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Guide for considering necessity of data on one-year dog study at toxicological evaluation of pesticide

1. Introduction

Toxicological evaluations of pesticide residue have been conducted based on data from various types of toxicity studies using rodents (rats and mice) and non-rodent species (rabbits and dogs). In order to assess chronic toxicity by long-term treatment of a pesticide, one-year toxicity studies in rodents (usually rats) as well as in non-rodents (usually dogs) have been mandated for a registration of pesticide in Japan. However, recently, many countries' regulatory authorities do not mandate chronic dog studies for the registration outside of Japan.

The Expert Committee on Pesticides, the Food Safety Commission of Japan (FSCJ), made a guide for the necessity of a chronic dog study at an evaluation regarding effects of a pesticide residue on health, based on the scientific evidences gained from the FSCJ's contract research report titled "Development of the new tiered approach for toxicity studies of pesticide considering species difference in "toxicity profile" and "dose-response"- Evaluation of necessity of 1-year toxicity study in dogs and carcinogenicity study in mice -" (Research Program No. 1501), and from the current international situations on this issue. This guidance will contribute to the aspect of animal welfare.

This guide is based on the most recently recognized scientific findings. Therefore, the guide will be revised depending on the shifts and changes on the guide-related internationally methodology for assessments, or new scientific evidences.

2. The guide for considering a chronic study in dogs to be applied for the evaluation of pesticide residues effect on health

(1) Basic concept

In principle, the Expert Committee can proceed to conduct toxicological evaluation of pesticide residues without available information on one-year dog studies. When a one-year dog study is already

included in the data package for application of a pesticide, this study is used for the assessment. For further information on the occasions where a one-year dog study is thought to be essential, please refer to section (2). Even when such one-year studies are not in the data package, additional submission of information on chronic toxicity study in dogs will be requested by the Expert Committee if they judge the information to be important for the assessment.

(2) Necessity of a one-year dog study

- ① There is a gap between toxicology profiles of rodents and dogs in subacute toxicity studies.
- ② Dogs and rodents share the same target organs for toxicological effects, but the obvious dose-sensitivity lag exists between those two groups of species for advent of signs, and dogs appear to be more sensitive than rodents.
- ③ Tissue accumulation of pesticide is predicted in dogs
- ④ Regarding the dog-specific kinetics, its related toxicological profile is expected in dogs as described ① to ③.

The Expert Committee should carefully consider inclusion of a chronic dog study for relevancy to human, when the Committee makes judgement of its necessity for the toxicological evaluation.

If a NOAEL is not specified by a 90-day dog study of a pesticide, and if a chronic dog study with lower doses are likely to result in descriptions ① to ④ above, it is preferable to conduct a chronic dog study rather than repeating the 90-day dog studies.

References

- 1) The contract research report titled “Development of the new tiered approach for toxicity studies of pesticide considering species difference in “toxicity profile” and “dose-response” - Evaluation of necessity of 1-year toxicity study in dogs and carcinogenicity study in mice -” (Research Program No. 1501, Chief Researcher, Prof. Atsushi Ono, Okayama Univ.)
- 2) Commission Regulation (EU) No 283/2013 of 1 March 2013, setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market.
- 3) U.S.: Code of Federal Regulations Title 40, Chapter I, Subchapter E, Part 158, Subpart F – Toxicology.