Pest Management Regulatory Agency
Agence de réglementation de la lutte antiparasitaire

Regulatory Directive

Guidelines for Efficacy Assessment of Chemical Pesticides

Efficacy data are fundamental to establishing the value component of pesticides, which must be balanced against risks identified by Health and Welfare Canada and Environment Canada in the regulatory management/decision-making process.

Memorandum to Registrant R-92-02 invited comments on proposed guidelines for efficacy assessment of chemical pesticides. All comments have been considered and the draft document has been modified and reissued as Regulatory Directives Dir93-07a and Dir93-07b.

This document contains general principles for efficacy assessment for chemical pesticides. The intent is to:

(1) clearly outline the general requirements for efficacy trials;

(2) provide guidance on reporting of efficacy data; and

(3) establish procedures and criteria for efficacy data evaluation.

Specific procedures applicable to herbicides, plant growth regulators, insecticides, fungicides, nematicides, and vertebrate control agents are under development, and will be published when available.

This Regulatory Directive replaces parts 1 and 2 of Memorandum to Registrant R-92-02 dated April 30, 1992.

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1.0 Introduction

The aim of pesticide regulation is to ensure that pesticides offered for sale and use in Canada meet the requirements for safety, merit and value. For merit and value assessment, Section 9 of the Pest Control Product (PCP) Regulations requires that applicants for registration provide scientific information to support the effectiveness of each control product for its intended purposes, and thus avoid unnecessary pesticide exposure to the environment, applicators and bystanders, as a result of the use of ineffective products or excessive dosages.

Efficacy data have always been required and evaluated by the pesticide regulatory agency. However, no written guidelines in this area have ever been established. The lack of guidelines can result in uncertainty, confusion or misunderstanding regarding both the quantity and quality of efficacy data required.

The intent of these guidelines is to:

(1) outline the general requirements for efficacy trials;
(2) provide guidance on the organization and reporting of efficacy data; and
(3) establish procedures and criteria for efficacy data evaluation by Product Managers of Agriculture Canada.

These guidelines consist of general principles which apply primarily to chemical control products for pest control in the field. Specific procedures applicable to herbicides, plant growth regulators, insecticides, fungicides, nematicides, and vertebrate control agents are under development, and will be published when available.

For the purpose of these guidelines, efficacy or effectiveness is defined as the ability of a pesticide to fulfil the claims made for it on the proposed label. It includes the extent of control of the pests and considers any adverse effects on the host, i.e., toxicity to animals and phytotoxicity to plants.

It should be noted that these guidelines provide general guidance only, rather than a check list or rigid criteria. Scientific judgment should be exercised in using them in conducting research and evaluating the results. Furthermore, it is not the intent of these guidelines to provide detailed study protocols. Registrants should consult with scientific authorities familiar with the area of research, and refer to American Society for Testing and Materials' (ASTM) protocols, current published literature, biological and statistical reference texts, etc. for more specific information on experimental design and procedures.

Note:

(1) These guidelines concern efficacy assessment of conventional chemical pesticides only. They may not apply to biological, microbial or biotechnological pest control agents, which will be dealt with in separate documents when available.

(2) Efficacy evaluation is only one facet of the registration process. The fact that a product is efficacious does not ensure registration.

2.0 General Principles

2.1 Test Procedures

Test procedures employed in developing data to support the registration of a control product will vary according to the characteristics of the chemical, the type of formulation, the target pest, the use pattern, the methods and timing of application, and many other factors. However, there are certain basic principles and techniques that should be employed in carrying out the efficacy trials and certain information must be reported in support of registration of a use claim. The basic elements which apply to most chemical control products are outlined below in this section. For more specific procedures, refer to the relevant sections dealing with specific classes of pesticides and use patterns.

2.1.1 Experimental design

Trial objectives and the criteria by which they are to be judged should be clearly defined. Treatments in the trial should be selected carefully in keeping with the objectives set.

Efficacy tests should be designed so that appropriate statistical analysis of the data can be performed to ensure that any differences are attributable to the pesticide treatments. The number of replicates used in the experiment should be large enough to furnish a confidence level of 95 percent (differences between the treatment and the untreated check are detected as statistically significant at the 5 percent level), where possible.

The number of treatments in a trial should be kept as low as possible: the more treatments, the larger the trial area, and the larger the variation in uncontrolled variables and, therefore, the lower the accuracy of treatment comparisons. However, the number of treatments and replications should provide enough degrees of freedom for proper statistical analysis. The essential treatments should be the product(s) to be evaluated, a reference product (i.e., a currently registered and commercially used product) and non-treated plots.

