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# ACVM RESEARCH STANDARD

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**Endorsement:**

**Date:**

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# ACVM RESEARCH STANDARD

## 1 INTRODUCTION

The *ACVM Research Standard* defines the minimum requirements for designing, conducting, monitoring and reporting of laboratory, field and clinical studies to enable the Agricultural Compounds and Veterinary Medicines (ACVM) Group of the New Zealand Food Safety Authority (NZFSA) to assess an application to register a trade name product or to vary the conditions on a registered trade name product.

This standard is based on OECD GLP guidelines and VICH GCP guidance as listed in section 1.2. Unless stated in this document, accreditation to those international standards is not an NZFSA requirement. However, studies conducted in accordance with them (with the additional requirement for Animal Ethics Committee approval) will satisfy the requirements of the *ACVM Research Standard*.

Applicants should note that they are responsible for providing all information required by the ACVM Group to make a decision on an application. Applications that do not contain the required information will not be assessed. If further advice is required, applicants are advised to contract the services of an appropriate consultant prior to submitting their application.

### 1.1 Scope

This standard must be followed by:

- all persons applying to register a trade name product or to vary the conditions on a registered trade name product;
- all persons accredited under the Agricultural Compounds and Veterinary Medicines Act 1997 to undertake a risk assessment of applications made to register a trade name product or vary the conditions on a registered trade name product.

This standard provides specifications for:

- study conduct;
- the final study report.

## 1.2 Definitions and abbreviations

### **Blinding**

A procedure to reduce potential bias in which designated study personnel are kept uninformed of the treatment assignment(s).

### **Field study**

A study that includes experimental activities carried out outside the usual laboratory situation, e.g. on land plots, in outdoor ponds or in greenhouses. They often occur in combination or in sequence with activities carried out in a laboratory.

### **Final study report**

A comprehensive description of a study that is written after the collection of all raw data is completed or the study is discontinued. It completely describes the study, presents the study results (including analysis), raw data and quality assurance reports, and contains a critical evaluation of the study results. It encompasses the study protocol with amendments and deviations.

### **Good clinical practice (GCP)**

An international standard for designing, conducting, monitoring, auditing, recording, analysing, and reporting clinical studies that provides assurance that the data and reported results are complete, correct and accurate, and that the welfare of the study animals and the safety of the study personnel involved in the study are ensured, and the environment and the food chain are protected.

### **Good laboratory practice (GLP)**

An international quality system concerned with the organisational process and the conditions under which non-clinical health and environmental safety studies are planned, performed, monitored, recorded, archived and reported.

### **Investigator**

The individual responsible for all aspects of the conduct of a study. See also **study director**.

### **Monitor**

An individual responsible for overseeing a study, and ensuring that it is conducted, recorded and reported in accordance with the study protocol, standard operating procedures (SOPs), *ACVM Research Standard*, and the applicable regulatory requirement(s). See also **quality assurance**.

### **Principal investigator**

An individual responsible for the conduct of certain defined phases of the field or laboratory study, acting on behalf of the study director.

**Quality assurance (QA)**

A planned and systematic process established to ensure that a study is performed and the data are collected, recorded and reported in compliance with this standard and any applicable regulatory requirement(s). The **monitor** of a study is part of the QA team.

**Randomisation**

The process of assigning test systems to treatment or control groups using an element of chance to determine the assignments in order to reduce bias.

**Raw data**

Any original worksheets, calibration data, records, memoranda and notes of firsthand observations and activities of a study that are necessary for the reconstruction and evaluation of the study. Raw data may include, but are not limited to, photographic materials, computer printouts, magnetic, electronic, or optical media, information recorded from automated instruments, and hand recorded data sheets. Facsimile transmissions and transcribed data are not considered raw data.

**Reference (control) substance**

Any substance or mixture used to provide a basis for comparison with the test substance. In the context of field studies, this includes analytical standards.

**Sponsor**

An individual (or organisation) who takes responsibility for the initiation, management, and/or financing of a study, and is liable for the test substance under investigation.

**Study**

A single scientific experiment conducted to test at least one hypothesis relevant to the proposed claim(s) made for a test substance under investigation.

