

Guidelines for Safety Evaluation of Microbial Pesticides

NOTICE TO USERS:

All of the translation provided in this document are unofficial. Only the original Japanese texts of the notification are official, and the translation is to be used solely as reference materials to aid in the understanding of the Japanese notification. FAMIC is not responsible for the accuracy, reliability or currency of the translation provided in this document, or for any consequence resulting from use of the information in this document.

(The notification No. 9-Seisan-5090, issued on August 29, 1997 by Director-General,
Agricultural Production Bureau, Ministry of Agriculture, Forestry and Fisheries)

Standards for safety evaluation of microbial pesticides

The present standards introduce basic approaches for safety evaluation of microbial pesticides, and specify date which shall be submitted by a registration applicant for safety evaluation.

1. Basic approaches for safety evaluation

- (1) In the present standards, "microbial pesticides" shall mean pesticides containing virus, bacterium, fungus, protozoan or nematode (limited to those containing like as the symbiotic bacterium as active ingredient) in a viable state which are manufactured or imported for sale for pesticidal purpose. Microbe-derived pesticides which are natural enemies to parasitic bees, predatory insects, etc. and antibiotics do not come under the category of microbial pesticides.

Genetically modified microbes are not included in it either for the moment.

- (2) Safety in humans and effects on the organisms etc. in the environment, the safety shall be demonstrated or confirmed on the basis of scientific data shown in paragraph 2 below.
- (3) Toxicological studies for safety evaluation shall be performed in compliance with the GLP standard notified by "Notification concerning standards for proper toxicological studies on Agricultural Chemicals (Notification 59 Nohsan No. 3850 * dated August 10, 1984), of Director-General of Agricultural Production Bureau, Ministry of Agriculture, Forestry and Fisheries)."
- (4) If, as a result of after evaluation based on the data submitted, it becomes necessary to prove or confirm the safety from the standpoint of biological properties of the microbe and method of using the microbial pesticide, the applicant shall be required to submit additional data.

2. Data serving as the basis for safety evaluation

- (1) Data necessary for safety evaluation of microbial pesticides are stipulated for in the Attached List "Data required, by type of microbe, for safety evaluation of microbial pesticides."
- (2) When the data for safety evaluation have already been submitted for the registration application of other microbial pesticides formulation, the said data can be used for the registration application of new formulation. In addition, when one applicant agrees that other applicant uses the said data, which have already been submitted for registration, new applicant is required to submit a certificate indicating that the said data is allowed to use by a former applicant.

(*) the notification was replaced to the Notification No. 11-Nousan-6283, issued on October 1, 1999.

