STATUTORY INSTRUMENTS

1997 No. 654

HEALTH AND SAFETY

The Good Laboratory Practice Regulations 1997

Made - - - -	*6th March 1997*
Laid before Parliament	*7th March 1997*
Coming into force - -	*1st April 1997*

The Secretary of State, being the Minister designated(**1**) for the purposes of section 2(2) of the European Communities Act 1972(**2**) in relation to measures relating to the control of laboratories carrying out tests on chemical products, in exercise of the powers conferred by the said section 2(2) and, with the consent of the Treasury, the powers conferred by section 56(1) and (2) of the Finance Act 1973(**3**), and of all other powers enabling him in that behalf, hereby makes the following Regulations—

Citation and commencement

1. These Regulations may be cited as the Good Laboratory Practice Regulations 1997 and shall come into force on 1st April 1997.

Interpretation

2.—(1) In these Regulations, unless the context otherwise requires—

"batch" means a specific quantity or lot of a test or reference substance 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;

"the GLP Inspection and Verification Directive" means Council Directive 88/320/EEC of 9th June 1988 on the inspection and verification of Good Laboratory Practice (GLP)(**4**), as amended by Commission Directive 90/18/EEC of 18th December 1989 adapting to technical progress the Annex to Council Directive 88/320/EEC on the inspection and verification of good laboratory practice (GLP)(**5**);

"laboratory" means a test facility which conducts or which intends to conduct safety studies;

(**1**) S.I.1991/755.
(**2**) 1972 c. 68.
(**3**) 1973 c. 51.
(**4**) OJ No. L145, 11.6.88, p. 35.
(**5**) OJ No. L11, 13.1.90, p. 37.

"monitoring authority" means any national authority which is responsible (either solely or jointly with other such authorities) for monitoring adherence to the principles of good laboratory practice;

"OECD" means the Organisation for Economic Co-operation and Development;

"OECD test guideline" means a test guideline which the OECD has recommended for use in its member countries;

"operator", in relation to a laboratory, means the person having control of the laboratory;

"premises", in relation to a laboratory, includes field sites at which safety studies are conducted;

"principles of good laboratory practice" means the principles of good laboratory practice set out in Schedule 1 to these Regulations, which are based on the principles of good laboratory practice contained in Annex 2 to the Decision of the Council of the OECD of 12th May 1981 on the mutual acceptance of data for the evaluation of chemical products(**6**), read with the guidance on inspection procedures and study audits set out in Schedule 2 to these Regulations, which is based on Annex B of the GLP Inspection and Verification Directive;

"quality assurance programme" means an internal control system designed to ascertain that the safety study is in compliance with these principles of good laboratory practice;

"raw data" means all original laboratory records and documentation, or verified copies thereof, which are the result of the original observations and activities in a safety study;

"reference substance" means any well defined substance or any mixture other than the test substance used to provide a basis for comparison with the test substance;

"regulatory authority" means any national authority with legal responsibility for aspects of the control of chemicals;

"safety study" means a non-clinical experiment or set of experiments—

(a) in which a substance is examined to evaluate its safety with respect to human health, animal health or the environment; and

(b) in relation to which a Community provision provides for the application of the principles of good laboratory practice in respect of that experiment or set of experiments;

"sample" means any quantity of a test or reference substance;

"specimen" means any material derived from a test system for examination, analysis, or storage;

"sponsor" means a person or entity who commissions or pays for a safety study;

"standard operating procedures" means written procedures which describe how to perform certain routine laboratory tests or activities normally not specified in detail in study plans or test guidelines;

"study director" means the individual responsible for the overall conduct of the safety study;

"study plan" means a document which defines the entire scope of the safety study;

"test substance" means a substance or a mixture which is under investigation;

"test system" means any animal, plant, microbial, cellular, sub-cellular, chemical, or physical system or a combination thereof used in a safety study;

"vehicle" means any agent which serves as a carrier used to mix, disperse, or solubilise the test or reference substance to facilitate the administration to the test system.

(2) In these Regulations, unless the context otherwise requires, a reference—

(**6**) The text of this Annex is included in chapter 2 of "Good Laboratory Practice in the Testing of Chemicals—Final Report of the OECD Group of Experts on Good Laboratory Practice"(ISBN 92-64-12367-9), which may be obtained from the OECD Publications Office, 2 rue André-Pascal, 75775 Paris Cedex 16.

(a) to a numbered regulation or Schedule is to the regulation in or Schedule to these Regulations bearing that number;

(b) in a regulation to a numbered or lettered paragraph is to the paragraph of that regulation bearing that number or letter; and

(c) in a paragraph to a numbered or lettered sub-paragraph is to the sub-paragraph in that paragraph bearing that number or letter.

Functions of the Secretary of State

3. The Secretary of State—

(a) is designated as the authority within the United Kingdom responsible for—

(i) the verification of compliance with the principles of good laboratory practice within the United Kingdom,

(ii) the inspection of laboratories within the United Kingdom and the audit of studies carried out by laboratories to assess compliance with the principles of good laboratory practice, and

(iii) any other functions of the United Kingdom's good laboratory practice monitoring authority arising out of or related to any Community obligation or the United Kingdom's enjoyment of rights deriving from the Community's cooperation with the OECD under or by virtue of the Treaties; and

(b) shall enforce compliance with these Regulations.

