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GUIDELINES ON RESIDUE DATA REQUIREMENTS FOR PESTICIDE REGISTRATION

PESTICIDE BOARD

MALAYSIA

GLOSSARY

pesticide residue	"Pesticide residue" means any specified substances 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. (Note: The term "pesticide residue" includes residues from unknown or unavoidable sources (e.g., environmental), as well as known uses of the chemical).
MRL	Maximum Residue Limit "MRL" is the maximum concentration of a pesticide residue (expressed as mg/kg), recommended to be legally permitted in or in food commodities and animal feeds. MRLs are based on GAP data and commodities that comply with the respective MRLs are intended to be toxicologically acceptable
PHI	Pre Harvest Interval “Pre Harvest Interval” is the time interval between the last pesticide application and harvest of the treated crops.
PSI	Pre Slaughter Interval “Pre Slaughter Interval” is the time interval between the last pesticide application and slaughter of the treated animal.
proprietary products	Any pesticide registered in Malaysia less than ten years
commodity products	Any pesticide which is not a proprietary pesticide
new recommendations	New crop recommended for any commodity pesticide
supervised residue trials	Residue trial designed in line with the requirements stated in ‘Supervised Residue Trials in Crops and Plant Products, part 3 of ‘FAO/WHO Codex Alimentarius Commission Guidelines on Producing Residues Data from Supervised Trials, 1990’.

local conditions	Local agriculture conditions that follow national GAP, which include weather, rainfall broadcast and climatic changes.
ADI	Acceptable Daily Intake "ADI" of a chemical is the daily intake which, during an entire lifetime, appears to be without appreciable risk to the health of the consumer on the basis of all the known facts at the time of the evaluation of the chemical. It is expressed in milligrams of the chemical per kilogram of body weight.
NOAEL	No Adverse Effects Level “No Adverse Effects Level” is the highest level of continual exposure to a chemical which causes no significant adverse effect on morphology, biochemistry, functional capacity, growth, development or life span of individuals of the target species which may be animal or human
Limit of Determination	"Limit of determination" is the lowest concentration of a pesticide residue or contaminant that can be identified and quantitatively measured in a specified food, agricultural commodity, or animal feed with an acceptable degree of certainty by a regulatory method of analysis.
pre-mixture product	Combination of an authorised pre-mix and one or more active ingredient which are intended for the subsequent manufacture of a ready to use crop protection product
field experiments	Experiment, research or trial conducted under actual use condition, instead of other controlled condition in the laboratory.

Guidelines On
Residue Data Requirements
For Pesticide Registration

A. INTRODUCTION

Residue data is required for registration of pesticides in order to:

(a) ensure that any residue of pesticides at the time of harvest does not exceed the maximum residue limits (MRLs), or in the absence of MRLs, either to enable MRLs to be established or to establish that MRLs are not necessary;

(b) recommend a suitable waiting period between the last application and harvest/slaughter (pre-harvest interval, PHI/ pre-slaughter interval, PSI) or consumption of the commodity so that residues of pesticides would not exceed MRLs or in the absence of MRLs, are at levels which would not be of concern to human and animal health, and

(c) ensure that a workable method is available to analyze for pesticide residues in food and/ or in the environment.

B. REQUIREMENTS

The following requirements must be submitted:

1. **For all products**, a proposed label with clear instructions on how the pesticide is to be used. This is to enable correlation of the proposed use patterns with the method of application used in obtaining the residue data. The following must be clearly stated:

   (a) The target crop, stored product or livestock.

(b) The method of application. This includes information on the equipment used, dosage (expressed as unit a.i. per unit area/volume), number of applications, timing of applications, etc.;

(c) The stage of growth of the crop or the livestock when the pesticide is applied, if applicable; and

(d) The recommended PHI, PSI, re-entry time, aeration period and other observations and limitations.

2. **For proprietary products only**, information on the physical, chemical and biological properties of the pesticide, nature and amounts of isomers, impurities and by-products which may be present in the technical or formulated products.

3. **For proprietary products only**, information on the behavior and metabolism/ degradation of the pesticide in crops and plant/ animal products and soil and the nature of the residues as well as its degradability as indicated by its half-life ($t_{½}$) in soil and water at 25^{o} C and its mobility in soils as indicated by adsorption studies. The metabolism studies are to characterize the residues, usually by employing radio-labeled compounds. Information on the amount of bound residues in soil and plants and their bio-availability may also be requested. For studies with livestock, the study should indicate the distribution of residues in tissues, milk or eggs and whether the residues are accumulated in any part of the animal.

4. **For proprietary products, and commodity products with new recommendations**, detailed reports on supervised residue trials. Trials must be carried out on the recommended crops, livestock and stored products with the pesticides applied in the same manner as in the proposed label. In addition to the proposed label rates, an exaggerated rate (usually 2 times the proposed rate) should be studied. Studies should preferably be conducted under local conditions or in locations with similar conditions.

5. In addition the design and implementation of supervised residue trials should follow proposed critical Good Agriculture Practice (GAP) (maximum number of applications, timing of application(s) at the latest stage permitted within application scope, maximum application rate, minimum PHI/PSI), which would likely result in maximum residue. Other factors such as weather condition and agronomic/husbandry practice should also be considered when designing supervised residue trials.

