Notification on the Good Laboratory Practice for Agricultural Chemicals

(The notification No. 11-Nousan-6283, issued on October 1, 1999 by the Director-General of Agricultural Production Bureau, the Ministry of Agriculture, Forestry and Fisheries)

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The Good Laboratory Practice for Agricultural Chemicals

Section 1: The Good Laboratory Practice for Agricultural Chemicals

The Good Laboratory Practice (GLP) for Agricultural Chemicals is to further ensure the reliability of the study reports on agricultural chemicals submitted for the application for registration of agricultural chemicals in accordance with the provision of Paragraph 2 of Article 2 as well as Paragraph 6 of Article 15-2 and Paragraph 1 of Article 6-2 as well as Paragraph 6 of Article 15-2 of the Agricultural Chemicals Regulation Law (Law No. 82, 1948) (hereinafter referred to as "the Law") through systematically ensuring the observance of the standards of the GLP for Agricultural Chemicals (hereinafter referred to as "the GLP standards". For details, please refer to the annex to this document) self-observance by the test facility

Section 2: The scope and area of studies applied by the GLP

The GLP shall be applied to the following scope/area of the studies;

(1) Toxicity / Mutagenicity:

The applied studies are those stipulated in (a)-(s) of I. (3) of the "Data Requirements for Supporting Registration of Agricultural Chemicals" (Ref. No. 12-Nousan-8147 notified by the Director-General, Agricultural Production Bureau, the Ministry of Agriculture, Forestry and Fisheries (MAFF) on 24 November, 2000) (hereinafter referred to as "Data requirements") and the studies stipulated in "3. Results of studies of safety in humans" in the annex of "Standards for safety evaluation of microbial pesticides" attached to "Guidelines for Safety Evaluations of microbial pesticides" (Ref. No. 9-Nousan-5090 notified by the Director-General, Agricultural Production Bureau, MAFF on 29 August, 1997).

(2) Metabolism studies in animals and plants and behavior studies in soil and water:

The applied studies are those stipulated in (t)-(x) of I. (3) of the "Data requirements".

(3) Physical/chemical property:

The applied studies are those stipulated in (aa) of I. (3) of the "Data requirements" (excluding test results regarding color, physical form and odor.)

(4) Aquatic organism effects:

The applied studies are those stipulated in (y) of I. (3) of the "Data requirements"

(5) Residues

The applied studies are those stipulated in (a) and (b) of I. (4) a. of the "Data requirements"

Section 3: Acceptance of the Studies Conducted in Accordance with the GLP

(1) The studies listed in Section 2 out of the studies submitted for the application for registration of agricultural chemicals in accordance with the provision of Paragraph 2 of Article 2 and Paragraph 1 of Article 6-2 of the Law, shall meet any of the following (i) to (iii).

(i) The study shall be conducted in the domestic test facilities which are accredited by the Director-General of Food Safety and Consumer Affairs Bureau (hereinafter referred to as " the Director-General") for "in compliance" with the GLP standards at a frequency

of once or more times every three years; or

(ii) The study shall be conducted in the test facility which is accredited by the governmental agencies or the other alternative agencies having the authority to conduct the accreditation of the compliance of GLP (which shall be complied with the GLP principle of the Organisation for Economic Co-operation and Development (OECD)); or

(iii) When any question arises as a result of the evaluation or by other information about the quality of the study reports which are applied by the GLP and submitted in accordance with the provision of Paragraph 2 of the Article 2 and Paragraph 1 of Article 6-2 of the Law and the question is notified to the applicant for agricultural chemical registration by the Director-General, the resolution of the question is accredited by the Director-General.

(2) When the applicant for agricultural chemical registration submits the study reports applied by the GLP to the MAFF in accordance with Paragraph 2 of Article 2 and Paragraph 1 of Article 6-2 of the Law, the following documents shall be attached:

(i) A GLP compliance statement by the study director which verifies that the study report(s) were conducted in compliance with the GLP standards, the standards for the GLP concerning agricultural chemicals in the country concluding a bilateral agreement on the GLP or the OECD Principles of GLP; and/or

(ii) For multi-site studies, a document that clearly describes the interrelationship among all test facilities involved.

Section 4: Application for GLP accreditation

(1) When any representative of the test facility (hereinafter referred to as "the GLP applicant") who applies for the accreditation of the GLP compliance by the Director-General under the aforementioned Section 3 (1) (i), the GLP applicant shall use the form of Annex 1, or the applicant for agricultural chemical registration under the aforementioned Section 3 (1) (iii) shall use the form of Annex 2, and submit it to the Director-General with the documents concerning the following (i) to (iv);

(i) The outline of the test facility (including the name, address, the established date, the organization and personnel (its position in the organization and in the GLP shall be clearly described.), the site area (m^2) and building area (m^2) of the test facility, the building layout and floor layout of the test facility and the type and content of the apparatus arranged);

(ii) The summary of the capacity of the test facility conducting the studies and of the studies conducted in the past three year;

(iii) The lists of the Standard Operation Procedures (SOP); and

(iv) The document recording the personnel career (e.g. Curriculum vitae and research history) and the academic societies to which they belong concerning Test Facility Management(s) (Test Site Management(s), if applicable), Study personnel (including Study Director(s), Principal Investigator(s)), Quality Assurance Programme personnel (QAP) (including the QAP manager) and Archivist.