Requirement to be a member or a prospective member of the United Kingdom good laboratory practice compliance programme

4. A safety study shall not be conducted at any premises of a laboratory unless—

(a) the operator of the laboratory is regarded by virtue of regulation 5 or 6 as a member or a prospective member of the United Kingdom good laboratory practice compliance programme; and

(b) the operator's membership or prospective membership of that programme is or is partly in respect of those premises,

and if a safety study is conducted at any premises of a laboratory in contravention of this regulation, the operator of that laboratory shall be guilty of an offence.

Prospective membership of the United Kingdom good laboratory practice compliance programme

5.—(1) An operator of a laboratory shall, for the purposes of these Regulations, be regarded as being a prospective member of the United Kingdom good laboratory practice compliance programme in respect of particular laboratory premises only if—

(a) he has informed the Secretary of State by notice in writing of the intention to conduct safety studies at those premises;

(b) the Secretary of State has in writing—

(i) acknowledged receipt of that notification, and

(ii) informed the operator that he is a prospective member of the programme in respect of those premises,

and he has not ceased to be regarded as a prospective member of the programme in respect of those premises by virtue of paragraph (2).

(2) Subject to paragraph (3), an operator of a laboratory shall cease to be regarded as a prospective member of the United Kingdom good laboratory practice compliance programme in respect of particular laboratory premises if—

(a) he is admitted to membership of the programme in respect of those premises by the Secretary of State;

(b) he informs the Secretary of State in writing that he no longer conducts or intends to conduct safety studies at those premises; or

(c) the Secretary of State informs him in writing that he is not prepared to admit him to membership of the programme in respect of those premises.

(3) The Secretary of State shall, before informing a prospective member of the United Kingdom good laboratory practice compliance programme under paragraph (2)(c) that he is not prepared to admit him to membership of the programme in respect of particular laboratory premises—

(a) inform the prospective member that he is considering taking such action and explain to him in writing the reasons why such action is being considered;

(b) give the operator a specified period within which to make representations to him; and

(c) consider any representations which are duly made and not withdrawn,

unless either there is a failure to adhere to the principles of good laboratory practice at those premises which, in the opinion of the Secretary of State, may contribute towards precipitating a danger to animal or human health or to the environment or in order to ensure fulfilment of any Community obligation, it is necessary for the Secretary of State to inform the prospective member immediately that he is not prepared to admit him to membership of the programme in respect of those premises.

Membership of the United Kingdom good laboratory practice compliance programme

6.—(1) Subject to paragraph (2) and except where paragraph (5) applies, the operator of a laboratory shall be regarded as being a member of the United Kingdom good laboratory practice compliance programme in respect of particular laboratory premises if—

(a) he is regarded by the Secretary of State as being a member of the programme in respect of those premises immediately before these Regulations come into force; or

(b) after having inspected those premises, the Secretary of State has informed the operator in writing that he is admitting the operator to membership of the programme in respect of those premises.

(2) The operator of a laboratory shall cease to be a member of the United Kingdom good laboratory practice compliance programme in respect of particular laboratory premises if—

(a) he has informed the Secretary of State by notice in writing that safety studies are no longer conducted at those premises; or

(b) membership of the programme in respect of those premises has been withdrawn from him by the Secretary of State in accordance with paragraph (3).

(3) Subject to paragraph (4), the Secretary of State may by a notice in writing served on the operator of a laboratory withdraw the operator's membership of the United Kingdom good laboratory practice compliance programme in respect of particular laboratory premises if—

(a) the operator is, in the opinion of the Secretary of State, not capable of ensuring that the principles of good laboratory practice are adhered to at those premises; or

(b) at those premises there is a failure to adhere to the principles of good laboratory practice which, in the opinion of the Secretary of State, may contribute towards precipitating a danger to animal or human health or to the environment.

(4) Before serving a notice on an operator of a laboratory under paragraph (3)(a), the Secretary of State shall—

(a) inform the operator in writing that he is considering serving such a notice and explain to him in writing the reasons why he is considering serving such a notice;

(b) give the operator a specified period within which to make representations to him; and

(c) consider any representations which are duly made and not withdrawn,

unless, in order to ensure fulfilment of any Community obligation, it is necessary for the Secretary of State to serve the notice immediately.

(5) Where membership of the United Kingdom good laboratory practice compliance programme has been withdrawn from an operator of a laboratory in respect of particular laboratory premises in accordance with paragraph (3), he shall again be regarded as being a member of that programme in respect of those premises if—

(a) he has informed the Secretary of State by notice in writing of the intention to conduct further safety studies at those premises;

(b) the Secretary of State is of the opinion—

(i) if membership of the good laboratory practice compliance programme was withdrawn on the grounds set out in paragraph (3)(a), that the operator is capable of ensuring that the principles of good laboratory practice are adhered to at those premises, or

(ii) if membership of the good laboratory compliance programme was withdrawn on the grounds set out in paragraph (3)(b), that the possible danger to animal or human health or to the environment which led to membership being withdrawn is no longer present; and

(c) the Secretary of State has informed the operator by notice in writing of his readmission to membership of the programme.

Requirement to adhere to the principles of good laboratory practice

7.—(1) No person shall conduct a safety study at any premises of a laboratory unless with regard to that study the principles of good laboratory practice are adhered to—

(a) as respects the organisational structure surrounding the study; and

(b) as respects the conditions under which the study is planned, performed, monitored, recorded and reported.