Attached List

Data required, by type of microbe, for safety evaluation of microbial pesticides

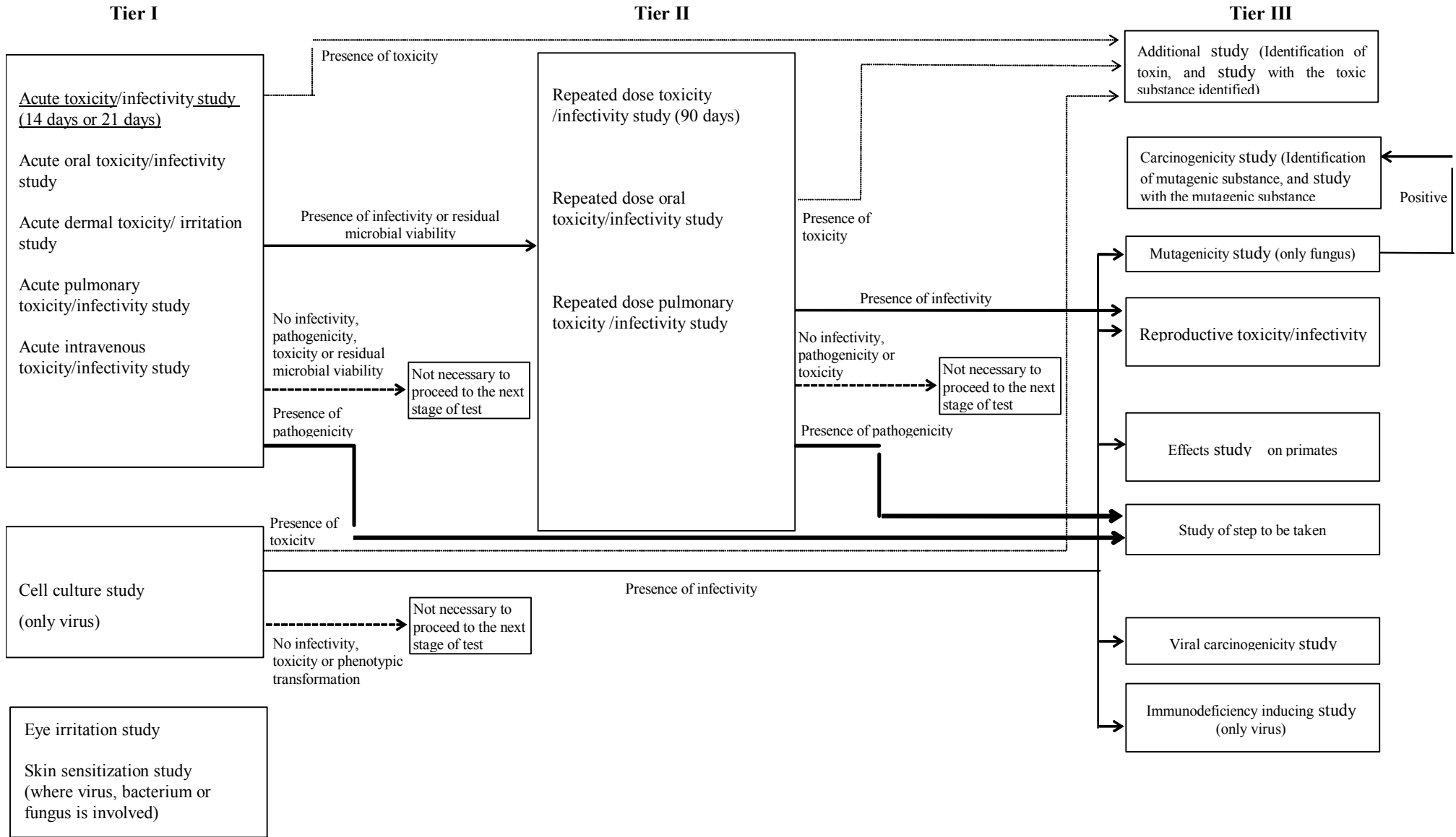
Data required	Type of microbe		Remarks
	Virus	Others	
1. Data concerning specification and properties of microbial pesticides			
(1) Name and taxonomic position of microbe	○	○	
(2) Biological properties of microbe	○	○	
(3) Composition of technical grade of the active ingredient	○	○	
(4) Production method for technical grade of the active ingredient	○	○	
(5) Composition of end-use product	○	○	
(6) Production method for end-use product	○	○	
2. Data concerning method of use			
(1) Diseases, pests and weeds for which the microbial pesticide is to be used, and crop plants to which the microbial pesticide is to be applied	○	○	
(2) Method of use and use level	○	○	
3. Results of studies of safety in humans			
(1) Acute oral toxicity/infectivity study	○	○	
(2) Acute dermal toxicity/ irritation study	○	○	
(3) Acute pulmonary toxicity /infectivity study	○	○	
(4) Acute intravenous toxicity/infectivity study	○	○	
(5) Eye irritation study	○	○	
(6) Skin sensitization study	○	○	Test should be performed where virus, bacterium or fungus is involved.
(7) Cell culture study	○	×	
(8) Repeated dose toxicity /infectivity study	△	△	This test should be performed if any infectivity or residual microbial viability has been found in the acute toxicity/infectivity study
(9) Mutagenicity study	×	▲	If, in the case of fungi, any infectivity has been observed in the repeated dose toxicity /infectivity study, this test should be performed.
(10) Reproductive toxicity/infectivity study	▲	▲	If the repeated dose toxicity /infectivity study has revealed any infectivity etc., this test should be performed.
(11) Viral carcinogenicity study	▲	▲	If any infectivity etc., has been noted in mammalian animal cells in the cell culture study, this study should be performed.
(12) Immunodeficiency inducing study	▲	×	If the cell culture study has revealed any infectivity etc. in mammalian animal cells, this study should be performed.
(13) Effect test on primates	▲	×	- ditto -

Data required	Type of microbe		Remarks
	Virus	Others	
4. Data concerning cases of hypersensitive reactions that occurred in production and use of microbial pesticides	○	○	
5. Results of studies of residual microbial viability on crop plants	△	△	If, in the case of microbial pesticides for food crops, any effects have been observed in the Tier I of safety in humans, excluding primary eye irritation and dermal sensitization studies, this test should be performed.
6. Results of effect test on the organisms in the environment			
(1) Toxicity study on freshwater fish	○	○	When there is no possibility of exposure, because of scientific grounds from the viewpoint of biological properties of the microbe or judging from the method of use, this test may be omitted.
(2) Toxicity study on freshwater invertebrates	○	○	- ditto -
(3) Avian toxicity study	○	○	- ditto -
(4) Study of effects on non-target plants	○	○	- ditto -
(5) Study of effects on non-target insects	○	○	- ditto -
(6) Study of effects on honey bees	○	○	- ditto -
(7) Study of effects on silkworms	○	○	- ditto -
(8) Study of effects on soil microbes	○	○	- ditto -
7. Results of studies of fate in the environment	△	△	If any effects have been observed in the effect test on the organisms in the environment, required tests should be performed.
○: Required in the Tier I △: Required in the Tier II ▲: Required in the Tier III ×: Not required			

