constituents</u> Geraniol eugenol, linalool, limonene, citronellal, thymol, carvone, 1,8-cineole, p-cymene, ar-turmerone, gingerols, pinene, terpene-ol,
	12. <i>Annona</i> spp. (Annonins, Squamocin)
	13. <i>Azadirachta indica</i> (Neem leaf and seed kernel oil)
	14. Brassinolides
	15. Chenopodium oil and extract
	16. Garlic extract
	17. Giberellic acid (GA3)
	18. Karanjin
	19. <i>Ryania</i> spp. (Ryanodines)
	20. <i>Reynoutria sachalinensis</i> extract
	21. Rocaglamides (Aglaia spp.)
	22. Soaps (fatty acid salts)
	23. <i>Sophora flavescens</i> (Matrine, oxymatrine)
	24. Sulphur
	25. Triacontanol
	26. <u>Pheromones</u>

Criterion	Examples of substances/microorganisms
Criterion 3. Substances for which no consumer exposure linked to the mode of application is foreseen	27. (Z)-8-Dodecen-1-yl-acetate
	28. (E)-8-Dodecen-1-yl-acetate
	29. (Z)-8-Dodecen-1-ol
	30. (E/z)-8-Dodecen-1-yl-acetate
	31. (E, E)-8,10-Dodecadien-1-ol
	32. 1-Dodecanol
	33. (E)-11-Tetradecen-1-ol
	34. Gossypure
	35. 9- Hexadecenal, 11-Hexadecenal, and Hexadecenol
	36. Hexadecadienyl acetate
	37. Rescalure
38. (E)-11-Tetradecen-1-yl-ol acetate	
Criterion 4. Microorganisms which are not pathogenic and do not produce mammalian toxins or other potentially toxic secondary metabolites of human health concern.	39. <i>Trichoderma asperellum</i> (formerly <i>T. harzianum</i>) strains ICC012, T25 and TV1
	40. <i>Trichoderma atroviride</i> (formerly <i>T. harzianum</i>) strains IMI 206040 and T11
	41. <i>Trichoderma gamsii</i> (formerly <i>T. viride</i>) strain ICC080
	42. <i>Trichoderma harzianum</i> strains T-22 and ITEM 908
	43. <i>Trichoderma polysporum</i> IMI-206039
	44. <i>Streptomyces</i> strain K61 (formerly <i>S. griseovirides</i>)
	45. <i>Bacillus amyloliquefaciens</i> strain FZB24
	46. <i>Bacillus amyloliquefaciens</i> strain MBI600
	47. <i>Bacillus amyloliquefaciens</i> subsp. <i>Plantarum</i> D747
	48. <i>Bacillus firmus</i> I – 1582
	49. <i>Bacillus subtilis</i> str. QST 713
	50. <i>Beauveria bassiana</i> strain ATCC 74040
	51. <i>Beauveria bassiana</i> strain GHA
	52. <i>Helicoverpa armigera</i> nucleopolyhedrovirus
	53. <i>Bacillus sphaericus</i>
	54. <i>Chaetomium globosum</i>
	55. Entomopathogenic nematodes (EPNs)
	56. <i>Fusarium oxysporum</i> strain Fo47
	57. <i>Metarhizium anisopliae</i>
	58. <i>Plaecilomyces lilacimus</i>
	59. <i>Pseudomonas fluorescens</i>
	60. <i>Trichoderma viride</i>
	61. <i>Trichoderma virens</i>
	62. Nucleopolyhedro virus (NPV) of <i>Spodoptera litura</i>
	63. <i>Verticillium lacanii</i>