Guidelines for Change in Source of Pesticides

Pursuant to the Sections 6 through 13 and the Section 23 of the Control of Pesticides Act No. 33 of 1980 as amended by the Control of Pesticides (Amendment) Act No. 06 of 1994. The purpose of this document is to provide overall guidance to the registrant on necessary steps to be followed when changing the source of pesticide or amendments proposed. Applicants are requested to refer to the specific details of relevant guidelines in submitting applications for registration of pesticides for further details of documentation and the format.

Office of the Registrar of Pesticides
Department of Agriculture

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INTRODUCTION

All pesticides imported to the country and/or manufactured or formulated within the country are registered under the Control of Pesticides Act No. 33 of 1980 as amended by the Act No. 06 of 1994. The range of products covers to agricultural pesticides (insecticides, fungicides, weedicides, nematicides etc.), household pesticides, veterinary pesticides, industrial biocides, wood preservatives, public health related pesticides and rodenticides, but the list is not necessarily exhaustive. Applications submitted with relevant technical documents are evaluated for the product's credibility in terms of authenticity of data submissions, with the view of safety, efficacy and suitability under the local conditions, is being met. Since the suitability of pesticides is evaluated with technical merits of individual product's performance, separate registrations are mandated for each product and assign a separate registration number.

As has been practiced over the years, all specialty products are considered as new registrations and assign a new registration number and all commodity products are registered either as new registrations or "third-party" registrations, subjected to the preference of submitting a complete data package from the pesticide manufacturer and/or the formulator. The Office of the Registrar of Pesticides receives occasional requests for amendments to the source of pesticides during or after the registration of pesticides. The Office of the Registrar of Pesticides views that it is necessary to adopt strict procedures and compliance by the pesticide registrants on the various aspects of changes as they are providing crucial role in regulatory management of pesticides. The following guidance document explains the regulatory approach to the source of the technical active ingredient and/or the formulation used in approved products and the actions required of registrant when making changes to the source. All registrants are advised that any change in technical aspects of pesticides must be informed to the Office of the Registrar of Pesticides without any delay and if they are unclear as to what action is required for previous changes in any of the following categories, then they should contact the Office of the Registrar of Pesticides for clarification.

NEW GUIDANCE

COMMON SCENARIOS AFFECTING SOURCES

1. A new source

In order to recognize as a new source of manufacturing and/or formulation of pesticide (i.e. technical material or formulation), it is necessary to submit a certified copy of the factory license issued by the competent authority of respective government (with appropriate supporting documentation to demonstrate the nature of business, preferably indicating the types of pesticides manufactured and/or formulated in the facility) to the Office of the Registrar of Pesticides for consideration. The details required under the new source must include the name and the complete postal address (number, street, city, province/state postal code (if any) and the country), telephone, fax and e-mail (web address, if any) and the name(s) of authorized personnel for correspondence.

2. Change in active ingredient specification

This probably involves changes in active ingredient purity (e.g. changes in metalaxyl-M and S-isomer) or impurity profile in the technical material. The changes in active ingredient composition would lead to improved efficacy and/or improved human health and the environmental safety. Similarly, impurities in the technical material with new specification have connotations both in their toxicological and eco-toxicological properties and an increase (or decrease) in these impurities will result in the new specification invalidating the previous data assessment of a registered product. Should this be the case then further toxicological or eco-toxicological data may be required accordingly.

Therefore, these changes have the potential to invalidate any previously conducted bio-efficacy and data assessments, and most likely require a new application to be submitted. Toxicological results may be accepted if the composition of the product is comparable. Additional toxicological studies are required if comparability cannot be confirmed. Any changes that clearly would not invalidate a previously conducted assessments, for example if the minimum purity is considered to only increase slightly from the original purity of the same active from the same manufacturer (and there are no additional impurities), can be notified to the Office of the Registrar of Pesticides in a letter with full justification[1] as to why the new specification does not invalidate previously conducted tests or a previous data assessment.