**Study animal**

Any animal that participates, as a recipient of either the test or reference substances or as a control, in a study.

**Study director**

The individual responsible for all aspects of the conduct of a field or laboratory study. Where more than one site is involved in the study, the study director may delegate responsibilities to a principal investigator. See also **investigator**.

**Study plan**

See **study protocol**.

**Study protocol (aka study plan)**

A document, signed and dated by the investigator and sponsor, that fully describes the objective(s), design, methodology, statistical considerations, and organisation of a study. The study protocol may also give the background and rationale for the study, but these could be provided in other study protocol-referenced documents.

**Study protocol amendment**

A written change or modification of the study protocol effected prior to the implementation of the protocol or execution of the changed or modified task. It is signed and dated by the investigator and sponsor, and incorporated into the protocol.

**Study protocol deviation**

A departure from the procedures stated in the study protocol.

**Target species**

The species of animal or plant for which the test substance is intended for final use.

**Test substance**

A substance or mixture that is under investigation.

**Test system**

Any biological, chemical or physical system or a combination thereof used in a study, e.g. plant, soil, animal.

**Unanticipated event**

Any abnormal response associated with the use of a test substance, whether or not considered to be product related, that may impact on the results of a study.

## 1.3 References

No other documents are required to be read in conjunction with this document to aid in understanding it.

## **2 GENERAL REQUIREMENTS FOR EFFICACY STUDIES**

### **2.1 Study conduct**

- 2.1.1 All analytical laboratory studies must be conducted by a GLP compliant laboratory.
- 2.1.2 All studies must be conducted under the authority of a single study director/investigator.
- 2.1.3 All studies must be conducted in accordance with a fully comprehensive detailed study protocol which shall be recorded in writing prior to the commencement of the study.
- 2.1.4 Amendments to and deviations from the study protocol must be justified and approved by the study director/investigator.
- 2.1.5 All data generated during the conduct of the study must be recorded directly, accurately and legibly in ink by the individual entering the data who also signs or initials, and dates the entry.
- 2.1.6 Any changes in the raw data must be made so as not to obscure the previous entry, and must be signed or initialled, and dated by the individual making the change. A reason for the change must be indicated.
- 2.1.7 There must be sufficient qualified personnel, appropriate facilities, equipment and materials available for the timely and proper conduct of the study.
- 2.1.8 Each study must be conducted under the auspices of a QA programme to ensure that studies performed comply with the principles of this document.
- 2.1.9 QA personnel must not be involved in the conduct of the study being assured.
- 2.1.10 All studies must be reported separately.

## 2.2 Final study report

All documentation must be complete, clearly written, free from errors and available in hard copy. Entries on all documents must be hand signed and dated.

The following information must be supplied:

- 2.2.1 Study title and identifier unique to the applicant.
- 2.2.2 A clearly defined objective in conducting the study.
- 2.2.3 Titles, names, qualifications and roles of all people involved in conducting key elements of the study.
- 2.2.4 Place(s) and date(s) of treatment.
- 2.2.5 A full description of the study design including:
  - specification of the type of study, e.g. controlled study, pilot study;
  - description of the randomisation method(s) used;
  - description of the study design (e.g. crossover design), and the blinding technique used;
  - objective criteria for the exclusion from, inclusion in, and removal subsequent to inclusion in the study of test systems;
  - specification of any other bias-reducing factors implemented;
  - description of the experimental unit(s);
  - detailed information on the experimental design, including a description of the chronological procedure of the study, all methods and materials and conditions, type and frequency of analysis, measurements, observations and examinations performed.
- 2.2.6 A full description of test systems involved in the study including:
  - characterisation, e.g. species, strain, location, age/stage of growth, and other pertinent information;
  - numbers used;
  - justification for the selection of the test system.
- 2.2.7 Details of test system management, including the method of individually identifying each test system, or part thereof.
- 2.2.8 Full information on any test system, or part thereof, withdrawn from the study.
- 2.2.9 The precise identification of the test and reference substances used in the study, e.g. code, CAS number, name, biological parameters.