6. **For proprietary products and commodity products with new recommendations,** a method of analysis for residues of the pesticide in the relevant matrix. For pesticides not used on food or on animals for consumption, a method of analysis for residues in the environment is required. The method can be a company method or a published method for which the source must be given. For methods to be accepted, the % recovery must be within the range of 70%-120%. If 70%-120% recovery is not attainable, methods having lower recoveries may be accepted if consistency can be shown. The recovery tests should be at levels found in practice and actual analysis of treated samples. Evidence on the workability, reproducibility, selectivity and sensitivity of the method must be submitted.

7. Information on MRL enforcement method (or known as post-registration method) should also be provided if possible. MRL enforcement method is usually in the form of multi-residue method used by regulatory authorities in enforcement of MRLs. Single-residue method may not be suitable for MRL enforcement as enforcement laboratories do not have sufficient capacity to perform single-residue methods on all pesticides. However certain active ingredients may not be suitable to be detected by enforcement method. Registrant should consult the Pesticide Board for possible establishment of enforcement method.

8. **For proprietary products, and commodity products with new recommendations,** proposals of PHI/PSI, other limitations and MRLs. The basis of the proposals must be clearly given and related to the residue and other data submitted. A statement on the Acceptable Daily Intake (ADI) and No Observed Adverse

Effect Level (NOAEL) as derived from the toxicological data must be submitted. Similar information from other countries or international organizations should also be submitted as additional information.

9. Additional information in the form of summaries of residue trials may also be submitted but the complete report must be available on request. Evaluations by the FAO/WHO Joint Meeting on Pesticide Residues (JMPR) are acceptable as additional information ONLY and cannot replace actual residue studies.

10. If residue trial information on a particular commodity is not available, the applicant may request for information on a representative commodity to be accepted. See Appendix I for the grouping of commodities and the commodity which may be regarded as representative of those in the group. The onus is on the applicant to request for extrapolation of the data.

11. Residue data generated under local conditions is preferred but data from other countries/locations with similar condition which reflect the principal growing regions of the recommended crop may be accepted. Published reports on relevant trials by researchers are acceptable as additional information.

12. For major crops, which are paddy, palm oil, cocoa beans, and black pepper, at least one field experiment must be generated under local condition.

13. Residue trials on certain commodities may not be required under certain situations such as when an insecticide/ fungicide is applied as a seed treatment or at the nursery stage of a perennial crop. (see Appendix III for the list of residue data exemption)

C. RESIDUE TRIALS

1. The FAO Guidelines on Producing Pesticide Residues Data from Supervised Trials, 1990, Part 3 on Residue Trials in Crops should be used as a basis in the design and execution of residue field trials. Where appropriate, Good Laboratory Practices (GLP) should be followed in carrying out the studies.

2. For crops not included in the Codex Classification of Foods and Animal Feeds (Guide to Codex Recommendations concerning Pesticide Residues, Part 4), the applicant is advised to submit a proposed residue trial protocol to the Pesticides Board for approval before commencing the trial. Appendix II contains examples of protocols for residue trials on oil palm and cocoa and residue requirements.

3. Field experiments must reflect the proposed use with respect to:
   - The rate and mode of application;
   - The number and timing of applications and
   - The formulations proposed

4. The location of the field experiments should reflect the principal growing regions of the crop.

   The field experiments must provide for residue dissipation or decline studies in which samples are taken at intervals during the period from the last applications of the pesticide to normal harvest. Sample for residue analysis must be taken at different period after the last application of the pesticide. The first sampling shall be done 2 hour after application (0 day). Sample shall be taken at least 4 times at various intervals depending on characteristic of pesticide and crop. The data obtained should indicate the pattern of uptake of the pesticide and its decline.

5. For pre-mixture product, a residue trial data based on a single active ingredient of the pre-mixture product is not accepted.

6. At least three field experiments done at different sites must be submitted. Replicate treatment of individual sites is usually not necessary since within-site variations are usually small compared to the variation between sites.

7. For fumigation trials on store products, the studies should adequately represent those commodities which might be treated, such as oily foods (nuts, copra), and high surface area foods (flour). The studies should reflect the effect of parameters such as temperature, time of exposure, dosage, pressure, aeration time etc. on the residue reduction.

8. For studies on livestock, data must show the level of residues that will result in the meat (muscle, liver, kidney and fat), poultry, (muscle, liver, kidney and fat), eggs and milk. The FAO Guidelines on Producing Pesticide Residues Data from Supervised Trials, 1990, Part 4 on Metabolism Studies and Supervised Residue Trials in Animals may be used in carrying out the studies.

9. Additional information on the reduction or concentration of residues due to post-harvest processing or household cooking would also be useful.

10. All data belonging to another company can only be evaluated if a letter of authorization is given.

D. RESIDUE TRIAL REPORT

1. The behavior of the pesticide deposit from application until harvest, possible formation of metabolites and identity of the metabolites should be reported in order to predict residue levels at harvest and to reach a preliminary judgement on the acceptability of the residues. The report should be certified by an authorized person of the agency or research institution carrying out the field trial and must contained the following information.