(Note) As regards the Tier I, II or III, if any infectivity etc. have been found in the Tier I in any of the tests, the test proceeds to the Tier II, and Tier III of test is performed if any infectivity etc. have been observed in any of the Tier II or if any infectivity etc. have been noted in the Tier I of the cell culture test. Proceeding of the test stage in studies of safety in humans is shown in Attached Fig. 1, and effect test on the organisms in the environment (Tier I) and studies of fate in the environment (Tier II) are shown in Attached Fig. 2.

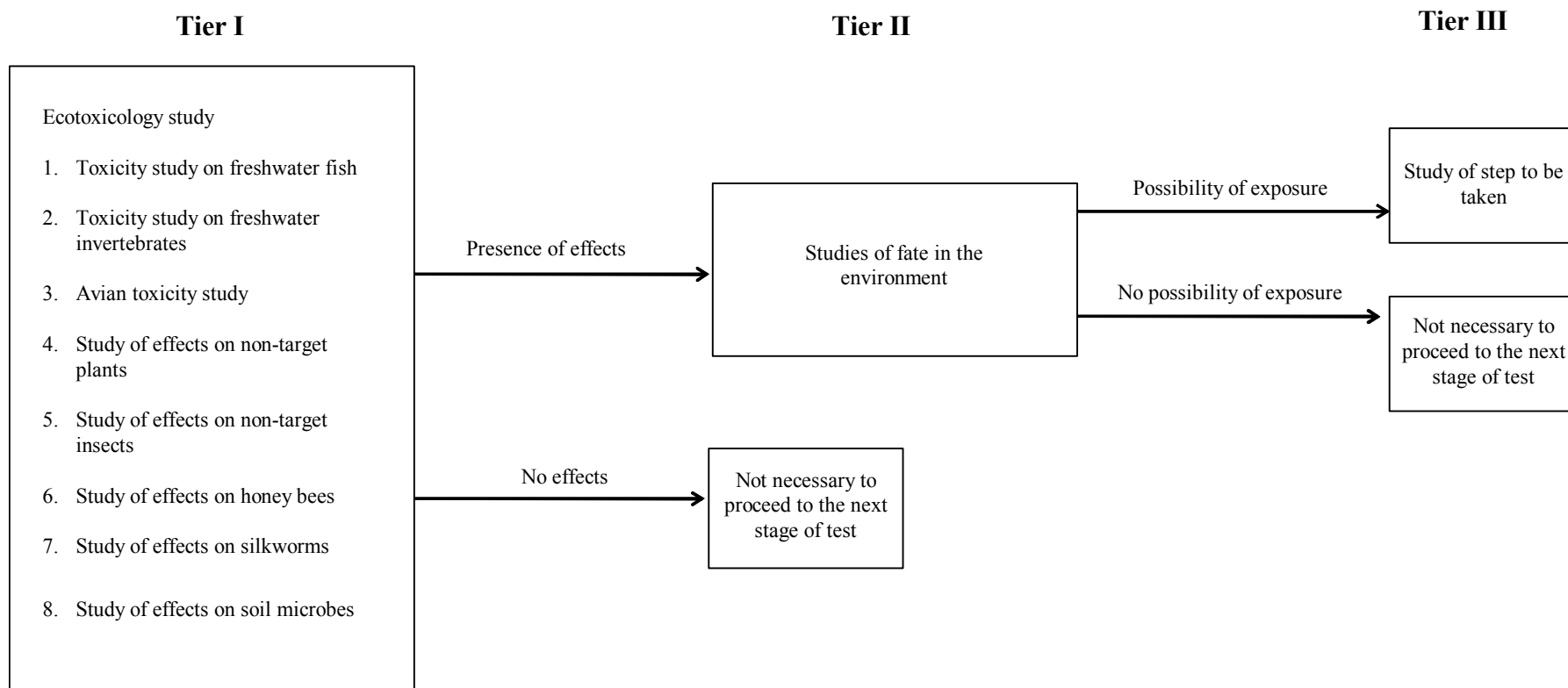
Attached Fig. 1

Toxicological studies for safety evaluation



Attached Fig. 2

Ecotoxicology study and Environmental fate study



(Note) Where there is no possibility of exposure, because of scientific grounds from the viewpoint of biological properties of the microbe or judging from the method of use, test may be omitted.