CODEX ALIMENTARIUS
INTERNATIONAL FOOD STANDARDS

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World Health Organization

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GUIDELINES 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 MAXIMUM RESIDUE LIMITS OR DO NOT GIVE RISE TO RESIDUES

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PREFACE

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, nematicides, molluscicides and repellents.

Pesticides contain active substances that can be of chemical or biological origin.

Chemical pesticides can be synthetic or of natural origin.

For the purpose of these guidelines, pesticides of biological origin, also known as biopesticides, include active substances based on microorganisms (microbial pesticides), compounds made from plants like plant extracts (botanical pesticides), pheromones (semiochemicals) and substances of animal origin. 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.

Sometimes authorized uses of pesticides on food crops result in residues. The Codex Alimentarius Commission (CAC) has set maximum residue limits (MRLs) for pesticides on specific foodstuffs or food groups traded internationally to protect the health of consumers based on 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.

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). These guidelines establish criteria for the exemption of substances, or specific authorized uses of substances, from the establishment of MRLs when the establishment of MRLs is not necessary to protect consumer health. The question of whether an active substance or a specific authorized use of an active substance fulfills one or more criteria with the aim to exempt the substance or a specific authorized use of an active substance from the setting of MRLs is the result of an evaluation of toxicology and residue behaviour.

When authorized uses of pesticides do not produce residues or result in residues that 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.

These guidelines represent a first step towards harmonization 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

These guidelines apply without prejudice to any other provisions of the CAC establishing MRLs for pesticides on foodstuffs.

These guidelines aim to make use of the different criteria used by some countries and international organizations to decide that it is not necessary to establish MRLs for an active substance or a specific authorized use of an active substance because a risk assessment concludes that they are of low risk and low public health concern.

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 need for establishment of MRLs.

The guidelines do not cover uses of toxic substances that do not give rise to residues, for example use of fungicides or insecticides as seed treatments.

These guidelines are intended to be used by competent authorities in countries that do not have established criteria for MRL exemption for active substances or specific authorized uses of active substances in their respective legislation.

SECTION 2. DEFINITIONS

Acceptable daily intake (ADI): The estimate of the amount of a chemical in food or drinking water, expressed on a body-weight basis, which can be ingested daily over a lifetime without appreciable health risk to the consumer. It is derived on the basis of all the known facts at the time of the evaluation. The ADI is expressed in milligrams of the chemical per kilogram of body weight (a standard adult person weighs 60 kg). It is applied to food additives, residues of pesticides and residues of veterinary drugs in food.

Active substance/ingredient: The part of the product that provides the pesticidal action.

Active substances of low public health concern: Active substances and their relevant metabolites considered of low or no toxicity to human and animal health based on risk assessments.

Acute reference dose (ARfD): The ARfD of a chemical is an estimate of the amount of a substance in food and/or drinking water, normally expressed on a body-weight basis, that can be ingested in a period of 24 hours or less without appreciable health risk to the consumer on the basis of all known facts at the time of the evaluation.

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 generally take into account public and occupational health and environmental safety considerations.

Biological pesticide (biopesticide): A pesticide containing active substances made from living or dead microorganisms such as bacteria, algae, protozoa, viruses and fungi (see microbial pesticides definition), pheromones and other semiochemicals (see semiochemicals pesticides definition), and plants or parts of plants (see botanical pesticides definition), designed to repel, destroy or control any pest or regulate the growth of plants (for example *Bacillus amyloliquefaciens* strain FZB24, *Trichoderma atroviride* (formerly *T. harzianum*) strains IMI 206040 and T11).

Botanical pesticide: A pesticide containing 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/altered by chemical and/or microbial processes (for example *Annona* spp. (Annonins, Squamocin), neem (*Azadirachta indica*)).

Environmental exposure: Levels of substances, including levels arising from past human activities in the environment (e.g. agriculture), present in the environment in situations relevant for the respective environmental compartment.

Feed: Any single or multiple materials, whether processed, semi-processed or raw, which is intended to be fed directly to food-producing animals.

Food group/Crop group: A collection of foods/crops subject to MRLs that have similar characteristics 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.

Good agricultural practice (GAP) in the use of pesticides: This 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.

Joint FAO/WHO Meeting on Pesticide Residues (JMPR): The JMPR is an expert ad hoc body administered jointly by Food and Agriculture Organization of the United Nations and the World Health Organization. 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.

Maximum limit for pesticide residues (MRL): A MRL is the maximum concentration of a pesticide residue (expressed as mg/kg), recommended by the CAC to be legally permitted in or on food commodities and animal feeds. MRLs are based on GAP data and foods derived from commodities that comply with the respective MRLs are intended to be toxicologically acceptable.

CXLs 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 GAPs. 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, CXLs 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 CXLs are safe for human consumption.

Microbial pesticide: A pesticide containing 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.

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.

Pest: 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.

Pesticide: 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. The term normally excludes fertilizers, plant and animal nutrients, food additives, and animal drugs.

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 significance.

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 9 to 18 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 MAXIMUM RESIDUE LIMITS

To grant the exemption from the establishment of MRLs to an active substance or a specific authorized use, the active substances or the specific use should meet the requirements of at least one of the following criteria.

Special consideration should be given in those situations where the MRL exemption is linked to a certain pesticide GAP use.

It can be GAP-dependent whether or not residues are expected; if residues are expected or will occur according to GAP, expected/measured residue levels should be assessed in comparison with possible environmentally relevant exposure levels.

Therefore, every time a new use is requested, the 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 for other uses).

According to the criteria below, active substances or specific authorized uses for which a risk assessment process conducted by competent authority concludes that there are not immediate or delayed harmful effects on human or animal health, directly or through drinking water, foods, or through aggregate effects, may be exempted from the need to establish MRLs.

Criterion 1. Active substances without hazardous properties identified

Active substances and their relevant metabolites[i] for which, according to risk assessments, it has been considered that it is not necessary to establish health-based guidance values (ADI/ARfD). This excludes active substances that do not have ADI/ARfD established because they are genotoxic substances or due to lack of data to define these values.

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 environmentally relevant levels.

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

Active substances which, by themselves, are food components or have low-toxicity and present no human or animal health concern.

Active substances for which environmental exposure associated with the food substance cannot be differentiated from that linked to the use as a pesticide (botanical pesticides, natural chemical substances).

Food and/or feed items which are known allergens should be subject to additional requirements, not related to risk from pesticides.

Measurable environmental levels should be assessed carefully and taken into consideration when deciding on the use of this criterion. For instance, when the exposure through residues from pesticides use does not add significantly to the exposure from environmentally relevant levels or other authorized uses, exemptions from establishing MRLs may be granted. Case-by-case considerations are needed taking into account the specificities of each substance and the exposure levels.

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

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 is similar to the environmental exposure level to the substance.

Criterion 4. Microorganisms that are not of human or animal health concern

This criterion also concerns microbial-active substances that may potentially produce toxins/metabolites. Such microorganisms should only be considered exempted from the establishment of MRLs if it can be proven that such toxins/metabolites are not present on edible parts of the treated crops, at levels on or in the treated crop that will exceed environmental relevant levels or potentially cause harm to human and animal health.

Microorganisms that are primary human or animal pathogen (excluding target species)[ii] should not be considered exempted from the establishment of MRLs. For microorganisms that are taxonomically close relatives to such pathogenic microorganisms, a MRL exemption would be possible only if evidence is provided that they do not negatively affect human or animal health.

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[i] Compounds of toxicological interest when they are present in significant concentrations.

[ii] A species that is intentionally targeted for control by a pesticide.