2.1.2 Test substances

The test substance shall generally be the formulated product for which the registrant is seeking registration. Whenever possible, the trial should include a reference product. If the formulated product is to be mixed with

other product(s) or spray adjuvant(s), test data must be produced to support the compatibility, effectiveness and safety (to the host) of the mixture (see section 2.1.13).

2.1.3 Dosage rates

The pesticide should be tested at various dosage levels including rates above and below that being suggested for commercial use. The development of a dosage range serves two purposes, i.e., (1) to ensure that the use rate is effective but not excessive; and (2) to permit the opportunity for using alternate pest control strategies, e.g., integrated pest management (IPM) programs.

The dosage should be reported as the amount of active ingredient (a.i.) in metric units, e.g., kg or grams a.i. per hectare, or grams a.i. per 100 litres.

2.1.4 Selection of trial sites

Climatic conditions, soil conditions and agricultural practices may have a significant influence on the effectiveness of a pesticide product. Field trials for efficacy testing must be conducted in appropriate geographic areas in Canada. Results of studies conducted at appropriate sites in northern states of USA under climatic conditions similar to those in the proposed use regions of Canada may have some value. Greenhouse and laboratory studies may be conducted under appropriate testing conditions outside Canada.

A number of variables relating to the soil, such as texture, moisture content, fertility, organic matter content and pH, may measurably influence the effectiveness of the product, especially in the case of a soil treatment. Thus these factors must be considered in selecting the sites of the tests, and recorded.

2.1.5 Plot sizes

Plot size may vary depending on the particular combination of crop and pest situation, the equipment used, or the kind of data required. The individual plot must be large enough to provide meaningful data and sampling to adequately represent the effects of the factors or variables being measured.

2.1.6 Large field or farm-level trials

Whenever possible or practical, the results obtained in small plot tests should be confirmed by data obtained in large field or farm-level trials under normal field-use conditions. These large trials serve the useful purpose of demonstrating the performance of the product under varying commercial conditions using the equipment and techniques usually used in application. Data obtained from these large trials should be considered

as complementary to those obtained in the small plot tests. To make the results more useful, a small untreated strip should be kept to aid in efficacy evaluation. Also, quantitative measurements should be taken from several locations in the field.

2.1.7 Application technique

The effectiveness of a pesticide can often be influenced by the way the treatment is applied. Therefore, the methods of application used in the test and those given in the label claim directions must be in agreement. A detailed record should be kept of application equipment; carrier volume; the placement of the pesticide; date of treatment and harvest; treatment time in relation to number of days before or after planting, emergence or harvest; the stage of growth of the crop when treatment was made; the stage of growth or expected appearance of the pest at treatment time; duration of exposure to pesticide treatment; treatment-to-observation intervals commonly referred to as days after treatment (DAT).

2.1.8 Aerial applications

Label recommendations involving aerial applications should be supported by data from aerial-applied trials. When extending label directions from ground spray to aerial application, test results from aerial applications should be compared with those from ground applications, where possible (see section 2.1.15 for comparability studies).

In conducting aerial trials, consideration should be given to the dimensions of the trial plots. As there is usually considerable overlap of adjacent swaths, a plot consisting of a single swath will not reflect deposit under operational conditions. There should be a minimum of three swaths, but five is preferable. When flow to the boom is switched on, it usually takes at least two seconds for full operating pressure to be attained and stabilize. During that time, an aircraft travelling at 160 kph covers 44 m/sec. Spray blocks should be long enough to ensure that assessment plots are not located in this region of uncertain application rate. Using swath markers is important in research tests to minimize stripping.

Efficacy of an aerial trial can be markedly affected by the delivery system and meteorological conditions. The following information should be recorded: aircraft type and model, speed, flying height, swath width, boom position, number of nozzles, nozzle type and size, nozzle space and orientation (e.g., back 45E below horizontal), the specific carrier (including thickening agent where applicable), spraying pressure, flow rate, wingspan or rotor length, distance from wing or rotor tip to outermost nozzles, wind speed, wind direction, temperature, relative humidity, atmospheric stability (a smoke bomb will detect the presence of an inversion).

One of the most common faults in aerial trials is uncertainty about the application rate. The researchers should perform their own calibration (speed, swath width and flow rate). A final check of application rate should also be made by dividing the amount of pesticide used by the area treated.

2.1.9 Weather conditions

Weather conditions around the time of application, precipitation (type and daily amount in mm), temperature (daily average, maximum and minimum in degrees Celsius) and wind speed should be recorded on the trial site or, as a last resort, obtained from a nearby weather station. Extreme weather conditions such as severe and prolonged drought, storms, or hail, occurring a few weeks prior to or after application, which are likely to influence the effect of the product(s) to be tested should also be recorded.