(2) If the Secretary of State has reasonable grounds for believing that a person has contravened paragraph (1) and is responsible for a serious deviation from the principles of good laboratory practice which may have affected the validity of a safety study, he may by a notice served on the operator of the laboratory at whose premises the alleged contravention took place (in these Regulations referred to as a "warning notice")—

(a) state the Secretary of State's grounds for believing that the person—

(i) has contravened paragraph (1), and

(ii) is responsible for a serious deviation from the principles of good laboratory practice which may have affected the validity of a safety study;

(b) specify the measures which, in the opinion of the Secretary of State, the operator of the laboratory must take in order to ensure that the serious deviation from the principles of good laboratory practice which may have affected the validity of a safety study will not recur;

(c) require the operator of the laboratory to take those measures, or measures which are at least equivalent to them, within such period as may be specified in the warning notice; and

(d) inform the operator of the laboratory of—

(i) his right of appeal against the warning notice under regulation 8,

(ii) the period within which such an appeal may be brought, and

(iii) the effect that such an appeal will have on any criminal proceedings relating to the operator's alleged failure to comply with the warning notice.

(3) Any operator of a laboratory who fails to comply with a warning notice shall, unless that notice has been withdrawn by the Secretary of State or cancelled by a court, be guilty of an offence.

Appeals against warning notices

8.—(1) An operator of a laboratory who is aggrieved by a decision to serve a warning notice on him may appeal—

(a) in England, Wales or Northern Ireland, to a magistrates' court, and such an appeal shall be by way of complaint for an order; or

(b) in Scotland, to a sheriff, and such an appeal shall be by summary application.

(2) The period during which such an appeal may be brought is—

(a) one month from the date on which the warning notice was served on the operator desiring to appeal; or

(b) the period specified in the warning notice,

whichever ends the earlier.

(3) On an appeal against a warning notice, a magistrates' or sheriff court may either cancel or affirm the notice and, if it affirms it, may do so either in its original form or with such modifications as the court may, in the circumstances, think fit.

(4) Pending the final disposal of an appeal, or unless or until the appeal is withdrawn, any criminal proceedings relating to the operator's alleged failure to comply with a warning notice shall be stayed or suspended.

Powers and duties of inspectors

9.—(1) The Secretary of State may arrange for the discharge of any of his functions under regulation 3 by an inspector duly appointed in accordance with regulation 10.

(2) In enforcing compliance with these Regulations, a duly appointed inspector shall, on production, if required, of his credentials, have a right—

(a) at any reasonable hour to enter any premises other than premises used only as a private dwelling house which he has reason to believe it is necessary for him to visit for the purposes of enforcing compliance with these Regulations;

(b) to carry out on those premises during that visit such inspections, examinations, tests and analyses as he considers necessary for the purpose of establishing whether or not these Regulations are being complied with;

(c) to require the production of and take, without payment, samples of any substances on the premises for the purpose of establishing whether or not these Regulations are being complied with, but where an inspector takes a sample pursuant to this sub-paragraph, he shall give a portion of it, noted in a manner sufficient to identify it, to a responsible person at the premises;

(d) to require the production of, inspect and take copies of or extracts from any book, document, data or record (in whatever form it is held) which may be relevant in relation to the proper exercise by the inspector of his powers to enforce compliance with these Regulations;

(e) subject to paragraphs (6) and (7), to take possession of any books, documents, data, records (in whatever form they are held), articles or substances which are on the premises and which may be relevant in relation to the proper exercise by the inspector of his powers under these Regulations, and to detain them for as long as he considers necessary for the purposes of the proper exercise of those powers;

(f) to question any person whom he finds on the premises and whom he has reasonable cause to believe is able to give him information which is relevant to the proper exercise by the inspector of his powers under these Regulations;

(g) to require any person to afford him such facilities and assistance with respect to any matter within that person's control or in relation to which that person has responsibilities as are necessary in order to enable the inspector to establish whether or not these Regulations are being complied with;

(h) to exercise any of the functions of the Secretary of State arising out of or related to his responsibility for assessing compliance with the principles of good laboratory practice under or by virtue of these Regulations,

but nothing in this paragraph shall be taken to compel the production by any person of a document of which he would, on grounds of legal professional privilege, be entitled to withhold production on an order for discovery in an action in the High Court or, as the case may be, on an order for the production of documents in an action in the Court of Session.

(3) If a justice of the peace is satisfied by any written information on oath that there are reasonable grounds for entry into any premises other than premises used only as a private dwelling house for any purpose mentioned in paragraph (1), and—

(a) admission to the premises has been or is likely to be refused and that notice of intention to apply for a warrant under this subsection has been given to the occupier; or

(b) that an application for admission, or the giving of such notice, would defeat the object of the entry or that the premises are unoccupied or that the occupier is temporarily absent and it might defeat the object of the entry to await his return,

the justice may by warrant signed by him, which shall continue in force for a period of one month, authorise any duly appointed inspector to enter the premises, if need be by force.

(4) An officer entering any premises by virtue of paragraph (2) or of a warrant under paragraph (3) may take with him when he enters those premises such equipment as may appear to him necessary and any person who is authorised by the Secretary of State to accompany him on that visit.

