SCHEDULE 1 Regulation 2(1)

PRINCIPLES OF GOOD LABORATORY PRACTICE (BASED ON ANNEX 2 TO THE DECISION OF 12TH MAY 1981 OF THE COUNCIL OF THE OECD ON THE MUTUAL ACCEPTANCE OF DATA FOR THE EVALUATION OF CHEMICAL PRODUCTS)

PART I

LABORATORY ORGANISATION AND PERSONNEL

The management's responsibilities

1.—(1) Laboratory management should ensure that the principles of good laboratory practice are complied with in laboratory premises.

(2) At a minimum it should—

(a) ensure that qualified personnel, appropriate facilities, equipment, and materials are available;

(b) maintain a record of the qualifications, training, experience and job description for each professional and technical individual;

(c) ensure that personnel clearly understand the functions they are to perform and, where necessary, provide training for those functions;

(d) ensure that health and safety precautions are applied according to national and/or international regulations;

(e) ensure that appropriate standard operating procedures are established and followed;

(f) ensure that there is a quality assurance programme with designated personnel;

(g) where appropriate, agree the study plan in conjunction with the sponsor;

(h) ensure that amendments to the study plan are agreed upon and documented;

(i) maintain copies of all study plans;

(j) maintain a historical file of all standard operating procedures;

(k) for each safety study ensure that a sufficient number of personnel is available for its timely and proper conduct;

(l) for each safety study designate an individual with appropriate qualifications, training, and experience as the study director before the safety study is initiated. If it is necessary to replace a study director during a safety study, this should be documented;

(m) ensure that an individual is identified as responsible for the management of the archives.

The study director's responsibilities

2.—(1) The study director has the responsibility for the overall conduct of the safety study and for its report.

(2) These responsibilities should include, but not be limited to, the following functions—

(a) agreeing to the study plan;

(b) ensuring that the procedures specified in the study plan are followed, and that authorisation for any modification is obtained and documented together with the reasons for them;

(c) ensuring that all data generated are fully documented and recorded;

(d) signing and dating the final report to indicate acceptance of responsibility for the validity of the data and to confirm compliance with the principles of good laboratory practice;

(e) ensuring that after termination of the safety study, the study plan, the final report, raw data and supporting material are transferred to the archives.

Personnel responsibilities

3.—(1) Personnel should exercise safe working practices. Chemicals should be handled with suitable caution until their hazard has been established.

(2) Personnel should exercise health precautions to minimise risk to themselves and to ensure the integrity of the safety study.

(3) Personnel known to have a health or medical condition that is likely to have an adverse effect on the safety study should be excluded from operations that may affect the safety study.

PART II

QUALITY ASSURANCE PROGRAMME

General

4.—(1) The laboratory should have a documented quality assurance programme to ensure that studies performed are in compliance with the principles of good laboratory practice.

(2) The quality assurance programme should be carried out by an individual or by individuals designated by and directly responsible to management and who are familiar with the test procedures.

(3) This individual or these individuals should not be involved in the conduct of safety study being assured.

(4) This individual or these individuals should report any findings in writing directly to management and to the study director.

Responsibilities of the quality assurance personnel

5.—(1) The responsibilities of the quality assurance personnel should include, but not be limited to, the following functions—

(a) ascertaining that the study plan and standard operating procedures are available to personnel conducting the safety study;

(b) ensuring that the study plan and standard operating procedures are followed by periodic inspections of the laboratory and/or by auditing the safety study in progress. Records of such procedures should be retained;

(c) promptly reporting to management and the study director unauthorised deviations from the study plan and from standard operating procedures;

(d) reviewing the final reports to confirm that the methods, procedures, and observations are accurately described, and that the reported results accurately reflect the raw data of the safety study;

(e) preparing and signing a statement, to be included with the final report, which specifies the dates inspections were made and the dates any findings were reported to management and to the study director.

PART III

FACILITIES

General

6.—(1) The laboratory should be of suitable size, construction and location to meet the requirements of the safety study and minimise disturbances that would interfere with the validity of the safety study.

(2) The design of the laboratory should provide an adequate degree of separation of the different activities to ensure the proper conduct of each safety study.

Test system facilities

7.—(1) The laboratory should have a sufficient number of rooms or areas to ensure the isolation of test systems and the isolation of individual projects, involving substances known or suspected of being biohazardous.

(2) Suitable facilities should be available for the diagnosis, treatment and control of diseases, in order to ensure that there is no unacceptable degree of deterioration of test systems.

(3) There should be storage areas as needed for supplies and equipment. Storage areas should be separated from areas housing the test systems and should be adequately protected against infestation and contamination. Refrigeration should be provided for perishable commodities.

Facilities for handling test and reference substances

8.—(1) To prevent contamination or mix-ups, there should be separate areas for receipt and storage of the test and reference substances, and for the mixing of the test substances with a vehicle.