2.1.10 Performance assessment

Performance assessment includes evaluation of effectiveness in controlling the pest and the tolerance of or injury to the host, as described below:

(a) Effectiveness: In the assessment of efficacy, observations should be scored using convenient quantitative and qualitative methods such as percent controlled, extent of remaining pest population, quantity and quality of yield. Regardless of the type of assessment chosen, it should be clearly described.

In trials for crops, yield data are very important. Researchers should attempt to obtain yield information whenever possible.

The effectiveness of the product should be measured against an untreated control. The untreated control provides a measure of the degree of pest infestation or development that would occur in the absence of treatment. In those very few cases where inclusion of untreated control is not practical (e.g., to avoid spread of certain diseases in disease control trials) the pesticide must be tested against some other base, such as another product of known efficacy used as a reference standard or conditions measured before the start of the test.

The procedures followed in sampling or assessing must be such that all of the various characteristics of the population are represented. The size of the sample must be large enough to give reliable estimates and it will vary depending upon the effect to be measured or characterized. For example, to accurately measure yields it may be necessary to harvest entire plots whereas representative portions of each plot may be sufficient to measure pest control.

(b) Effects on the host: Pesticide applications may result in injury to the host at certain dosage rates or under certain conditions. Injury to host plants (phytotoxicity) may appear as chlorosis, malformed plant parts, leaf burning, wilting, death of plant parts or entire plants, delayed emergence or maturity, reduced growth, reduced yield, or other abnormalities. Any injury observed including any effects due to treatment on maturity date, size, quality and appearance of edible parts, should be noted and described.

Likewise, a pesticide may cause various toxic symptoms or other injuries to host animals, which should be noted and described in detail.

(c) Effects on non-target organisms: The use of a pesticide product could have beneficial or hazardous effects to non-target species such as beneficial plants, beneficial insects, soil microorganisms. While these side effects are not considered in efficacy evaluation, such information should be recorded and reported in the environmental toxicity data submission for the assessment of environmental impact.

2.1.11 Data analysis and interpretation

Whenever possible, test data should be analyzed statistically as per the objectives and criteria established prior to conducting the experiment. The statistical method(s) used for analysis must be reported.

Based on analysis of the results, the researcher should draw conclusions of the trial. Based on the results from a series of trials, conclusions on the performance of a product can be made. Conclusions must be clear, precise, and drawn on the basis of representative data.

2.1.12 Source of research

A good efficacy data submission should consist of studies conducted by as many researchers as possible including researchers from the pesticide industry, private consultants, government, colleges and universities. In developing data to support registration, the pesticide companies should include independent research in their efficacy testing programs.

2.1.13 Pesticide combinations/Tank-mixing

Pesticide combinations refer to the use of two or more products at the same time, including tank-mix treatment and concurrent application from separate spray tanks connected to the same set of spray nozzles. Use of pesticide combinations may result in additive, synergistic or antagonistic effects. Product labelling which recommends or implies the use of pesticide combinations may require supporting physical compatibility information and efficacy data (including phytotoxicity). Efficacy studies should be conducted on each component tested separately as well as the combination. If the products are to be used as a tank-mix, physical compatibility tests should be conducted to determine the method and order of mixing the specific formulations in the spray tank.

Labelling of pesticide combinations may be made by (1) listing the specific pest species supported by data from actual testing of the proposed combination, or (2) claiming all pest species from the label of each product involved in the combination, and supporting these claims with performance comparability data (see 2.1.15 below). In the latter case, the appropriate rates (as they are used alone) are to be used in the combination, if no additive, antagonistic or synergistic effect has been indicated in the comparability tests (lower rates of the components should be included in the test to determine possible additive or synergistic effect).

2.1.14 Sequential applications

The label use directions may specifically direct sequential applications of one or more pesticide products preceding or following the application of another pesticide on the same crop area in the same growing season. These use recommendations should be supported by tests designed to compare the efficacy of each product alone with applications of the products applied sequentially. Special emphasis should be directed toward determining whether or not a minimum time interval between applications of the respective chemicals is necessary. In most instances comparability data will be sufficient (see 2.1.15 below).