(5) On leaving any premises which an inspector is authorised to enter by a warrant under paragraph (3), that inspector shall, if the premises are unoccupied or the occupier is temporarily absent, leave the premises as effectively secured against trespassers as he found them.

(6) Where, pursuant to paragraph (2)(e), an inspector takes possession of any book, document, data, record, article or substance, he shall leave on the premises with a responsible person a statement giving particulars of the book, document, record, data, article or substance sufficient to identify it and stating that he has taken possession of it.

(7) Before taking possession of any substance pursuant to paragraph (2)(e), an inspector shall, where it is reasonably practicable to do so, take a sample of it pursuant to paragraph (2)(c).

(8) In enforcing compliance with these Regulations, the Secretary of State or a duly appointed inspector shall have regard to any relevant provision of—

(a) the guides for compliance monitoring procedures for good laboratory practice set out in Annex A to the GLP Inspection and Verification Directive(**7**); and

(b) the guidance for the conduct of laboratory inspections and study audits set out in Annex B to that Directive.

Appointment of inspectors

10.—(1) The Secretary of State may appoint as inspectors such persons as he thinks necessary for the proper discharge of his functions under regulation 3.

(2) Every appointment of a person as an inspector shall be made by notice in writing specifying or referring to the functions of the Secretary of State under regulation 3 which that person is expected to discharge.

(3) An inspector shall be appointed upon such terms and conditions as the Secretary of State may determine and the Secretary of State may pay to or provide for inspectors such remuneration, benefits, allowances or reimbursement for expenses as he thinks fit.

Disclosure of confidential information

11.—(1) A person who in the course of enforcing compliance with these Regulations gains access to commercially sensitive or other confidential information shall be guilty of an offence if without lawful authority he discloses that information.

(2) A person may disclose commercially sensitive or confidential information to which he has had access in the course of enforcing compliance with these Regulations to—

(a) the European Commission;

(b) a monitoring authority;

(c) a regulatory authority;

(d) a laboratory or sponsor concerned with the inspection or study audit during the course of which that person gained access to that information.

(3) For the purposes of this regulation—

(a) the names of laboratories which are or have been subject to an inspection as part of the United Kingdom's good laboratory practice compliance programme;

(b) the level of adherence of a laboratory to the principles of good laboratory practice as assessed by the United Kingdom's monitoring authority; and

(c) the dates upon which laboratory inspections or study audits have been conducted,

shall not be considered to be confidential.

Obstruction etc. of inspectors

12.—(1) Subject to paragraph (2)—

(a) any person who—

(i) intentionally obstructs an inspector, or

(ii) without reasonable cause fails to comply with any requirement made of him by an inspector,

in circumstances where the inspector is acting in pursuance of any of his functions under these Regulations; or

(**7**) *See* article 1 of Commission Directive 90/18/EEC and the Annex thereto.

(b) any person who, in purported compliance with any such requirement as is mentioned in sub-paragraph (a)(ii), intentionally or recklessly furnishes information which is false or misleading in a material particular,

shall be guilty of an offence.

(2) Nothing in paragraph (1)(a)(ii) shall be construed as requiring any person to answer any question or give any information if to do so might incriminate him or, in the case of a person who is married, his spouse.

Offences by bodies corporate and Scottish partnerships

13. Where an offence under these Regulations is committed by a body corporate or Scottish partnership and is proved to have been committed with the consent or connivance of, or to be attributable to any neglect on the part of—

(a) any director, manager, secretary, partner or similar officer of the body corporate or Scottish partnership; or

(b) any person who was purporting to act in any such capacity,

he as well as the body corporate or Scottish partnership shall be deemed to be guilty of that offence and he shall be liable to be proceeded against and punished accordingly.

Defence of due diligence

14. In any proceedings for an offence under any of the preceding provisions of these Regulations, it shall be a defence for the person charged to prove that he took all reasonable precautions and exercised all due diligence to avoid the commission of the offence.

Penalties

15.—(1) A person guilty of an offence under regulation 12(1)(a) shall be liable on summary conviction to a fine not exceeding level 3 on the standard scale.

(2) A person guilty of any other offence under these Regulations shall be liable on summary conviction to a fine not exceeding level 5 on the standard scale or to imprisonment for not more than three months.

Fees

16.—(1) The Secretary of State may, in respect of allaying the disbursements incurred in connection with inspecting laboratories and auditing safety studies to assess compliance with the principles of good laboratory practice, charge operators of laboratories, and operators of laboratories shall, if so charged, pay to the Secretary of State such reasonable fees as he may determine to cover the cost of carrying out such laboratory inspections and study audits.

(2) The Secretary of State may set those fees at levels such that they also cover the cost of such of his overheads as are reasonably attributable to carrying out such laboratory inspections and study audits.

(3) Any such fee shall be payable within fourteen days following written notice from the Secretary of State requiring payment of the fee.

(4) All unpaid sums due by way of, or on account of, any fees payable under this regulation shall be recoverable as debts due to the Crown.

(5) The Secretary of State may in exceptional circumstances—

(a) waive payment of any fee or reduce any fee or part of a fee otherwise payable under this regulation;

(b) refund the whole or part of any fee paid pursuant to this regulation.

