GUIDELINES FOR

THE REGISTRATION OF BIOLOGICAL PEST CONTROL AGENTS

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

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Rome - October 1988

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1. INTRODUCTION

Biological pest control agents are naturally occurring or genetically modified agents that are distinguished from conventional chemical pesticides by their unique modes of action, low use volume, and target species specificity. There are two major categories of biological pest control agents: the biochemical pest control agents and the microbial pest control agents.

1.1 Biochemical pest control agents

A chemical must meet the following two criteria in order to be classified as a biochemical pest control agent and to be subject to the data requirements for this class of compounds:

- The chemical must exhibit a mode of action other than direct toxicity in the target pest (e.g. growth regulation, mating disruption, attraction). Pesticides such as strychnine, rotenone, nicotine, and pyrethrin which exhibit direct toxicity, are not considered biochemical pest control agents; and

- A biochemical must be naturally occurring, or if the chemical is synthesized by man, then it must be structurally identical to a naturally occurring chemical. For a synthetic chemical to be identical in chemical structure to a naturally occurring chemical, the molecular structure of the major component of the synthetic chemical must be the same as the molecular structure of the naturally occurring analog. Minor differences between the stereochemical isomer ratios (found in the naturally occurring compound compared to the synthetic compound) will normally not rule out a chemical being classified as a biochemical pest control agent unless an isomer is found to have significantly different toxicological properties than another isomer.

There are situations where a candidate chemical possesses many characteristics of a biological pest control agent, but does not technically meet the two criteria established for defining biochemical pest control agents. The regulatory authority should evaluate such chemicals on a case-by-case basis to determine whether it should be classified as a biochemical pest control agent or a conventional pesticide. For example, a case-by-case evaluation would be required if the exact molecular structure of the naturally occurring compound is unknown, or if the synthetic chemical is closely related to but not identical in structure to the naturally occurring compound, or if the mode of action is different in the target, compared to non-target organisms.

In these case-by-case situations, the criteria to be used to determine whether the chemical is a biochemical pest control agent, include:

- the chemical and toxicological significance of the differences in chemical structure;

- the mode of action of the synthetic analog in the target species as compared to the mode of action of the naturally occurring compound;

- differences in toxicity between the naturally occurring chemical and the synthetic analog.

Biochemical pest control agents fall into four general biologically functional classes:

1.1.1 Semiochemicals

Chemicals emitted by plants or animals that modify the behaviour of receptor organisms of like or different kinds are termed semiochemicals. They include pheromones, allomomes, and kairomomes. Pheromones are substances emitted by members of one species which modify the behaviour of others within the same species. Allomones are chemicals emitted by one species which modify the behaviour of a different species, to the benefit of the emitting species. Kairomones are chemicals emitted by one species which modify the behaviour of a different species to the benefit of the receptor species.

1.1.2 Hormones

Hormones are biochemical agents that are synthesized in one part of an organism and translocated to another where they have controlling, behavioural or regulating effects.

1.1.3 Natural plant regulators and insect growth regulators

Natural plant regulators are chemicals produced by plants that have inhibitory, stimulatory, or other modifying effects on the same or other species of plants. Some of these are termed "plant hormones" or "phytohormones". Insect growth regulators are chemicals that have toxic, inhibitory, stimulatory, or other modifying effects on the insect growth cycle.

1.1.4 Enzymes

For the purposes of these guidelines, enzymes are defined as protein molecules that are the instruments for expression of gene action and that catalyze chemical reactions.

1.2 Microbial pest control agents

The pesticides referred to as microbial pest control agents include naturally occurring agents such as bacteria, fungi, viruses, and protozoa, or genetically modified micro-organisms.

Because of the nature of biological pest control agents, some data requirements would have to be different from those necessary for registration of chemical pesticides, but the general principle that the product should demonstrate effectiveness and will not present unacceptable hazard to users, consumers of treated foods, or the environment still applies.

2. DATA REQUIREMENTS

2.1 Biochemical Pesticide

When necessary, an initial evaluation to determine whether the proposed pesticide would fall into the category of biochemical or conventional chemical pesticides should be done. The data requirements for biochemical pesticides should include:

2.1.1 Identity of the Product

In order to establish the identity and biological purity of the biochemical agent, it is necessary to provide information on the taxonomy of the product, and its physical and chemical properties. Information on the composition of the finished product should also be given.

a. Active agent

- Chemical or systematic name, whichever is applicable
- Physical and chemical properties
- Analytical methods
- Manufacturing process
- Discussion of formation of unintentional ingredients

b. Finished product

- Formulation type, composition of formulation, nature and quantity of diluent, purpose and identify of non-active ingredients
- Physical and chemical properties
- Stability of product and effect of storage and other conditions on biological activity
- Process of formulation
- Analytical methods

2.1.2 Biological Properties of the Active Agent

Information on the following should be supplied:

a. Intended Uses and Method of Application

- Mode of action and degree of specificity
- Target pest(s) and crops or premises to be protected Application rate
- Manner, rate and frequency of application

b. Experimental Data

- Description of trials protocols and data
- Limitations of use
- Stability of biochemical agent under different climatic conditions

2.1.3 Toxicology Data

a. Primary toxicology data

Active Agent

- Acute oral toxicity
- Acute dermal toxicity
- Inhalation toxicity
- Acute genotoxicity
- Immunotoxicity where applicable, depending upon the type of biochemical agent.