(2) Submission of the documents mentioned in Section 4 (1) should be made through "Incorporated Administrative Agency, Food and Agricultural Materials Inspection Center" (hereinafter referred to as "the Center"). In this case, the Center may make a comment to the application.

(3) The Director-General may request the GLP applicant to submit further information/document to accredit the GLP compliance, if necessary. In this case, the GLP applicant may submit them to the Director-General through the Center.

Section 5: Review of the document submitted and conduct of the GLP inspection

When the Director-General evaluates the documents submitted in accordance with the aforementioned Section 4 and considers that the GLP inspection is necessary for the Test Facility, the Director-General may make, with the GLP applicant's agreement, those corresponding to any

of the following persons conduct GLP inspection to the test facility;

(1) The personnel designated by the Director-General among Agricultural Chemicals regulation officers stipulated in "the order on the inspection and the report stipulated in article 13 in the Agricultural Chemicals Regulation Law (the ordinance of the Prime Minister's office and the MAFF (Ref. No. 2, 1971)) who have the expert knowledge or experience of the inspection concerning test facility, study report, specimens etc.; or

(2) The staff of the Center; or

(3) Academic experts who are familiar with the studies of toxicology or residue in crops on Agricultural Chemicals and are designated by the Director-General.

Section 6: Procedure for the GLP Inspection

(1) The Director-General shall notify the GLP applicant of the date of the inspection and other information concerned in advance.

(2) The GLP inspection shall be conducted concerning the following items with the agreement of the GLP applicant:
   (i) Evaluation on compliance of the test facility with the GLP standards; and
   (ii) Audit of the studies covered by the GLP inspection.

(3) The GLP inspection shall be conducted in accordance with the following steps:
   (i) Evaluation of the general management of the test facility;
   (ii) Inspection tour in the test facility and evaluation of the condition of the apparatus;
   (iii) Evaluation of the operations;
   (iv) Evaluation of the management of Study Plan(s), SOP, Final Report(s), etc.;
   (v) Evaluation of the activities of Quality Assurance Programme;
   (vi) Evaluation of the archiving management of raw data, specimens, etc.; and
   (vii) Audit of the study(s) covered by the inspection with the relevant raw data, specimens, final reports, etc.

(4) The inspector(s) may require, with the GLP applicant's agreement, the GLP applicant to submit the sample of test item(s), specimens, raw data and any other related materials as necessary.

(5) The inspector(s) may give any advice and instruction to the test facility at the end of the GLP inspection, if necessary. In this case, those advice and instructions shall be recorded by the inspector(s).

Section 7: Report of the GLP Inspection

(1) The inspector(s) shall prepare the GLP inspection report including the following items and then submit it to the Director-General immediately after conducting the GLP inspection:
   (i) The name and affiliation of the inspector(s);
   (ii) The name and address of the test facility inspected;
   (iii) The date and/or period of the GLP inspection;
   (iv) The purpose of the inspection;
   (v) The outline of the test facility;
   (vi) The kind of the study(s) audited;
   (vii) The name and affiliation of the personnel of the test facility who attended the GLP inspection;
   (viii) The compliance of the test facility with the GLP standards;
   (ix) The compliance of the study(s) audited with the GLP standards;
   (x) The advice and/or the instructions taken to the test facility at the end of the GLP inspection;
   (xi) Comprehensive evaluation; and
   (xii) Any other remarks;

(2) Based on the inspection reports, the Director-General shall verify whether or not the test facility is in compliance with the GLP standards and notify the applicant of the result.

Section 8: Others

(1) The representative of the test facility accredited by the Director-General concerning Section 3 (1) (i) or (iii), shall report the changes to the Director-General with the form of Annex 3, when there is any change in the contents of the application for verification of compliance of a test facility with the GLP standards.

(2) The representative of the test facility accredited by the Director-General concerning Section 3 (1) (i) or (iii) shall submit the notification of the closure with the form of Annex 4 to the Director-General, when closing the GLP operation of the test facility.

Supplementary provision (1 October 1999):

This notification shall be applied to those studies defined in Section 2 which are initiated after 1 October, 1999.