Amendment of the Medicines (Applications for Grant of Product Licences—Products for Human Use) Regulations 1993

17. The Medicines (Applications for Grant of Product Licences—Products for Human Use) Regulations 1993(**8**) shall be amended as follows—

(a) in paragraph (2) of regulation 1 (citation, commencement and interpretation), after the definition of "expert" there shall be inserted the following definition—

> ""principles of good laboratory practice" has the same meaning as in the Good Laboratory Practice Regulations 1997;"; and

(b) in paragraph 17 of Schedule 1 (information, documents, samples and other material required in respect of applications), the words "referred to in that sub-paragraph" shall be omitted.

Amendment of the Notification of New Substances Regulations 1993

18. The Notification of New Substances Regulations 1993(**9**) shall be amended as follows—

(a) in paragraph (1) of regulation 2 (interpretation), after the definition of "preparations" there shall be inserted the following definition—

> ""principles of good laboratory practice" has the same meaning as in the Good Laboratory Practice Regulations 1997;";

(b) in paragraph (b) of regulation 4 (full notifications), the words "referred to in regulation 14(1)" shall be omitted;

(c) in paragraph (2) of regulation 5 (requirements for further testing for substances notified under regulation 4), the words "referred to in regulation 14(1)" shall be omitted;

(d) in paragraph (1) of regulation 14 (tests under these Regulations to conform to principles of good laboratory practice), the words from "referred to in" to the end of that paragraph shall be omitted; and

(e) paragraph (4) of regulation 14 shall be omitted.

Amendment of the Marketing Authorisations for Veterinary Medicinal Products Regulations 1994

19. The Marketing Authorisations for Veterinary Medicinal Products Regulations 1994(**10**) shall be amended as follows—

(a) in paragraph (4) of regulation 1 (title, commencement and interpretation), after the definition of "the Ministers" there shall be inserted the following definition—

> ""principles of good laboratory practice" has the same meaning as in the Good Laboratory Practice Regulations 1997;";

(b) in paragraph 3 of Schedule 1 (requirements in respect of products other than immunological products), the words "as referred to in the second paragraph of Part 3" shall be omitted; and

(c) in paragraph 1 of Schedule 2 (requirements in respect of immunological products) the words from "as referred to" to the end of that paragraph shall be omitted.

(**8**) S.I. 1993/2538; there are no relevant amending instruments.
(**9**) S.I. 1993/3050; there are no relevant amending instruments.
(**10**) S.I. 1994/3142; there are no relevant amending instruments.

Department of Health

Stephen Dorrell
One of Her Majesty's Principal Secretaries of State

6th March 1997

We consent,

Patrick McLoughlin
Richard Ottaway
Two of the Lords Commissioners of Her Majesty's Treasury

6th March 1997

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.

SCHEDULE 2 Regulation 2(1)

INSPECTION PROCEDURES AND STUDY AUDITS (BASED ON ANNEX B TO THE GLP INSPECTION AND VERIFICATION DIRECTIVE)

PART I

INSPECTION PROCEDURES

Pre-inspection

1.—(1) *Purpose:* To familiarise the inspector with the facility which is about to be inspected in respect of management structure, physical layout of buildings and range of studies.

(2) Prior to conducting a laboratory inspection or study audit, inspectors should familiarise themselves with the facility which is to be visited. Any existing information on the facility should be reviewed. This may include previous inspection reports, the layout of the facility, organisation charts, study reports, protocols and *curricula vitae*(CVs) of key personnel. Such documents would provide information on—

— the type, size and layout of the facility,

— the range of studies likely to be encountered during the inspection,

— the management structure of the facility.

(3) Inspectors should note, in particular, any deficiencies from previous laboratory inspections. Where no previous laboratory inspections have been conducted, a pre-inspection visit can be made to obtain relevant information.

(4) Laboratories should be informed of the date and time of inspectors' arrival, the objective of their visit and the length of time they expect to be on the premises. This will allow the laboratory to ensure that the appropriate personnel and documentation are available. In cases where particular documents or records are to be examined, it may be useful to identify these to the laboratory in advance of the visit so that they will be immediately available during the laboratory inspection.

Starting conference

2.—(1) *Purpose:* To inform the management and staff of the facility of the reason for the laboratory inspection or study audit that is about to take place, and to identify the laboratory areas, study(ies) selected for audit, documents and personnel likely to be involved.

(2) The administrative and practical details of a laboratory inspection or study audit should be discussed with the management of the facility at the start of the visit. At the starting conference, inspectors should—

— outline the purpose and scope of the visit,

— describe the documentation which will be required for the laboratory inspection, such as lists of on-going and completed studies, study plans, standard operating procedures, study reports, etc. Access to and, if necessary, arrangements for the copying of relevant documents should be agreed upon at this time,

— clarify or request information as to the management structure (organisation) and personnel of the facility,

— request information as to the conduct, side-by-side, of studies subject to good laboratory practice principles with others for which they are not applied,

— make an initial determination as to the parts of the facility to be covered during the laboratory inspection,

— describe the documents and specimens that will be needed for on-going or completed study(ies) selected for study audit.

(3) Before proceeding further with a laboratory inspection, it is advisable for the inspector to establish contact with the laboratory quality assurance unit.

(4) As a general rule, when inspecting a facility, inspectors will find it helpful to be accompanied by a member of the quality assurance unit.