2.1.15 Comparability tests

Extensive full scale efficacy testing is required for new active ingredients and/or major new uses. In certain circumstances, however, the registrant may have the option of establishing comparable performance between proposed and registered uses of a product (bridging data), rather than conducting a full scale testing program in which all variables are again extensively reevaluated. These circumstances may apply to an amendment of a registered label by altering directions for use, rates, or application techniques, or by adding tank-mixes, sequential applications, adjuvants, or alternate carriers, or when a registrant desires initial registration of an alternate formulation of a product. Prior to initiating this alternate approach, the registrant is encouraged to

consult with the responsible Product Manager of the Plant Industry Directorate to determine the appropriateness of this approach and the performance data required in the specific situation.

Comparison evaluation should be based on direct comparisons of results from plots (preferably adjacent) subjected to identical test conditions. Since tests may be fewer in number and smaller in size than those involved in full scale testing programs, more emphasis should be placed on selection of test conditions such that comparisons will be evaluated under the most rigorous test conditions. As an example of rigorous conditions for a herbicide, plots should be selected which contain the more tolerant weed species of those claimed on the label.

2.1.16 Adjuvants

Products with labelling which recommends the addition of separately packaged adjuvants to the spray tank should be supported with data indicating benefits and detrimental effects, if any, of these adjuvants. Efficacy studies should be designed to test specific adjuvant/pesticide/ host/pest situations and the product should be labelled as such. The trials should include a pesticide-alone treatment (without adjuvant) in order to assess merit/value of adding adjuvant. If a range of adjuvant rates is recommended, the maximum and minimum rates should be evaluated in conjunction with the intended pesticide product.

2.1.17 Pesticides used with fertilizers

Pesticides may be used in tank-mixes with fluid fertilizers or be impregnated onto dry fertilizers. When a pesticide and fertilizer combination is sold as one product in a package, the product is subject to regulation under the Fertilizers Act and Regulations; the pesticide itself must have been registered under the PCP Act and Regulations. When a pesticide is sold separately for use as a tank-mix with fluid fertilizers or for impregnation on to dry fertilizers, this use is subject to regulation under the PCP Act and Regulations. In either case, field test data must be provided to support the compatibility and efficacy of the combination. Efficacy trials should be conducted for the pesticide alone as well as in combination with the specific fertilizer(s).

In the case of using fluid fertilizer as a carrier for pesticide application, field test data should indicate spray volume, fertilizer analysis, compatibility, efficacy and detrimental effects, on a specific crop basis.

Laboratory tests are of value in determining the physical compatibility of the tank-mix. This information should be directed, via labelling, towards use of a "jar test" by the applicator prior to large-scale mixing.

2.1.18 Minor uses

Minor uses of pesticides are defined as those necessary uses of registered pesticides for which the anticipated increase in the volume of sales is not sufficient to persuade the registrant to carry out the research required for registration.

Efficacy data are required to support the registration of minor uses. The general principles and special procedures outlined in these guidelines would also apply to the efficacy trials for minor use registration. However, because of the nature of the minor use (e.g., small geographic areas), the number of required efficacy trials may be reduced compared to those for regular uses. For details, refer to the "Minor Use of Pesticides Program" published by Agriculture Canada.

2.2 Reporting of Efficacy Data

2.2.1 General remarks

To facilitate efficacy evaluation for registration purposes, it is essential that the data submission be presented in an orderly manner and contains complete and accurate information. The data submitter should review and screen the data very carefully to ensure that: (a) all relevant tests, regardless of positive or negative results, are submitted; (b) studies irrelevant to the proposed registration are not submitted; and (c) there is no double counting, i.e., test results must be reported only once.

2.2.2 Format of the data submission

Consistent with guidelines for Organization of Data for End Use Products (Dir93-03), efficacy data should be presented as Part 8 of the registration submission and include the following sections:

8.0 Table of contents
8.1 Summaries
8.2 Efficacy
8.3 Adverse effects (e.g., phytotoxicity)

For the table of contents, an index should be prepared to list the contents of the submission including the summaries and individual studies. It is recommended that numbered tabs be used to identify the individual topics.

In addition to the report of individual trials, the data submission should include summarized conclusions related to label claims. The conclusions must be clear and precise, and drawn on the basis of data analysis and evaluation.

To allow quick review of a comprehensive data submission, table summaries are essential. Summary tables present a condensed and simplified overview of the scope of the test program and the level of product performance obtained. These summaries should be organized primarily according to the year/site/researcher combinations and secondarily according to pertinent variables, such as treatment, method of application, site-specific conditions and results. Tables should be clear, concise and complete so that they can stand alone.

In addition to the general summaries, it is important to provide summary tables for a specific treatment to present the frequency distribution of pest control or crop tolerance. Extreme weather conditions, such as severe and prolonged drought, hail, and heavy rainfall immediately following foliar application, are likely to influence the effect of the treatment. While results from all tests must be submitted, individual tests under these unusual conditions may be excluded from the specific rating summaries, if justified; such justifications must be clearly noted.