3. Change in formulant and formulation specification

This probably involves changes in formulant and/or adjuvant. The changes in formulation composition would lead to change in toxicology with respect to human health and the environmental. These changes have the potential to invalidate any previously conducted data assessments of a registered product (e.g. change in solvents known to have properties, or be subjected to legislation by governments or international agencies may impact on the use of the product or result in proclamation of hazards to some groups of consumers using it such as pregnant women, then a more detailed assessment of this aspect may be

[1] (a) The justification would require submission of technical specifications to include the certified manufacturing limits in terms of minimum/maximum content of the active ingredient and related isomers (if appropriate), and maximum contents of all impurities and additives (if appropriate). All impurities and additives should be identified in terms of their IUPAC nomenclature and structural formula. Only impurities and additives of a content >0.1% w/w need to be identified unless there are suspected impurities at a lower level that may be of cause for concern.

(b) Additional quantitative analysis report(s) is/are required on metal and non-metal impurities for arsenic, cadmium, cobolt, chromium, mercury, nickel, lead, tin, thalium and cyanide, from an accredited laboratory.

(c) Comparison of the composition of the technical product used for toxicological evaluations with that manufactured by a different procedure or under different conditions. The composition of the new and original product is comparable if the active ingredient content in the technical-grade product is equal to or higher and the concentrations of relevant impurities are equal or lower than they were in the original product that had been used for the complete toxicological tests. The composition is not comparable if a relevant impurity occurs in the new product, but not in the original product.

needed), and most likely require a new application to be submitted. It is also known that the type of solvent is a key determinant of acute toxicity of some of the formulations. Any changes that clearly would not invalidate a previously conducted data assessments, for example if the formulation composition is considered to only change slightly from the original composition of the same active ingredient from the same manufacturer (and there are no additional formulant and/or adjuvant), can be notified to the Office of the Registrar of Pesticides in a letter with full justification as to why the new specification does not invalidate previously conducted tests or a previous risk assessment. In some cases, the formulation adjustments could lead to decreased efficacy (e.g. some colouring compounds are known to cause some polymerization in granular products) and/or phytotoxicity, which must be averted at all, and be subjected to data requirements as may be applicable. In case of slight formulation changes, which do not require new applications to be submitted will be requested to submit a report of bio-efficacy test conducted under the farmer field conditions for confirmation of the equal or better efficacy compared with a standard practice.

4. Change in manufacturer and/or manufacturing site

If the active ingredient is obtained from a new manufacturer or manufacturing site (e.g. toll manufacture) it may be the case that the existing data package still applies (i.e. no change in a.i. specification or impurity profile). Nevertheless, the Office of the Registrar of Pesticides would still require proof that this is the case and therefore it would be necessary to submit a letter by the original manufacturer before requesting for importation of pesticides that the specifications submitted earlier in this regard does not invalidate. This must be accompanied with a letter from the new manufacturer or the toll manufacturer that they are adhering to the specifications given by the original manufacturer. In this case, additional information and/or documentation is required as per (1) above.

5. Change in formulator and/or formulation site

If the formulated pesticide (i.e. end use product) is obtained from a new formulator or formulation site (e.g. toll formulation) it may be the case that the existing data package still applies (i.e. no change in formulation composition or product specifications). Nevertheless the Office of the Registrar of Pesticides would still require proof that this is the case and therefore it would be necessary to submit a letter by the original formulator before requesting for importation of pesticides that the specifications submitted earlier in this regard does not invalidate. This must be accompanied with a letter from the new formulator or the toll formulator that they comply to the specifications given by the original formulator and/or the manufacturer. In this case, additional information and/or documentation is required as per (1) above.

6. Change in supplier

If the pesticide technical material or the formulation is supplied by a new supplier or through a new supplying point (of the same supplier) it may be the case that the existing data package still applies (i.e. no change in product). Nevertheless the Office of the Registrar of Pesticides would still require proof that this is the case and therefore it would be necessary to submit a letter by the original manufacturer or formulator before requesting for importation of pesticides that the product is supplied by the new supplier or through new supplying point.