(5) Inspectors may wish to request that a room be set aside for examination of documents and other activities.

Organisation and personnel

3.—(1) *Purpose:* To determine whether: the laboratory has sufficient qualified personnel, staff resources and support services for the variety and number of studies undertaken; the organisational structure is appropriate; and management has established a policy regarding training and staff health surveillance appropriate to the studies undertaken in the facility.

(2) The management should be asked to produce certain documents, for example—

— floor plans,

— facility management and scientific organisation charts,

— CVs of key personnel involved in the type(s) of studies selected for the study audit,

— list(s) of on-going and completed studies with information on the type of study, initiation/ completion dates, test system, route of administration and name of study director,

— staff training and health surveillance policies, where such policies have been established,

— staff training records where available,

— an index to the facility's standard operating procedures,

— specific standard operating procedures related to the studies or procedures being inspected or audited,

— list(s) of the study directors associated with the study(ies) being audited.

(3) The inspector should check, in particular—

— lists of on-going and completed studies to ascertain the level of work being undertaken by the laboratory,

— the identity and qualifications of the study directors, the head of the quality assurance unit and other key personnel,

— existence of standard operating procedures for the relevant areas of testing.

Quality assurance programme

4.—(1) *Purpose:* To determine whether the mechanisms used to assure manage ment that laboratory studies are conducted in accordance with good laboratory practice principles are adequate.

(2) The head of the quality assurance unit should be asked to demonstrate the systems and methods of quality assurance inspection and monitoring of studies, and the system for recording observations made during quality assurance monitoring. Inspectors should check—

— the qualifications of the head of quality assurance and of all quality assurance staff,

— that the quality assurance unit functions independently from the staff involved in the studies,

— how the quality assurance unit schedules and conducts inspections, how it monitors identified critical phases in a study, and what resources are available for quality assurance inspections and monitoring activities,

— that, where studies are of such short duration and monitoring of each study is impracticable, arrangements exist for monitoring on a sample basis,

— the extent and depth of quality assurance monitoring during the practical phases of the study,

— the quality assurance procedures for checking the final report to ensure its agreement with the raw data,

— that management receives reports from quality assurance concerning problems likely to affect the quality or integrity of a study,

— the actions taken by quality assurance when deviations are found,

— the quality assurance role, if any, of studies or parts of studies done in contract laboratories,

— the part played, if any, by quality assurance in the review, revision and updating of standard operating procedures.

Facilities

5.—(1) *Purpose:* To determine whether the laboratory is of suitable size, construction, design and location to meet the demands of the studies being undertaken.

(2) The inspector should check that—

— the design enables an adequate degree of separation so that, e.g. test substances, animals, diets, pathological specimens etc., of one study cannot be confused with those of another,

— environmental control and monitoring procedures exist and function adequately in critical areas, e.g. animal and other biological test systems rooms, test substance storage areas and laboratory areas,

— the general housekeeping is adequate for the various facilities and that there are, if necessary, pest control procedures.

Care, housing and containment of biological test systems

6.—(1) *Purpose:* To determine whether the laboratory, if engaged in studies using animals or other biological test systems, has support facilities and conditions for their care, housing and containment, adequate to prevent stress and other problems which could affect the test system and hence the quality of data.

(2) A laboratory may be carrying out studies which require a diversity of animal or plant species as well as microbial or other cellular or sub-cellular systems. The type of test systems being used will determine the aspects relating to care, housing or containment that the inspector will monitor. Using his judgment, the inspector will check, according to the test systems that—

— there are facilities adequate for the test systems used and for testing needs,

— there are arrangements to quarantine animals and plants being introduced into the facility and that these arrangements are working satisfactorily,

— there are arrangements to isolate animals (or other elements of a test system, if necessary) known to be, or suspected of being, diseased or carriers of disease,

— there is adequate monitoring and record-keeping of health, behaviour or other aspects, as appropriate to the test system,

— the equipment for maintaining the environmental conditions required for each test system is adequate, well maintained and effective,

— animal cages, racks, tanks and other containers, as well as accessory equipment, are kept sufficiently clean,

— analyses to check environmental conditions and support systems are carried out as required,

— facilities exist for removal and disposal of animal waste and refuse from the test systems and that these are operated so as to minimise vermin infestation, odours, disease hazards and environmental contamination,

— storage areas are provided for animal feed or equivalent materials for all test systems; that these areas are not used for the storage of other materials such as test substances, pest control chemicals or disinfectants, and they are separate from areas in which animals are housed or other biological test systems are kept,

— stored feed and bedding are protected from deterioration by adverse environmental conditions, infestation or contamination.

Apparatus, materials, reagents and specimens

7.—(1) *Purpose:* To determine whether the laboratory has suitably located, operational apparatus in sufficient quantity and of adequate capacity to meet the requirements of the tests being conducted in the facility and that the materials, reagents and specimens are properly labelled, used and stored.

(2) The inspector should check that—

— apparatus are clean and in good working order,

— records have been kept of apparatus operation, maintenance, standardisation and calibration,

— materials and chemical reagents are properly labelled and stored at appropriate temperatures and that expiry dates are not being ignored. Labels for reagents should indicate their source, identity and concentration and/or other pertinent information.

— specimens are well identified by test system, study, nature and date of collection,

— apparatus and materials used do not interfere with the test systems.

