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Title of research project	Preparation of Guidance for ARfD Setting for Pesticides, Etc., in Japan
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【Abstract】

the last 8 years. Our conceptual principles were based on the concepts written by Solecki et al. (2005) and were adapted for toxicological data required in Japan. Through this process, we were able to set the ARfDs for over 90% of the 201 pesticides tested. The studies that provided the rationale for ARfD setting were primarily reproductive and developmental toxicity studies, acute neurotoxicity studies, and pharmacology studies. For approximately 30% of the pesticides simulated in the present study, it was not necessary to establish ARfDs. Some of the simulated ARfDs resulting from their endpoints may be conservative estimates, because the evaluation reports were written for acceptable daily intake settings. Thus, it was sometimes difficult to distinguish acute toxic alerts from repeated toxicities. We were unable to set an ARfD for 14 pesticides because of insufficient data on acute toxicities. This could be improved by more complete recordkeeping. Furthermore, we categorized the 201 pesticides by mechanism of action or chemical structure. Our simulation indicates that the conceptual framework presented here can be used as a basis for the development of guidelines on ARfD settings for pesticides in Japan.

Based on the simulation described above, basic principles for acute reference dose (ARfD) setting were defined as follow The principles were:

(1) Indicator of acute toxicity within 24 h after oral administration. (2) Rationale for setting toxicity that appears or could appear after single-oral administration. (3) ARfD setting is assumed to be necessary for all pesticides. (4)ARfD is not necessary when values are at or above the cutoff level. (5)The setting basically applies to general population. (6) ARfD is set based on the lowest NOAEL among all the available study data detected endpoints for acute effects. (7)Effects of exposure during critical period are applicable for endpoints for ARfD setting. (8)The way for the safety coefficient is the same as that of acceptable daily intake. (9) If available, human data are acceptable for an endpoint for the setting.