In addition, those studies of which the initiation date is before 30 September, 1999 and were conducted in the test facilities accredited by the Director-General in accordance with the GLP standards of the notification from the Director-General of Agricultural Production Bureau, MAFF "GLP for Agricultural Chemicals (59-nousan-No.3850, 10 August, 1984)", are regarded as meeting the GLP standards by this notification.

Supplementary provision (6 December, 2000):

(1) This notification shall be applied to those studies defined in Section 2 which are initiated after 6 December, 2000. However, the notification may be applied to the studies initiated after 1 February, 2001 for preparing the following test results:
   (i) Test results regarding acute neurotoxicity;
   (ii) Test results regarding repeated dose oral neurotoxicity;
   (iii) Test results regarding pharmacology;
   (iv) Test results in regard to metabolism in animals;
   (v) Test results in regard to metabolism in plants;
   (vi) Test results in regard to behavior in soil;
   (vii) Test results in regard to behavior in water; and
   (viii) Test results in regard to impact on aquatic animals and plants (except Daphnia. spp. reproduction toxicity).

(2) As of 6 December, 2000, the test facility accredited by the Director of Plant Protection Division of the Agricultural Protection Bureau on the test results regarding impact on aquatic animals and plants, may be regarded as being accredited by the Director-General of the Agricultural Protection Bureau in accordance with Section 3 of the revised notification.

(3) As of 6 December, 2000, the application for the GLP compliance concerning studies regarding the impact on aquatic animals and plants of the test facility to the Director of Plant Protection Division of the Agricultural Protection Bureau, may be regarded as the application to the Director-General of the Agricultural Protection Bureau in accordance with Section 3 of the revised notification.

Supplementary Provision (5 June, 2001):

This notification shall be applied since 5 June, 2001.

Supplementary Provision (April 1, 2007):

This notification shall be applied since April 1, 2007.

Supplementary Provision (April 1, 2008)

This notification shall be applied to the studies initiated since April 1, 2008.

Supplementary Provision (February 2, 2012)

This notification shall be applied since February 2, 2012.

Supplementary Provision (May 15, 2014)

This notification shall be applied to the studies initiated on and after the day on which six months have elapsed from the effective date.

Annex 1:

Application for verification of compliance of a test facility with the GLP standards

Date:

To: The Director-General,
Food Safety and Consumer affairs Bureau,
The Ministry of Agriculture, Forestry and Fisheries.

Address:
Name :
(For corporate body, the name of the corporate body and the representative.)
Contact point:
(TEL, FAX, E-mail, responsible division, name)

This is to apply for the compliance of the following test facility with the GLP standards. Attached are the documents required.

1. **Legal basis:**
2. **The name of the test facility :**
3. **The address of the test facility :**
4. **The area of the study(s) or the title of the study :**
5. **If the test facility was accredited by the Director-General previously, the date of the accreditation and the area of the study(s) or the title of the study**

NB: The form shall be JIS A4 size.

Annex 2:

Application for verification of compliance with the GLP standards

Date:

To: The Director-General,
Food Safety and Consumer affairs Bureau,
The Ministry of Agriculture, Forestry and Fisheries.

Address:
Name:
(For corporate body, the name of the corporate body and the representative.)

We received the notification that the following study was in suspicion of the reliability. Therefore, this is to apply for the inspection concerning the resolution of the suspicion with the relevant documents.

1. The name of the study report(s) in suspicion:

2. The name of the test facility:

3. The address of the test facility:

NB: The form shall be JIS A4 size.

(1) The documents defined in Section 4 by the Director-General shall be attached.

(2) If the name (for corporate body, the name of the representative) is signed, one's seal may be exempted.

(3) About" 2." and "3.", the name and address in English shall be written together with Japanese.

Annex 3:

Notification of the Change(s) in "Application for verification of compliance of a test facility with the GLP standards compliance"

Date:

To: The Director-General,
Food Safety and Consumer affairs Bureau,
Ministry of Agriculture, Forestry and Fisheries.

Address:
Name:
(For corporate body, the name of the corporate body and the representative.)

We report the following change(s) in the contents of "the Application" submitted in accordance with Section 8 (1).

1.The name of the test facility:

2.The content(s) of the change(s):

3. The reason for the change(s):

4. The date of the change(s):

NB: The form shall be JIS A4 size.

If the name (for corporate body, the name of the representative) is signed, one's seal may be exempted.

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Annex 4:

Notification of test facility closure

Date:

To: The Director-General,
Food Safety and Consumer affairs Bureau,
Ministry of Agriculture, Forestry and Fisheries.

Address:
Name:
(For corporate body, the name of the corporate body and the representative.)

Since we close (closed) the business, we notify the following information in accordance with Section 8 (2).

1.The name of the test facility:

2. The contents:
(1) The reason for the closure:
(2) The list(s) of the transferred place of the final reports, specimens and raw data, etc. after the closure:
(3) The (due) date of the closure:

NB: The form shall be JIS A4 size.