Test systems

8. *Purpose:* To determine whether adequate procedures exist for the handling and control of the variety of test systems required by the studies undertaken in the facility, e.g. chemical and physical systems, cellular and microbial systems, plants or animals.

Physical and chemical systems

9. The inspector should check that—

— where required by study plans, the stability of test and reference substances were determined and that the reference substances specified in test plans were used,

— standard operating procedures exist to cover laboratory activities and that their provisions are observed,

— in automated systems, data generated as graphs, recorder traces or computer print-outs are documented as raw data and archived.

Biological test systems

10. Taking account of the relevant aspects referred to above relating to care, housing or containment of biological test systems, the inspector should check that—

— test systems are as specified in study plans,

— test systems are adequately identified,

— animals are adequately and, if necessary and appropriate, uniquely identified throughout the study,

— housing or containers of test systems are properly identified with all the necessary information,

— there is an adequate separation of studies being conducted on the same animal species (or the same biological test system) but with different substances,

— the biological test system environment is as specified in the study plan or in standard operating procedures for aspects such as temperature or light/dark cycles,

— the recording of the receipt, handling, housing or containment, care and health evaluation is appropriate to the test systems,

— written records are kept of examination, quarantine, morbidity, behaviour, diagnosis and treatment of animal and plant test systems or other similar aspects as appropriate to each biological test system,

— there are provisions for the appropriate disposal of test systems at the end of tests.

Test and reference substances

11.—(1) *Purpose:* To determine whether the laboratory has procedures designed—

(i) to ensure that the identity, potency, quantity and composition of test and reference substances are in accordance with their specifications, and

(ii) to properly receive and store test and reference substances.

(2) The inspector should check that—

— there are standard operating procedures for recording the receipt, and for the handling, sampling, usage and storage of test and reference substances,

— test and reference substances containers are properly labelled,

— storage conditions are appropriate to preserve the concentration, purity and stability of the test and reference substances,

— there are standard operating procedures for the determination of identity, purity, composition, stability, and for the prevention of contamination of, test and reference substances, where applicable,

— records are kept of the composition, characterisation, concentration and stability of test and reference substances, where applicable,

— there are procedures for the determination of the homogeneity and stability of mixtures containing test and reference substances, where applicable,

— containers holding mixtures (or dilutions) of the test and reference substances are labelled and that records are kept of the homogeneity and stability of their contents, where applicable,

— when the test is of longer than four weeks' duration, samples from each batch of test and reference substances have been taken for analytical purposes and that they have been retained for an appropriate time,

— procedures for mixing substances are designed to prevent errors in identification or cross-contamination.

Standard operating procedures

12.—(1) *Purpose:* To determine whether the laboratory has written standard operating procedures relating to all the important aspects of the laboratory's operation, considering that one of the most important management techniques for controlling laboratory operations is the use of written standard operating procedures. These relate directly to the routine elements of tests conducted by the laboratory.

(2) The inspector should check that—

— each laboratory area has immediately available relevant, authorised copies of standard operating procedures,

— any amendments or changes to standard operating procedures have been authorised and dated,

— historical files of standard operating procedures are maintained,

— standard operating procedures are available for, but not necessarily limited to, the following activities—

(i) receipt, identification, labelling, handling, sampling, usage and storage of test and reference substances,

(ii) maintenance, cleaning and calibration of measuring apparatus and environmental control equipment,

(iii) preparation of reagents and dosing formulations,

(iv) record-keeping, reporting, storage and retrieval of records and reports,

(v) preparation and environmental control of areas containing the test systems,

(vi) receipt, transfer, location, characterisation, identification and care of test systems,

(vii) handling of the test systems before, during and at the termination of the study,

(viii) disposal of test systems,

(ix) use of pest control and cleaning agents,

— quality assurance programme operations.

Performance of the study

13.—(1) *Purpose:* To verify that written study plans exist and that the plans and the conduct of the study are in accordance with good laboratory practice principles.

(2) The inspectors should check that—

— the study plan was signed by the study director,

— any amendments to the study plan were signed and dated,

— the date of the agreement to the study plan by the sponsor was recorded (where applicable),

— measurements, observations and examinations were in accordance with the study plan and relevant standard operating procedures,

— the results of these measurements, observations and examinations were recorded directly, promptly, accurately and legibly and were signed (or initialled) and dated,

— any changes in the raw data, including data stored in computers, did not obscure previous entries, included the reason for the change and were signed and dated,

— computer-generated or stored data have been identified and that the procedures to protect them against unauthorised amendments or loss are adequate,

— the computer software used within the study is reliable, accurate, and can be validated,

— any unforeseen events recorded in the raw data have been investigated and evaluated,

— the results presented in the reports of the study (interim or final) are consistent and complete and that they correctly reflect the raw data.

Reporting of study results

14.—(1) *Purpose:* To determine whether final reports are prepared in accordance with good laboratory practice principles.

(2) When a final report is available, the inspector should check that—

— it is signed and dated by the study director and, where appropriate, by other principal scientists,

— the study director has signed a statement indicating acceptance of responsibility for the validity of the study and confirming that the study was conducted in accordance with good laboratory practice principles,

— a quality assurance statement is included in the report and that it is signed and dated,

— any amendments were made by the responsible personnel,

— it lists the archive location of all samples, specimens and raw data.