Examples of summary tables for each class of pesticides are provided at the end of the particular section as appendices.

2.2.3 Details of report

In the efficacy and injury sections, all details of the tests should be reported giving particular emphasis to variables that relate to the label directions and limitations. Such details may include, but are not limited to, the following, when appropriate:

(a) the objectives of the trial
(b) the location of the trial site
(c) chemical name and formulation
(d) target pest organisms and population levels
(e) host, e.g., crops and cultivars
(f) growth stage of the host and/or the pest
(g) soil factors (texture, organic matter, etc.)
(h) experimental design, size and number of plots
(i) application dates and rates
(j) application method and equipment, type and size of nozzles, and operating pressure, etc.
(k) volume of spray carrier, and water conditions (e.g., pH, hardness) if water is used
(l) weather conditions during and after treatment
(m) cultural practices including treatment of the plots with other pesticides

(n) dates of assessment
(o) size and frequency of sampling
(p) quantity and quality of yield of the treated commodity
(q) side effects (positive or negative)
(r) statistical analysis and data assessment
(s) performance evaluation including interpretation, discussion and conclusions that relate to label claims
(t) name of the responsible researcher and organization.

2.3 Evaluation Criteria and Procedures

2.3.1 Objective

These evaluation criteria and procedures are designed to aid Product Managers of Agriculture Canada in their evaluation of efficacy data for the purpose of pesticide registration. They also assist the registrants in their understanding of the review process and the basis for acceptance or rejection of a proposed registration.

The purpose of the efficacy review is to ensure that the proposed use of a pesticide product is supported by adequate scientific information. For a treatment to be acceptable for registration, the information submitted must prove that the proposed treatment is effective in pest control and safe to the host.

2.3.2 Sources of information

It is the responsibility of the registrant to produce, collect and submit all scientific information required to support the proposed registration. However, the Product Managers may use any relevant data available to them in addition to those submitted by the registrant. They may base their judgement on their own experience and knowledge of the pesticide product under consideration. They may also consult with research scientists and/or other personnel involved in the research being reviewed. It must be remembered, however, that only "scientific evidence" will be used in the assessment of the performance of a product. Testimonials from individuals, without documented evidence, are of no value in efficacy evaluation.

2.3.3 Scanning of data submissions

The registrant's submission should include all information necessary to provide a complete evaluation of the usefulness of a product. The Product Manager examines the complete data package and a judgement will be made as to whether any data omissions are significant enough to adversely affect the review. Those so identified should be communicated back to the registrant for supplemental data submissions before the evaluation can be carried out.

2.3.4 Assessing the appropriateness and adequacy of the data

If there are no apparent major data gaps which would prevent a meaningful evaluation of the submission, the reviewer will then consider the appropriateness of the submission, i.e., the intended use pattern and adequacy of the data that has been supplied. The following items should be considered in the assessment:

(a) Acceptability of the studies: The acceptability of a test is evaluated on the basis of whether it is designed and conducted following acceptable test procedures. Elements for consideration may include test material, test species, site of test, method and rate and timing of application, etc.

(b) Location, duration and number of tests: For field studies, the geographic distribution of the tests should adequately cover the various climate and soil conditions likely to be encountered. The duration of testing (number of years) should be long enough to reflect fluctuations and variances of conditions that normally occur from year to year. Generally, a minimum of two years is required.

The number of tests should be large enough to produce conclusive results with a high degree of confidence. It depends on many factors, such as pest/host combinations, the proposed use situation, and the consistency (reproducibility) of the results.

(c) Effectiveness: The data should demonstrate that the pesticide product, when used as directed, will have merit and value such as increases in marketable yields of desirable quality, a reduction of damage, a satisfactorily high degree of repellency or attraction, reduction of injury, or reduction of the pest population to acceptable low levels. The acceptable level of control may vary depending on the purpose of the proposed use.

2.3.5 Conclusion on efficacy evaluation

Based on the review of all scientific information available, the Product Manager will decide whether the proposed use of a product is acceptable for registration from the efficacy point of view:

(a) The proposed registration is acceptable if the data demonstrate an adequate level of pest control without unacceptable effect to the host and support all the label claims and statements;

(b) If the proposed registration is not fully supported by available data, changes to the draft label may be made, in consultation with the registrant, to improve use directions and precautions. Acceptance of the registration may then be considered based on the revised draft label; or

(c) If additional data/information are required to support claims and to resolve a particular point or item of concern, the Product Manager will identify the additional requirements and notify the registrant.