(1) About "2. (2)", the list(s) may be attached to this form.

(2) If the name (for corporate body, the name of the representative) is signed, one's seal may be exempted.

(Annex) The standards for the Good Laboratory Practice (GLP) for Agricultural Chemicals.

Chapter 1: General Provision

(Purpose)

Article 1.

The purpose of the GLP for Agricultural Chemicals is to ensure the reliability of the studies submitted to the Minister of Agriculture, Forestry and Fisheries in accordance with Paragraph 2 of Article 2 and paragraph 1 of Article 6-2 of the Agricultural Chemicals regulation Law (Law No.82. 1948. Hereinafter referred to as "the Law").

(Definition)

Article 2.

The following terms in the GLP for Agricultural Chemicals should be defined as follows:

(1) Test facility means the persons, premises and operational unit(s) that are necessary for conducting a study. For multi-site studies, the studies which are conducted at more than one site, the test facility includes the site at which the Study Director is located and all individual test sites, which individually or collectively can be considered to be test facilities.

(2) Test site means the location(s) at which a phase(s) of a study is conducted.

(3) Test facility management (hereinafter referred to as "TFM") means the person who has the authority and formal responsibility for organization and functioning of the test facility according to the GLP for Agricultural Chemicals.

(4) Test site management (if appointed) means the person(s) responsible for ensuring that the phase(s) of the study, for which he is responsible, are conducted in accordance with the GLP for Agricultural Chemicals.

(5) Sponsor means an entity which commissions a test facility to conduct a study.

(6) Study Director means the individual responsible for the overall conduct of the study.

(7) Principal Investigator means an individual who, for multi-site study, acts on behalf of the Study Director and has defined responsibility for delegated phases of the study. The Study Director's responsibility for overall conduct of the study cannot be delegated to the Principal Investigator(s); this includes approval of the study plan and its amendments, approval of the final report, and ensuring that all applicable principles of the GLP for Agricultural Chemicals are followed.

(8) Quality Assurance Programme means a defined system, which assures TFM that the studies conducted in the Test facility are in compliance with the GLP for Agricultural Chemicals.

(9) Standard Operating Procedures (hereinafter referred to as "SOPs") mean documented procedures which describe how to perform tests or activities normally not specified in detail in study plans or test guidelines which include the guidelines notified by the Director-General of Agricultural Production Bureau, the Ministry of Agriculture, Forestry and Fisheries (hereinafter referred to as "the Director-General") and the OECD Test Guidelines, etc.

(10) Master schedule means a compilation of the information to assist in the assessment of workload and for tracking of studies at a test facility.

(11) Study means an experiment or set of experiments in which a test item is examined to obtain data on its toxicity, etc. intended for submission to the Minister of Agriculture, Forestry and Fisheries.

(12) Study plan means a document which defines the objectives and experimental design for the conduct of the study, and includes any amendments.

(13) Study plan amendment means an intended change to the study plan after the study initiation date.

(14) Study plan deviation means an unintended departure from the study plan after the study initiation date.

(15) Test system means any biological, chemical or physical system or a combination thereof used in a study.

(16) Raw data means all original test facility records and documentation, or verified copies thereof, which are the result of the original observations and activities in a study. Raw data also may include photographs, microfilm, or microfiche copies, computer readable media, dictated observations, recorded data from automated instruments, or any other data storage medium that has been recognized as capable of providing secure storage of information for time period as defined in Article 17.

(17) Specimen means any material derived from a test system for examination, analysis, or retention.

(18) Experimental starting date means the date on which the first study specific data are collected.

(19) Experimental completion date means the last date on which raw data are collected from the study.

(20) Study initiation date means the date the Study Director signs or seals to the study plan.

(21) Study completion date means the date the Study Director Signs or seals to the final report.

(22) Test item means agricultural chemicals, its active ingredient or their related substance.

(23) Reference item ("Control item") means any substance used to provide a basis for comparison with the test item.

(24) Batch or Lot means a specific quantity of a test item or reference item produced during a defined cycle of manufacture in such a way that it could be expected to be of a uniform character and should be designated as such.

(25) Vehicle means any agent which serves as a carrier used to mix, disperse, or solubilise the test item or reference item to facilitate the administration/application to the test system.

Chapter 2 : Test facility Organisation and Personnel

(TFM's Responsibilities)

Article 3.

1. TFM should ensure that the GLP for Agricultural Chemicals is complied with, in its test facility. Thus, TFM should, at a minimum, conduct the items defined in the following events.

   TFM should:

   (1) Maintain a statement which identifies the individual(s) within a test facility who fulfil the responsibilities of management as defined by the GLP for Agricultural Chemicals.

   (2) Ensure that a sufficient number of personnel with acknowledge and experience concerning the study, appropriate facilities, equipment, and materials are available for the proper conduct of the study.