(a) General information

- Pesticide (active ingredient and trade name);
- Formulation;
- Trial number and type (field, glasshouse);
- Commodity (crop, animal etc);
- Variety;
- Test locations (country and site);
- Soil characteristics, pH, physical and chemical properties;
- Name(s) and signature(s) of the person(s) responsible for the trial.

(b) Application data for field trials.

- Crop planting or sowing date; & harvest date
- Plot plan, crop layout or cropping system;
- Plot size or number of plants per plot/unit area;
- Number of plots per treatment;
- Method of application and equipment;
- Number of applications and application dates;
- Application details (overall, banded or circle);
- Dose rate – weight of a.i. per hectare (in kg or g a.i/ha)

  - weight/volume of formulation/hectare

  - applied dilution

- Climatic conditions during and after applications preferably for the whole period of the trial;
- Other pesticides applied to the trial plot; and
- Growth stage at (last) treatment.

(c) Sampling data

- Growth stage at sampling;
- Method of sampling;
- Sampled part(s);
- Number of units in sample, if relevant;
- Sample weight and preparation (trimming, washing or other common practices in preparing the commodity);
- Control and treated samples;
- Date of sampling with time interval between last application and sampling;
- Storage conditions before transporting to laboratory and
- Date shipped.

E. RESIDUE ANALYSIS REPORT

Analysis of major metabolites should also be included. Data obtained from surface striping are not acceptable except for crops where other data on that crop have established that the total residues are in fact only surface residues.

(a) Details on the method used.

- Full description or adequate reference;
- Apparatus;
- Chemicals and reagents;
- Data on selectivity of method;
- Data on limits of determination and quantification of the method for the commodity in question;
- Adequate recovery data at levels corresponding to those found in practice. The raw agricultural commodity, or a macerate thereof, should be fortified for the recovery tests, and not the crop extracts. For data to be accepted, the % recovery must be within the range of 70%-120%. The recovery tests should

be at levels corresponding to those found in practice and actual analysis of treated samples. Evidence on the workability, reproducibility, selectivity and sensitivity of the method must be submitted.

- A statement on whether or not the results have been corrected for blanks, recoveries or both.
- In all cases, Good Laboratory Practices (GLP) or International Standard Scheme Accreditation must be adhered to.

(b) Preparation of sample.

Peeling, chopping, washing, removing of soil, drying, separation of oil or fat or juice, cooking, separation of seed from the pulp, milling.

(c) Presentation of data.

All analytical data obtained from the analysis of samples should be provided, and not just a summary or an average figure. It should be clearly stated how the residues are calculated and expressed. Chromatographic and/or spectrophotometric evidence to support the analysis data must be submitted. Raw data from the laboratory need not be submitted but must be available on request.

REFERENCES

1. Codex Alimentarius Commission Vol. 2 – Pesticides Residues in Food, 1993.

2. EPA Code of Federal Regulations, 40, Parts 150-189, 1986

3. EPA Good Laboratory Practices Standards, Code of Federal Regulations, 40, Part 160, 1990

4. FAO/WHO Codex Alimentarius Commission Guidelines on Producing Residues Data for Supervised Trials, 1990 in 5 Parts

5. FAO Manual on the Submission and Evaluation of Pesticide Residues Data for the Estimation of Maximum residue Levels in Food and Feed, 2009

6. Official Journal of the European Communities, Vol. 4.89, 1989

7. Principles for Identifying Unacceptable Pesticides, The Swedish National Chemicals Inspectorate 1992

8. Report on Short-term Consultancy by J.A.R. Bates to the Malaysian-German Pesticide Project 1987

9. United States Environment Protection Agency Pesticide Assessment Guidelines, Sub-division O, Residue Chemistry

IMPORTANT NOTES

1. **THE COMMODITY GROUPS OF APPENDIX I MAY CONTAIN THE NAMES OF ONLY THE MORE IMPORTANT OR FAMILIAR COMMODITIES. IF A COMMODITY IS NOT LISTED IN THE GROUP IT IS SUPPOSED TO BE, REFER TO THE PESTICIDES BOARD OR CODEX "INDEX OF FOOD AND ANIMAL FEED COMMODITIES" TO DETERMINE THE COMMODITY GROUP OF THAT COMMODITY.**

2. **IN SOME GROUPS, ANY COMMODITY IN A GROUP CAN REPRESENT ANOTHER COMMODITY IN THE SAME GROUP IN RESIDUE TRIALS. NOTWITHSTANDING THAT HOWEVER, IF THE PESTICIDES BOARD IS OF THE OPINION THAT THE RESIDUE TRIALS OF A COMMODITY DO NOT TRULY REPRESENT THE EXPOSURE TO PESTICIDES OF ANOTHER COMMODITY FOR WHICH THE PESTICIDE IS RECOMMENDED, THEN RESIDUE TRIALS OF THE SPECIFIC COMMODITY FOR WHICH THE PESTICIDE IS RECOMMENDED WILL BE REQUIRED.**