Storage and retention of records

15.—(1) *Purpose:* To determine whether the facility has generated adequate records and reports and whether adequate provision has been made for the safe storage and retention of records and materials.

(2) The inspector should check—

— the archive facilities for the storage of study plans, raw data, final reports, samples and specimens,

— the procedures for retrieval of archived materials,

— the procedures whereby access to the archives is limited to authorised personnel and records are kept of personnel given access to raw data, slides, etc.,

— that an inventory is maintained of materials removed from, and returned to, the archives,

— that records and materials are retained for the required or appropriate period of time and are protected from loss or damage by fire, adverse environmental conditions, etc.

PART II

STUDY AUDITS

16. Laboratory inspections will generally include *inter alia*(limited) study audits. These may be brief reviews of on-going or completed studies. When specific study audits are requested by regulatory authorities, the conduct and reporting of the study should be subjected to a detailed examination. Because of the wide variation in the types of studies which might be audited, only general guidance is appropriate, and inspectors and others taking part in study audits will always need to exercise judgment as to the nature and extent of their examinations. The objective should be to reconstruct the study from the study plan using relevant standard operating procedures, raw data and other archived material.

17. In some cases, inspectors may need assistance from other experts in order to conduct an effective study audit, e.g. where there is a need to examine tissue sections under the microscope.

18. When conducting a study audit, the inspector should—

— obtain names, job descriptions and summaries of training and experience for selected personnel engaged in the study(ies) such as the study director and principal scientists,

— check that there are sufficient staff trained in relevant areas for the study(ies) undertaken,

— identify individual items of apparatus or special equipment used in the study and examine the calibration, maintenance and service records for the equipment,

— review the records relating to the stability of the test substances, analyses of test substance and formulations, analyses of feed, etc.,

— attempt to determine, through the interview process if possible, the work assignments of selected individuals participating in the study to ascertain if these individuals had the time to accomplish the tasks specified in the study plan or report,

— obtain copies of all documentation concerning control procedures or forming integral parts of the study, including—

  (i) the study plan,

  (ii) standard operating procedures in use at the time the study was done,

  (iii) log books, laboratory notebooks, files, worksheets, print-outs of computer stored data, etc.,

  (iv) the final report.

19. In studies in which animals (i.e. rodents and other mammals) are used, the inspectors should follow a certain percentage of individual animals from their arrival at the laboratory to autopsy. They should pay particular attention to the records relating to—

— animal body weight, food/water intake, dose formulation and administration etc.,

— clinical observations and autopsy findings,

— clinical chemistry,

— pathology.

EXPLANATORY NOTE

(This note is not part of the Regulations)

These Regulations contain the legislative measures necessary for the implementation of Council Directive 87/18/EEC on the harmonization of laws, regulations and administrative provisions relating to the application of the principles of good laboratory practice and the verification of their applications for tests on chemical substances (OJNo. L15, 17.1.87, p. 29), Council Directive 88/320/EEC on the inspection and verification of Good Laboratory Practice (GLP) and Commission Directive 90/18/EEC adapting to technical progress the Annex to Council Directive 88/320/EEC on the inspection and verification of good laboratory practice.

Regulation 2 is an interpretation provision. Amongst other definitions, there is a definition of the principles of good laboratory practice, a concept which is defined with reference to the principles set out in the Schedule 1 to the Regulations and the operating procedures set out in Schedule 2 to the Regulations. Regulation 3 sets out certain functions of the Secretary of State, including enforcing compliance with the Regulations.

Regulation 4 contains a requirement that safety studies covered by the Regulations must only be conducted at laboratories which are part of the United Kingdom good laboratory practice compliance programme. Regulation 5 deals with prospective membership of the programme by laboratory operators in respect of particular laboratory premises, and regulation 6 deals with full membership of the programme.

Regulation 7 contains a requirement that safety studies covered by the Regulations shall be conducted in accordance with the principles of good laboratory practice. Where there are serious deviations from the principles, there is a procedure for serving warning notices on laboratory operators requiring them to ensure that the serious deviation will not recur. Breach of such a notice is an offence, although there is an appeals procedure, contained in regulation 8, if an operator of a laboratory is aggrieved by a decision to serve a warning notice on him.

Regulation 9 deals with the powers of inspectors who are discharging the enforcement functions of the Secretary of State. The conditions under which inspectors are to be appointed are governed by regulation 10.

Regulation 11 contains rules relating to the disclosure of commercially sensitive or other confidential information which may come to light as a result of enforcement action taken under the Regulations. Impeding the work of an inspector who is acting in pursuance of any of his functions under the Regulations is made an offence under regulation 12.

Regulation 13 relates to offences committed with the consent or connivance, or attributable to, bodies corporate or Scottish partnerships, and regulation 14 is a general defence of due diligence in relation to any of the offences contained in the Regulations.

Regulation 15 is a penalties provision, and regulation 16 gives the Secretary of State powers to charge fees to cover the cost of carrying out inspections and study audits.

Regulations 17 to 19 contain a set of consequential amendments to other Regulations.

An assessment of the cost to business of complying with these Regulations has been prepared and copies may be obtained from the Good Laboratory Practice Monitoring Authority, Room 1801, Market Towers, 1 Nine Elms Lane, London SW8 5NQ. A copy has also been placed in the library of each of the Houses of Parliament.