(2) Storage areas for the test substances should be separate from areas housing the test systems and should be adequate to preserve identity, concentration, purity, and stability, and ensure safe storage for hazardous substances.

Archive facilities

9. Space should be provided for archives for the storage and retrieval of raw data, reports, samples and specimens.

Waste disposal

10.—(1) Handling and disposal of wastes should be carried out in such a way as not to jeopardise the integrity of studies in progress.

(2) The handling and disposal of wastes generated during the performance of a safety study should be carried out in a manner which is consistent with pertinent regulatory requirements. This includes provision for appropriate collection, storage and disposal facilities, decontamination and transportation procedures, and the maintenance of records related to the preceding activities.

PART IV

APPARATUS, MATERIALS AND REAGENTS

Apparatus

11.—(1) Apparatus used for the generation of data and for controlling environmental factors relevant to the safety study should be suitably located and of appropriate design and adequate capacity.

(2) Apparatus used in a safety study should be periodically inspected, cleaned, maintained and calibrated according to standard operating procedures. Records of procedures should be maintained.

Materials

12. Apparatus and materials used in studies should not interfere with the test systems.

Reagents

13. Reagents should be labelled, as appropriate, to indicate source, identity, concentration and stability information, and should include the preparation date, earliest expiration date and specific storage instructions.

PART V

TEST SYSTEMS

Physical/chemical

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

(2) Reference substances should be used to assist in ensuring the integrity of the physical/chemical test systems.

Biological

15.—(1) Proper conditions should be established and maintained for the housing, handling and care of animals, plants, and microbial as well as other cellular and sub-cellular systems, in order to ensure the quality of the data.

(2) In addition, conditions should comply with appropriate national regulatory requirements for the import, collection, care and use of animals, plants, and microbial as well as other cellular and sub-cellular systems.

(3) Newly received animal and plant test systems should be isolated until their health status has been evaluated. If any unusual mortality or morbidity occurs, this lot of test systems should not be used in studies and, when appropriate, humanely destroyed.

(4) Records of source, date of arrival and arrival condition should be maintained.

(5) Animal, plant, and microbial as well as other cellular and sub-cellular test systems should be acclimatised to the test environment for an adequate period before a safety study is initiated.

(6) All information needed to properly identify the test systems should appear on their housing or containers.

(7) The diagnosis and treatment of any disease before or during a safety study should be recorded.

PART VI

TEST AND REFERENCE SUBSTANCES

Receipt, handling, sampling and storage

16.—(1) Records including substance characterisation, date of receipt and quantities received and used in studies should be maintained.

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

(3) Storage containers should carry identification information, earliest expiration date and specific storage instructions.

Characterisation

17.—(1) Each test and reference substance should be appropriately identified (e.g. code, chemical abstract number (CAS), name).

(2) For each safety study, the identity, including batch number, purity, composition, concentrations, or other characterisations to appropriately define each batch of the test or reference substances should be known.

(3) The stability of test and reference substances under conditions of storage should be known for all studies.

(4) The stability of test and reference substances under the test conditions should be known for all studies.

(5) If the test substance is administered in a vehicle, standard operating procedures should be established for testing the homogeneity and stability of the test substance in that vehicle.

(6) A sample for analytical purposes from each batch of test substance should be retained for studies in which the test substance is tested for longer than four weeks.

PART VII

STANDARD OPERATING PROCEDURES

General

18.—(1) A laboratory should have written standard operating procedures approved by management that are intended to ensure the quality and integrity of the data generated in the course of the safety study.

(2) Each separate laboratory unit should have immediately available standard operating procedures relevant to the activities being performed therein. Published text books, articles and manuals may be used as supplements to these standard operating procedures.

Application

19.—(1) Standard operating procedures should be available for, but not be limited to, the following categories of laboratory activities. The details given under each heading are to be considered as illustrative examples—

(a) Test and reference substances

receipt, identification, labelling, handling, sampling and storage;

(b) Apparatus and reagents

use, maintenance, cleaning, calibration of measuring apparatus and environmental control equipment; preparation of reagents;

(c) Record keeping, reporting, storage and retrieval

coding of studies, data collection, preparation of reports, indexing systems, handling of data, including the use of computerised data systems;

(d) Test system (where appropriate)

(i) room preparation and environmental room conditions for the test system,

(ii) procedures for receipt, transfer, proper placement, characterisation, identification and care of test system,

(iii) test system preparation, observation examinations before, during and at termination of the safety study,

(iv) handling of test system individuals found moribund or dead during the safety study,

(v) collection, identification and handling of specimens including necropsy and histopathol ogy;

(e) Quality assurance procedures

operation of quality assurance personnel in performing and reporting study audits, inspections and final study report reviews;

(f) Health and safety precautions

as required by national and/or international legislation or guidelines.