Finished product

- Acute oral toxicity
- Acute dermal toxicity
- Acute inhalation toxicity
- Eye irritation
- Skin irritation

b. Worker Exposure Studies (If substantial exposure of workers is expected)

c. Supplementary Toxicological Studies (Active Agent)

When expressions of hazard are found in the primary studies, the following supplementary data should be required:

- Detection of genotoxicity Immune response
- 90-day feeding (1 species)
- 90-day dermal toxicity (1 species)
- 90-day inhalation studies (1 species)
- Teratogenicity
- Mutagenicity
- Carcinogenicity

2.1.4 Residue Data

- Chemical identity of residues
- Nature of residues (in plants and livestock)
- Analytical methods
- Proposed Maximum Residue Limit (If expected concentrations greatly exceed levels from the naturally occurring biochemical agent).

2.1.5 Environmental Fate Studies (Active Agent)

- Acute oral toxicity to birds
- Toxicity to fish
- Non-target plant studies
- Non-target insect studies
- Degradation in water
- Absorption and binding to organic matter in water
- Degradation in soil
- Effects on soil organisms

2.2 Microbial Pesticides

The data requirements for microbial pesticides are designed to give basic hazard and exposure information for a micro-organism with totally unknown properties. In actual practice, present microbial pest control agents are usually well identified which enables a regulatory authority to predict their properties and behaviour. This is particularly true in the categories of human health and plant pathogenicity. Clinical medicine and agricultural science have identified many micro-organisms associated with many diseases. If the microbial pesticide under consideration is taxonomically similar to a clinically or agriculturally-significant micro-organism, its properties and effects should be examined in greater detail than suggested by the tests generally required.

The data requirements should apply to all microbial pesticides, including those that are naturally-occurring as well as those that are genetically modified. Each "new" variety, subspecies, or strain of an already registered microbial agent must be evaluated, and may be subject to additional data requirements. The data requirements for microbial pesticides should include:

2.2.1 Identity of the Product

Similar requirements as for biochemical pesticides should be followed to establish the identity and biological purity of microbial pesticides. The following detailed information must be supplied:

a. Active Agent

- Physical and chemical properties
- Systematic name and strain for bacteria, protozoa, fungi, etc. Common name
- Natural occurrence of the organism, its relationships to other species, and history
- Manufacturing process
- Appropriate test procedures and criteria used for identification, such as morphology, biochemistry, and/or serology
- Composition of unintentional ingredients, their nature and identity, and content of extraneous organisms
- Methods of analysis

b. Finished Product

- Physical and chemical properties
- Quantity of active agent
- Name and type of formulation
- Nature and quantity of diluent Purpose and identity of non-active ingredients such as UV protectors, water retaining agents, etc.
- Stability of product and effect of temperature and storage conditions on biological activity
- Methods of analysis

2.2.2 Biological Properties of the Active Agent

Information on which species are attacked, degree of specificity for target pest(s), genetic stability of the agent, areas and circumstances in which the agent is naturally occurring, and likely biological effects arising from use, should be supplied. The information should include:

- The natural occurrence and method of distribution of the active agent under different climatic conditions
- The target host species of the pest and the pathogenicity or antagonism to that pest
- The infective dose level, transmissibility and mode of action
- Indication of whether the agent is closely related to a crop pathogen or to a pathogen of a vertebrate species
- Types of crops or premises to be protected
- Manner, rate and frequency of application

2.2.3 Toxicology Data

It should be established that the active agent is not a known pathogen of man or other mammals and that the preparation does not contain such pathogens as contaminants or mutants as determined by acceptable tests.

a. Primary toxicology data

Active Agent

- Acute oral toxicity/pathogenicity
- Acute dermal toxicity
- Acute pulmonary toxicity/pathogenicity
- Eye irritation/infection study
- Hypersensitivity/allergy incident reports

Finished Product

- Acute oral toxicity/pathogenicity
- Acute dermal toxicity
- Acute pulmonary toxicity/pathogenicity

The dermal toxicity and eye irritation tests are designed primarily to detect toxicity due to chemical components of any preparation or finished product.

b. Supplemental Toxicological Data

In general, further studies may be required, depending on indications of toxin production or of significant signs of infectivity or unusual persistence of the microbial pesticide. Examples of such studies are:

- Subchronic toxicity/pathogenicity (if unusual persistence is observed)
- Reproductive effects
- Immunodeficiency (for viruses)
- Primate infectivity/pathogenicity (for intracellular parasites of mammalian cells).

2.2.4 Residue Data and Ecological Effects

In the case of microbial pesticides which leave a toxin, information on the identity and means of measuring residues of toxins remaining on an edible crop as a result of the use of the microbial pesticide should be submitted.

It is important to assess ecological risks due to microbial pesticides. In order to do this, their degree of species specificity and adverse effects on nontarget species must be given careful consideration. The following data are required to establish basic potential effects:

- Toxicity to fish
- Non-target plant studies
- Non-target insect studies
- Avian single dose oral toxicity and pathogenicity
- Avian inhalation pathogenicity

If adverse effects are seen in these tests then further testing is required to attempt to quantify levels of the microbial agent to which susceptible nontarget species may be exposed under conditions of use.