   (3) Maintain the record of qualifications, training, experience and job description for each personnel

involved in the studies.

(4) Ensure that personnel clearly understand the functions they are to perform and, where necessary, provide training for these functions.

(5) Establish SOPs, which the activities in the test facility are carried out in accordance with, and approve all SOPs from their original version to the latest version.

(6) Designate Quality Assurance Programme and assure that the quality assurance responsibility is being performed in accordance with the GLP for Agricultural Chemicals.

(7) Designate the Study Director with appropriate qualification, training, or experience for each study before the study is initiated. Replacement of a Study Director should be done in accordance with the established procedures, and should be documented.

(8) Ensure, in the event of a multi-site study, that, if needed, the Principal Investigator is designated who is appropriately trained, qualified and experienced to supervise the delegated phase(s) of the study. Replacement of a Principal Investigator shall be done in accordance with to established procedures, and should be documented.

(9) Ensure the documented approval of the study plan by the Study Director.

(10) Ensure Study Director distributes the copy of the approved study plan to the Quality Assurance Programme.

(11) Maintain a historical file of all SOPs.

(12) Designate personnel responsible for the management of the archive(s) (hereinafter referred to as "Archivist").

(13) Designate personnel responsible for the management of test and reference items.

(14) Designate personnel responsible for the management of the apparatus.

(15) Approve the master schedule and maintain it.

(16) Ensure that the test facility supplies meet requirements appropriate to their use in a study.

(17) Establish a close communication system among the Study Director, Principal Investigator(s), the Quality Assurance Programme and study personnel, particularly in the event of a multi-site study.

(18) Ensure that test and reference item are appropriately characterized.

(19) Establish procedures to ensure that computerized system are validated, operated and maintained in accordance with the GLP for Agricultural Chemicals.

2. When a phase(s) of a study is conducted at a test site, test site management (if appointed) will have the responsibilities as defined above with the following exceptions:1.(7), (9), (10) and (17).

(Study Director's Responsibilities)

Article 4.

1. The Study Director is the single point of study control and has the responsibility for the overall conduct of the study and for its final report.

2. The Study Director should:
   (1) Approve the study plan and any amendments to the study plan by dated signature or seal.

(2) Forward the copy of the approved study plan and any amendments to the Quality Assurance Programme in a timely manner and communicate effectively with the Quality Assurance Programme as required during the conduct of the study.

(3) Ensure the study plan and amendments and SOPs are available to study personnel.

(4) Ensure that the study plan and the final report for a multi-site study identify and define the role of any Principal Investigator(s), any test facilities and test sites involved in the conduct of the study.

(5) Conduct the study in accordance with the procedures specified in the study plan, assess and document the impact of any deviations from the study plan on the quality and integrity of the study, and take appropriate corrective action if necessary; acknowledge deviations from the SOPs during the conduct of the study, and documented them.

(6) Ensure that all raw data generated are fully documented and recorded and signed or sealed to the data with the date.

(7) Ensure that the computerized systems used in the study have been validated, if the system is used.

(8) Sign or seal and date the final report to indicate acceptance of responsibilities for the validity of the data and to indicate the extent to which the study complies with the GLP for Agricultural Chemicals.

(9) Ensure that after completion of the study, the study plan, the final report, raw data and supporting materials are archived.

(Principal Investigator's responsibilities)

Article 5.

The principal Investigator should conduct the delegated phases of the study in accordance with the GLP for Agricultural Chemicals.

(Study Personnel's responsibilities)

Article 6.

1. All personnel involved in the conduct of the study must be knowledgeable in those parts of the GLP for Agricultural Chemicals which are applicable to their involvement in the study.

2. Study personnel should:
   (1) Have access to the study plan and appropriate SOPs applicable to their involvement of the study. It is their responsibility to comply with the instructions given in these documents. Any deviations from these instructions should be documented and directly reported to the Study Director and/or the Principal Investigator(s) (if appointed)).

   (2) Be responsible for recording raw data promptly and accurately in accordance with the GLP for Agricultural Chemicals and be responsible for the quality of their data.

   (3) Exercise health precaution to minimize risk to themselves and to ensure the integrity of the study. They should report to the Study Director and/or Principal Investigator(s) about their relevant known health or medical condition, which can be considered to be related to the conduct of the study, in order that they can be excluded from operations that may affect the study.

(The responsibilities of Quality Assurance Programme)

Article 7.

1. The test facility should have a Quality Assurance Programme to assure that the studies performed are in compliance with the GLP for Agricultural Chemicals.

2. The Quality Assurance Programme, designated by and directly responsible to the TFM, should be familiar with study procedures.

3. The Quality Assurance Programme personnel should not be involved in the conduct of the studies being assured.

4. The Quality Assurance Programme should:
   (1) Maintain copies of all approved study plans and SOPs in use in the test facility and an up-to-date copy of the master schedule.