PART VIII

PERFORMANCE OF THE SAFETY STUDY

Study plan

20.—(1) For each safety study, a plan should exist in a written form prior to initiation of the study.

(2) The study plan should be retained as raw data.

(3) All changes, modifications, or revisions of the study plan, as agreed to by the study director, including justifications, should be documented, signed and dated by the study director, and maintained with the study plan.

Content of the study plan

21.—(1) The study plan should contain, but not be limited to, the following information—

(a) Identification of the test and reference substance

(i) a descriptive title,

(ii) a statement which reveals the nature and purpose of the safety study,

(iii) identification of the test substance by code or name (IUPAC, CAS number, etc.),

(iv) the reference substance to be used;

(b) Information concerning the sponsor and the laboratory

(i) name and address of the sponsor,

(ii) name and address of the laboratory,

(iii) name and address of the study director;

(c) Dates

(i) the date of agreement to the study plan by signature of the study director, and when appropriate, of the sponsor and/or the laboratory management,

(ii) the proposed starting and completion dates;

(d) Test methods

reference to OECD test guidelines or other test guidelines to be used;

(e) Issues (where applicable)

(i) the justification for selection of the test system,

(ii) characterisation of the test system, such as the species, strain, substrain, source of supply, number, body weight range, sex, age and other pertinent information,

(iii) the method of administration and the reason for its choice,

(iv) the dose levels and/or concentration, frequency, duration of administration,

(v) detailed information on the experimental design, including a description of the chronological procedure of the safety study, all methods, materials and conditions, type and frequency of analysis, measurements, observations and examinations to be performed;

(f) Records

a list of records to be retained.

Conduct of the safety study

22.—(1) A unique identification should be given to each safety study. All items concerning this safety study should carry this identification.

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

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

(4) Any change in the raw data should be made so as not to obscure the previous entry, and should indicate the reason, if necessary, for change and should be identified by date and signed 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 responsible for direct data entries. Corrections should be entered separately with the reason for the change, the date and the identity of the individual making the change.

PART IX

REPORTING OF SAFETY STUDY RESULTS

General

23.—(1) A final report should be prepared for the safety study.

(2) The use of the International System of Units (SI) is recommended.

(3) The final report should be signed and dated by the study director.

(4) If reports of principal scientists from co-operating disciplines are included in the final report, they should sign and date them.

(5) Corrections and additions to a final report should be in the form of an amendment. The amendment should clearly specify the reason for the corrections or additions and should be signed and dated by the study director and by the principal scientist from each discipline involved.

Content of the final report

24. The final report should include, but not be limited to, the following information—

(a) Identification of the test and reference substance

(i) a descriptive title,

(ii) identification of the test substance by code or name (IUPAC, CAS number, etc.),

(iii) identification of the reference substance by chemical name,

(iv) characterisation of the test substance including purity, stability and homogeneity;

(b) Information concerning the laboratory

(i) name and address,

(ii) name of the study director,

(iii) name of other principal personnel having contributed reports to the final report;

(c) Dates

dates on which the safety study was initiated and completed;

(d) Statement

a quality assurance statement certifying the dates inspections were made and the dates any findings were reported to management and to the study director;

(e) Description of materials and test methods

(i) description of methods and materials used,

(ii) reference to OECD test guidelines or other test guidelines;

(f) Results

(i) a summary of results,

(ii) all information and data required in the study plan,

(iii) a presentation of the results, including calculations and statistical methods,

(iv) an evaluation and discussion of the results and, where appropriate, conclusions;

(g) Storage

The location where all samples, specimens, raw data and the final report are to be stored.

PART X

STORAGE AND RETENTION OF RECORDS AND MATERIAL

Storage and retrieval

25.—(1) Archives should be designed and equipped for the accommodation and the secure storage of—

(a) the study plans;

(b) the raw data;

(c) the final reports;

(d) the reports of laboratory inspections and study audits performed according to the quality assurance programme;

(e) samples and specimens.

(2) Material retained in the archives should be indexed so as to facilitate orderly storage and rapid retrieval.

(3) Only personnel authorised by management should have access to the archives. Movement of material in and out of the archives should be properly recorded.

Retention

26.—(1) The following should be retained for the period specified by the appropriate authorities—

(a) the study plan, raw data, samples, specimens and the final report of each safety study;

(b) records of all inspections and audits performed by the quality assurance programme;

(c) summary of qualifications, training, experience and job descriptions of personnel;

(d) records and reports of the maintenance and calibration of equipment;

(e) the historical file of standard operating procedures.

(2) Samples and specimens should be retained only as long as the quality of the preparation permits evaluation.

(3) If a laboratory or an archive contracting facility goes out of business and has no legal successor, the archive should be transferred to the archives of the sponsor of the safety study.