- 2.2.10 A full description of the use of the test and reference substances used in the study including:
- method of administration/application;
  - frequency and duration of administration/ application;
  - dose level(s), concentration(s) or application rate(s) used;
  - rules for any concomitant administration/application of other substances;
  - precautions taken during administration/application, if any.
- 2.2.11 Details of any other substance(s) administered/applied during the study, either prior to, during or after the test substance, and the details of any interactions observed.
- 2.2.12 Full details of the materials and methods used in the study.
- 2.2.13 All raw data.
- 2.2.14 A full description of any deviations from the study protocol.
- 2.2.15 All results of the studies (including unfavourable or negative results) with a full statement of the observations and the results of any objective tests. Where appropriate, a statistical evaluation of the results must be included.
- 2.2.16 Statistical methods used including:
- sufficient description of the statistical methods employed for them to be understood;
  - the sample size and justification for its choice, including calculation of the power of the study where relevant;
  - the level of significance to be used and justification for its use.
- 2.2.17 All particulars of, and explanations for, any unanticipated events, whether harmful or not, and of any measures taken in consequence.
- 2.2.18 Conclusions based on results from each individual test system or group as appropriate.
- 2.2.19 A summary of the study including a statement of the objective, the materials and methods, the results, and the main conclusions that can be drawn from the results.
- 2.2.20 All QA audits conducted during, or relevant to, the study including laboratory audits, and a QA statement by an authorised person(s) attesting to adherence to the relevant QA standards.
- 2.2.21 A statement attesting to the accuracy and completeness of the final study report and stating whether the data were collected in compliance with this standard. This statement must be signed by the study director/investigator and the QA personnel involved.

## **3 ADDITIONAL REQUIREMENTS FOR STUDIES INVOLVING ANIMALS**

### **3.1 Study conduct**

- 3.1.1 All New Zealand studies must be conducted in accordance with approval from a valid Animal Ethics Committee.
- 3.1.2 Any animals that die in the course of a study must be subjected to a postmortem examination to determine the cause of death, or the cause of debilitation requiring euthanasia.

### **3.2 Final study report**

The following information must be supplied:

- 3.2.1 Animal Ethics Committee approval documentation.
- 3.2.2 For efficacy studies, the criteria to be met for efficacy to be claimed.
- 3.2.3 Case history (as full as possible), occurrence and course of any intercurrent diseases.
- 3.2.4 Diagnosis of the disease being treated, including a description of the clinical signs according to conventional criteria. Ancillary tests are to be summarised and appended.
- 3.2.5 Any effects on animal performance.
- 3.2.6 Results of postmortems of animals that die during the study.

## **4 ADDITIONAL REQUIREMENTS FOR STUDIES INVOLVING PLANTS/SOIL**

### **Final study report**

History of the land on which the plants are to be grown, e.g. use of crop or soil treatments, which could be of relevance to the present study.

## 5 ADDITIONAL READING

### OECD GLP Guidelines

- No.1 OECD Principles of Good Laboratory Practice (1998)
- No.2 Revised Guides for Compliance Monitoring Procedures for Good Laboratory Practice (1995)
- No.3 Revised Guidance for the Conduct of Laboratory Inspections and Study Audits (1995)
- No. 4 Quality Assurance and GLP (1999)
- No. 5 Compliance of Laboratory Suppliers with GLP Principles (2000)
- No. 6 The Application of the GLP Principles to Field Studies (1999)
- No. 7 The Application of the GLP Principles to Short-Term Studies (1999)
- No. 8 The Role and Responsibilities of the Study Director in GLP Studies (1999)
- No. 9 Guidance for the Preparation of GLP Inspection Reports (1995)
- No. 10 The Application of the Principles of GLP to Computerised Systems (1995)
- No. 11 The Role and Responsibilities of the Sponsor in the Application of the Principles of GLP (1998)
- No. 12 Requesting and Carrying Out Inspections and Study Audits in Another Country (2002)
- No. 13 The Application of OECD Principles of GLP to the Organisation and Management of Multi-Site Studies (2002)

FDA GLP for Non Clinical Studies (21CFR 58)

VICH Good Clinical Practice (2000)