   (2) Verify that the study plan contains the information required for compliance with the GLP for Agricultural Chemicals. The verification should be documented.

   (3) Conduct inspections to determine if all studies are conducted in accordance with the GLP for Agricultural Chemicals. Inspection should also determine that the study plans and SOPs have been made available to the study personnel and are being followed.

   (4) Clearly describe the methods of the following, relevant to inspection in the SOPs for the Quality Assurance Programme. However, inclusion of iii) is not required, if not applicable.
   i) Study-based inspections
   ii) Facility-based inspections
   iii) Process-based inspections
   Records of such inspections should be retained.

   (5) Inspect the final reports to confirm that the methods, procedures, and observations are accurately and completely described, and that the reported results accurately and completely reflect the raw data of the studies.

   (6) Promptly report any inspections in writing to the TFM and to the Study Director, and to the Principal Investigator(s) and the respective test site management, when applicable.

   (7) Prepare and sign or seal a statement, to be included with the final report, which specifies types of inspections and their dates, including the phase(s) of the study inspected and the dates inspection results were reported to the TFM, the Study Director and Principal Investigator(s), if applicable. .

Chapter 3: Facilities, Apparatus, Material and Reagents

(Facilities)

Article 8.

Test facilities should be in compliance with the items specified in the following, depending on the studies conducted:

1. The test facility should be of suitable size, construction and location to meet the requirements of the study and to minimize disturbance that would interfere with the validity of the study.

2. The design of the test facility should provide an adequate degree of separation of the different activities to assure the proper conduct of each study.

3. The test facility should have a sufficient number of rooms or areas in order to separate the individual test

systems and studies from those substances or organisms known to be or suspected of being bio-hazardous.

4. Test facility should have suitable rooms or areas available for diagnosis, treatment and control of diseases, in order to ensure that there is no unacceptable degree of deterioration of test systems.

5. Test facility should have storage rooms or areas for apparatus. Storage rooms or areas should be separated from rooms or areas housing the test systems and should provide adequate protection against infestation, contamination and/or deterioration.

6. To prevent contamination or mix-ups, there should be separate rooms or areas for receipt and storage of the test and reference items, and mixing of the test items with a vehicle.

7. Storage rooms or areas for the test and reference item should be separated from rooms or areas containing test systems. They should be adequate to preserve identity, concentration, purity and stability, and ensure safe storage for hazardous substances.

8. Archive facilities should be provided for the secure storage and retrieval systems of study plans, raw data, final reports, samples of test items and reference items, and specimens. Archive design and archive condition should protect contents from untimely deterioration.

(Handling and disposal of Wastes)

Article 9.

Handling and disposal of wastes should be carried out in such a way as not to jeopardise the integrity of the studies. This includes provision for appropriate collection, storage and disposal facilities, and decontamination and transportation procedures.

(Apparatus, Materials and Reagents)

Article 10.

1. Apparatus, including validated computerized systems, used for the generation, storage and retrieval of data, and for controlling environmental factors relevant to study should be suitably located and of appropriate design and adequate capacity.

2. Apparatus used in a study should be periodically checked, cleaned, maintained, and calibrated in accordance with SOPs. Records of these activities should be maintained. Calibration should, where appropriate, be traceable to national or international standards of measurement.

3. Apparatus and materials used in a study should not interfere adversely with the test systems.

4. Chemicals, reagents, and solution should be labelled to indicate identity (with concentration if appropriate), expiry date and specific storage instructions. Information concerning source, manufacture or preparation date and stability should be available. The expiry date may be extended on the basis of documented evaluation or analysis.

Chapter 4: Operation and Handling of Test item, etc.

(Test systems)
Article 11.

1. Physical/chemical

(1) Apparatus used for the generation of physical/chemical data should be suitably located and of appropriate design and adequate capacity.

(2) The integrity of the physical/chemical test systems should be ensured.

2. Biological (if applicable)
   (1) Proper condition should be established and maintained for the storage, housing, handling and care of biological test systems, in order to ensure quality of the data.

   (2) Newly received animal and plant test systems should be isolated until their health status has been evaluated.

   (3) If any unusual mortality or morbidity occurs, this lot should not be used in studies and, when appropriate, should be humanely destroyed.

   (4) At the experimental starting date of a study, it should be ensured that test systems should be free from any disease or condition that might interfere with the purpose or conduct of the study.

   (5) Test systems that become diseased or injured during the course of a study should be isolated and treated, if necessary to maintain the integrity of the study.

   (6) Any diagnosis and treatment of any disease before or during a study should be recorded.

   (7) Records of source, date of arrival, and arrival condition of test systems should be maintained.