7. Changes in the method of manufacture

If the change in the method of manufacture does not result in a change in the active ingredient specifications then notification of the change in method of manufacture is required by letter detailing the changes (additional data may still

be requested such as the reports of five-batch analysis[2] for consecutive production batches, gas chromatography fingerprint comparisons[3] etc.). If the specification does change then refer to (2) above.

8. Changes in the method of formulation

If the change in the method of formulation does not result in a change in the product specifications then notification of the change in method of formulation is required by letter detailing the changes (additional data may still be requested such as the reports of five-batch analysis[4], stability[5] etc.). If the specification does change then refer to (3) above.

9. Changes in methods of analysis

With improvements in analytical techniques there may be apparent changes in active substance specification. However provided the method of manufacture, raw materials and any other aspect of the production of the active substance

[2] Five-batch analysis of the technical material− This is used to demonstrate that the active material, isomers, impurities and additives are within the certified manufacturing limits detailed by the applicant. All components of each batch should be quantified, identified and reported. For the active component the range (minimum to maximum purity) demonstrated by the five batch analysis should also be reported. It is a requirement for the five batch analysis to be conducted in compliance with the principles of Good Laboratory Practice (GLP) in an accredited testing facility.

[3] The gas chromatography/spectrometric "fingerprint" can be successfully applied to distinguish between proprietary and generic products, as well as determining differentiation of impurity profiles during production.

[4] Five-batch analysis of the formulation− This is used to demonstrate that the active material is within the limits of specification detailed under the Food and Agricultural Organization or the World Health Organization, as may be applicable. All components of each batch should be quantified, identified and reported. For the active component(s) the range (minimum to maximum purity) demonstrated by the five batch analysis should also be reported. It is a requirement for the five batch analysis to be conducted in compliance with the principles of Good Laboratory Practice (GLP) in an accredited testing facility.

[5] Stability under elevated temperature or aged tests − This is used to demonstrate that the product composition and the performance is within the limits of specification during and at the end of stated shelf-life as detailed under the Food and Agricultural Organization or the World Health Organization, as may be applicable. All components of specifications should be quantified and reported. It is a requirement for the stability tests to be conducted in compliance with the principles of Good Laboratory Practice (GLP) in an accredited testing facility.

have not changed there should be no impact on the risk assessment. Improvements in the specification should be notified to the Office of the Registrar of Pesticides at the earliest convenience.

10. Technical specification is more detailed than one registered after the year 2000

The Office of the Registrar of Pesticides has initiated revitalizing of all registration documents which had been submitted and registered before the year 2000. In this case, the stipulated requirements in this guideline should be adopted completely when submitting information/ documents for the renewal of registration. Unless otherwise specifically requested for up-to-date technical documents, all registrants are required to submit updated registration documents (e.g. in case where (a) additional impurities have been identified due to refined methods of analysis, and/or (b) significant threat to non-targeted organisms have been elucidated which require special precautionary measures to be highlighted in product labels, etc.) during the course of registration in timely manner. In this case applicants should clarify what aspect/ component of the material has been actually changed.

The data assessment carried out initially has been based on the properties of the technical active ingredients, including all impurities, whether identified or not. Therefore a new data assessment may not be necessary in such situations. However, if the newly identified impurity or a change in any formulant is known to have properties, or be subject to legislation, which may impact on the use of the products containing it, then a further more detailed assessment of this aspect may be needed. The Office of the Registrar of Pesticides presumes that the information we hold is up-to-date, if technical specifications do change then the Office of the Registrar of Pesticides should receive a copy of the up-to-date technical specification as early as possible.

11. **Changes in data ownership** (by liquidation or merger in business etc.)

In this case providing there are no changes to the technical specification, formulation specification, manufacturer/formulator, and/or manufacturing/ formulation site then the change of ownership can be notified to the Office of the Registrar of Pesticides by a letter confirming that the technical specification and/ or product specification will not change. If there are changes to technical specification and/or product specification then refer to (2) and (3) above.

REFERENCES

(Relevant to the production of this guidance document)

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Office of the Registrar of Pesticides, Circular No. RP/2011-07 dated 18.10.2011 on Procedure for Issuing Import Permits.