   (8) Biological test system should be acclimatized to the test environment for an adequate period before the first administration/application of the test or reference item.

   (9) All information needed to properly identify the test systems should appear on their housing or containers. Individual test systems that are to be removed from their housing or containers during the conduct of the study should bear appropriate identification.

   (10) During use, housing or containers for test systems should be cleaned and sanitary condition of them should be maintained. Any material that comes into contact with the test system should be free of contaminants at levels that would interfere with the study. Bedding for animals should be changed as required by sound husbandry practice. Use of pest control agents or disinfectants should be documented.

   (11) Test systems used in field studies should be located so as to avoid interference in the study from spray drift and from past usage of Agricultural Chemicals.

(Receipt, handling, sampling and storage of test and reference items)

Article 12.

1. Records including test item and reference item characterization, date of receipt, expiry date, quantities received and used in studies should be maintained.

2. Handling, sampling, and storage procedures should be identified in order that the homogeneity and stability are assured to the degree possible and contamination or mix-up are precluded.

3. Storage container(s) should carry identification information, expiry date, and specific storage instructions.

4. Each test and reference item should be appropriately identified (e.g., code, Chemical Abstracts Service Registry Number [CAS number], name, biological parameters).

5. For each study, the identity of the test or reference items should be known (the identity includes batch or lot number, purity, composition, concentrations, or other characteristics to appropriately define each batch or lot of these items.).

6. In cases where the test item is supplied by the sponsor, there should be a mechanism developed in co-operation between the sponsor and the test facility to verify the identity of the test item subject to the study.

7. The stability of test and reference items under storage and test conditions should be known for all studies.

8. If the test item is administered or applied in a vehicle, the homogeneity, concentration and stability of the test item in that vehicle should be determined.

9. A sample for analytical purpose from each batch or lot of test item should be retained for all studies except those studies of which experimental period are shorter than 4 weeks.

(SOPs)

Article 13.

1. A test facility should have written SOPs approved by the TFM that are intended to ensure the quality and integrity of all data generated by that test facility. Revision to the SOPs should be approved by the TFM.

2. Each separate test facility unit or area should have available current SOPs relevant to the activities being performed therein. Published text books, analytical methods, article and manuals may be used as supplements to these SOPs.

3. Deviations from SOPs related to the study should be documented and should be acknowledged by the Study Director and the Principal Investigator(s), as applicable.

4. At a minimum, the following categories of test facility activities should be included in SOPs:
   (1) Test and reference items
   Receipt, identification, labelling, handling, sampling and storage.

   (2) Apparatus
   Use, maintenance, cleaning and calibration.

   (3) Computerized systems
   Validation, operation, maintenance, security, change control and back-up.

   (4) Materials, reagents and solutions
   Preparation and labeling

   (5) Record keeping, reporting, storage, and retrieval
   Coding of studies, data collection, preparation of report, indexing systems, handling of data, including the use of computerized systems.

   (6) Test system (where applicable)
   a) Room preparation and environmental room conditions for test system.
   b) Procedures for receipt, transfer, proper placement, characterization, identification and care of the test system.
   c) Test system preparation, observations and examinations, before, during and at the conclusion of the study.
   d) Handling of test system individuals found moribund or dead during the study.
   e) Collection, identification and handling of specimens including necropsy and histopathology.
   f) Sitting and placement of test systems in test plots.

   (7) Quality assurance procedures
   Operation of Quality Assurance personnel in planning, performing, documenting and reporting inspections.

Chapter 5: Study plan and performance of study

(Study plan)

Article 14.

1. For each study, a written study plan should be prepared prior to the initiation of the study. The study plan should be approved by the Study Director with his dated signature or seal and also verified for GLP compliance by Quality assurance personnel as specified in Article 7-4-(2) above.

2. Amendments to the study plan should be approved by the Study Director with his dated signature or seal, and should be maintained with the study plan.

3. Deviations from the study plan should be described, explained, and approved by the Study Director and/or Principal Investigator(s) with his (their) dated signature or seal and maintained with the study raw data.

4. At a minimum, the study plan should contain the following information:
   (1) Identification of the study, the test item and reference item
      a) A descriptive title
      b) A statement which reveals the nature and purpose of the study
      c) Identification of the test item by its name, abbreviation or code number
      d) The reference item to be used

   (2) Information concerning the sponsor and the test facility
      a) Name and address of the sponsor
      b) Name and address of any test facilities and test sites involved
      c) Name and affiliation of the Study Director
      d) Name and affiliation of the Principal Investigator(s), and the phase(s) of the study delegated by the Study Director and under the responsibility of the Principal Investigator(s).

   (3) Dates
      a) The study initiation date
      b) The proposed experimental starting and completion dates

   (4) Test methods
      Reference to the test guideline (e.g. the test guideline notified the Director-General, MAFF and the OECD test guideline) to be used.

   (5) Issues (where applicable)
      a) The justification for selection of the test system
      b) Characterization of the test system (e.g. the species, strain, substrain, source of supply, number, body weight range, sex, age and other pertinent information)
      c) The method of administration or application of test or reference item and the reason for the choice
      d) The dose levels and/or concentration(s), frequency, and duration of administration/applications
      e) Detailed information on the experimental design, including a description of the chronological procedure of the study, all methods, materials and conditions, type and frequency of analysis, measurements, observations and examinations to be performed, and statistical methods to be used.

   (6) Records
      A list of records to be retained

(Conduct of the study)

Article 15.

1. A unique identification should be given to each study. Specimens from the study should be identified to confirm their origin.

2. The study should be conducted in accordance with the study plan.

3. All data generated during the conduct of the study should be recorded promptly, accurately, and legibly by the individual entering the data. These entries should be signed or sealed and dated.

4. Any change in the raw data should be made so as not to obscure the previous entry, should indicate the reason for change and should be dated and signed or sealed by the individual making the change.

5. Data generated as a direct computer input should be identified at the time of data input by the individual(s) responsible for direct data entries. Computerized system should be designed to change the data without obscuring the original data

Chapter 6: Reporting of study results and storage.

(Reporting of study results)
Article 16.

1. A final report should be prepared for each study.

2. Reports of the Principal Investigator(s) or scientist(s) involved in the study should be signed or sealed and dated by them.

3. The final report should be signed or sealed and dated by the Study Director to indicate his responsibility for the validity of the data. A GLP compliance statement, which describes that the study was conducted in compliance with the GLP for Agricultural Chemicals, should be also signed or sealed and dated by the Study Director and be included in or attached to the final report.

4. Corrections and additions to a final report should clearly describe (specify) the reason for the corrections or additions in the final report and should be signed or sealed and dated by the Study Director.

5. At a minimum, the final report should include the following information:
   (1) Identification of the study, test item and reference item
      a) A descriptive title
      b) Identification of the test item by its name, abbreviation or code number
      c) The name of reference item to be used
      d) Characterization of the test item including purity, stability and homogeneity

   (2) Information concerning the sponsor and the test facility
      a) Name and address of the sponsor
      b) Name and address of any test facilities and test sites involved
      c) Name and affiliation of the Study Director
      d) Name and affiliation of the Principal Investigator(s) and the phase(s) of the study delegated, if applicable.
      e) Name and affiliation of scientists having contributed reports to the final report.

   (3) Dates
      a) Study initiation date
      b) Experimental starting and completion dates

   (4) Quality Assurance Pragramme Statement
      A Quality Assurance Programme statement listing the types of inspections made and their dates, including the phase(s) inspected, and their dates any inspection results were reported to the TFM (also to Test site management(s), if appointed) and the Study Director and the Principal Investigator(s), if applicable.

   (5) Description of materials and test methods
      a) Description of methods and materials used.
      b) Reference to the test guideline (e.g. the test guideline notified by the Director-General, MAFF and

the OECD test guideline) used.

(6) Results
   a) A summary of results
   b) All information and data required by the study plan
   c) A presentation of the results, including calculation and determination of statistical significance
   d) An evaluation and discussions of the results and, where appropriate, conclusions

(7) Storage
   The location(s) where the study plan, samples of test and reference items, specimens, raw data and the final report are to be stored.

(Storage and retention of records and materials)

Article 17

1. The following (1) should be retained for at least 5 years and (2) to (8) should be also retained for at least 15 years in the archives in the test facility, where the study was conducted, after the registration of the agricultural chemicals relevant to the study.
   After that, they may as well be moved to the proprietor like the sponsor. But, when moving them, the test facility should keep the record concerning the movement, and the proprietor should attempt to prevent their dissipation.
   (1) Samples of test and reference items, and specimens

   (2) The study plan, raw data and the final report of each study

   (3) Master schedule and records of all inspections performed by the Quality Assurance Programme.

   (4) Records of qualifications, training, experience and job description of personnel

   (5) Records and reports of the maintenance and calibration of apparatus

   (6) Validation documentation of computerized systems

   (7) The historical file of all SOPs

   (8) Environmental monitoring records

2. When samples of test and reference items and specimens are disposed before the expiry of the retention period required by the preceding paragraph, this should be justified and documented. Samples of test and reference items and specimens should be retained as long as the quality of the preparation permits evaluation.

3. Material retained in the archives should be indexed so as to facilitate orderly storage and retrieval.

4. Only Archivist and the personnel permitted by the Archivist should have access to the archives. Movement of the personnel and material in and out of the archives should be recorded.

(The provision for the closing of test facilities)

Article 18.

If a test facility goes out of business and has no legal successor, the material in the archives should be transferred to the archives of the sponsor(s) of the study(s).