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MEDICINES ACT
(CHAPTER 176)

MEDICINES (MEDICINAL PRODUCTS AS CLINICAL RESEARCH MATERIALS) REGULATIONS 2016

ARRANGEMENT OF REGULATIONS

In exercise of the powers conferred by sections 18, 34, 44 and 74 of the Medicines Act, the Minister for Health makes the following Regulations:

PART 1

GENERAL

Citation and commencement

1. These Regulations are the Medicines (Medicinal Products as Clinical Research Materials) Regulations 2016 and come into operation on 1 November 2016.

Definitions

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

"appropriate non-proprietary name", in relation to an active ingredient of a medicinal product, means —

(*a*) the name or synonym of the active ingredient described in the relevant monograph appearing in the latest edition of any of the following publications:

(i) the British Pharmacopoeia;

(ii) the European Pharmacopoeia;

(iii) the United States Pharmacopoeia and the National Formulary;

(*b*) where the active ingredient is not described in a monograph in any such publication, its international non-proprietary name; or

(*c*) where paragraph (*a*) or (*b*) is not applicable, the accepted scientific name or other name descriptive of the true nature of the active ingredient;

"Authority's website" means the Authority's Internet website at http://www.hsa.gov.sg;

"auxiliary CRM" means any clinical research material that is used for the needs of any clinical research as described in the protocol, but not as the material to be tested or used as a reference in the research;

"clinical research" means any research involving human beings (whether or not a regulated clinical trial);

"clinical research material" means any medicinal product or placebo, that is not specified in the First Schedule, that is manufactured, assembled, imported or supplied for the purpose of being used in any clinical research by way of administration to a subject in accordance with the protocol for the research;

"institutional review board" means an independent body which —

(*a*) is constituted of medical, scientific, and non-scientific members, whose responsibility is to ensure the protection of the rights, safety and wellbeing of subjects by, among other things, reviewing, approving and providing continuing review of the protocol, amendments, and the methods and materials to be used in obtaining and documenting informed consent of the subjects; and

(*b*) when Part 4 of the Human Biomedical Research Act 2015 (Act 29 of 2015) comes into operation, is appointed under that Act;

"investigational CRM" means any clinical research material that is to be tested or used as a reference in any clinical research;

"proprietary name" means a word or words used in connection with the supply of a medicinal product for the purpose of indicating that it is the product of a particular person who manufactures, selects the name of, certifies or deals with the medicinal product, or offers it for supply;

"protocol" means a document that describes the objectives, design, methodology, statistical considerations and organisation of any clinical research;

"regulated clinical trial" means a clinical trial that is —

(*a*) issued with a certificate under regulation 8 of the Medicines (Clinical Trials) Regulations 2016 (G.N. No. S 335/2016); or

(*b*) authorised by the Authority, or notified to the Authority and the notification accepted by the Authority, under regulation 8 or 9 of the Health Products (Clinical Trials) Regulations 2016 (G.N. No. S 331/2016);

"sponsor" means a person who takes responsibility for the initiation, management or financing of any clinical research;

"subject" means a human being, whether or not a patient, who participates in any clinical research —

(*a*) as a recipient of the clinical research material to which the research relates, or of some other treatment or procedure in that research; or

(*b*) as a control, without receiving any such clinical research material, or any such treatment or procedure.

PART 2

EXEMPTIONS FOR CLINICAL RESEARCH MATERIALS

Exemptions from Act

3.—(1) Subject to paragraphs (2), (3) and (4), sections 5 and 6 of the Act do not apply to any medicinal product that is not specified in the First Schedule, and that —

(*a*) is manufactured, assembled, imported or supplied as clinical research material; or

(*b*) is exported under regulation 7(5).

(2) Paragraph (1) applies to the import by a person (called in these Regulations an importer) of the clinical research material only if the importer gives the Authority notice of the import before importing the product.

(3) Where a person who manufactures (called a manufacturer in these Regulations) the clinical research material supplies the material, paragraph (1) applies to the supply only if the manufacturer gives the Authority notice of the supply before supplying the product.

(4) A notice under this regulation must be given in the form and manner, and within the time, specified on the Authority's website.

(5) A notice of the import mentioned in paragraph (2) is not required if —

(*a*) before 1 November 2016 —

(i) the clinical research material was a medicinal product under the Act; and

(ii) the import of the product was permitted by the licensing authority under the Act in connection with

any clinical trial regulated under the Medicines (Clinical Trials) Regulations (Rg 3) in force immediately before 1 November 2016; and

(*b*) the clinical research material is imported in accordance with the permission.

PART 3

MANUFACTURE, ASSEMBLY AND IMPORT OF CLINICAL RESEARCH MATERIALS

Manufacture, assembly and import of clinical research materials

4.—(1) A manufacturer of any clinical research material, or an importer of such material, must ensure that the material is of the correct identity and conforms with the applicable standards of strength, quality and purity for that material.

(2) A person who assembles any clinical research material must ensure that the material is of the correct identity.

PART 4

SUPPLIES, ETC., OF CLINICAL RESEARCH MATERIALS

Supply only as clinical research material

5.—(1) A person who manufactures, assembles, imports or is supplied with any clinical research material under regulation 3 must only supply the material for the purpose of being used in clinical research in accordance with the protocol for the research.

(2) Despite paragraph (1), the person may supply the clinical research material for a purpose other than that specified in that paragraph if the Authority has allowed such supply.

(3) To avoid doubt, as from the time that the Authority has allowed the supply for a purpose other than that specified in paragraph (1) —

(*a*) the clinical research material in question ceases to be clinical research material; and

(*b*) nothing in these Regulations prevents clinical research material which ceases to be such, from being subject to any law relating to medicinal products.

Supply of clinical research material properly labelled

6.—(1) For the purpose of section 44 of the Act, a person must not supply any clinical research material for the purpose of being used in any regulated clinical trial, unless it is labelled in accordance with the Second Schedule to the Medicines (Clinical Trials) Regulations 2016 (G.N. No. S 335/2016); except that paragraph 1(1)(*d*), (2)(*a*) to (*d*) and (*g*), (3)(*a*) to (*d*), (*g*) and (*j*) and (4)(*a*), (*b*), (*e*) and (*h*) of that Schedule does not apply if the supply is by wholesale.

(2) For the purpose of section 44 of the Act, a person must not supply any other clinical research material unless it is labelled in accordance with the requirements set out in the Second Schedule.

PART 5

DUTIES RELATING TO CLINICAL RESEARCH MATERIALS

Division 1 — Use and disposal, etc., of clinical research materials

Dealing with clinical research materials

7.—(1) This regulation applies to any clinical research material manufactured, assembled, imported or supplied, under regulation 3.

(2) Without prejudice to regulation 5, a person must not use the clinical research material in any clinical research, and the sponsor must ensure that no person involved in the research uses the material —

(*a*) except in accordance with the protocol for the research; and

(*b*) where the research requires the approval of an institutional review board, only after the approval has been obtained.

(3) Despite paragraph (2) —

(*a*) the clinical research material need not be used as referred to in paragraph (2) if the Authority has allowed some other use of the material; and

(*b*) the sponsor must ensure that the material is put to the other use.

(4) To avoid doubt, as from the time that the Authority has allowed the other use under paragraph (3) —

(*a*) the clinical research material in question ceases to be clinical research material; and

(*b*) nothing in these Regulations prevents clinical research material which ceases to be such, from being subject to any law relating to medicinal products.

(5) Unless the Authority otherwise allows, the sponsor must ensure that, within 6 months of the conclusion or termination of the clinical research, any unused clinical research material obtained for the research is disposed of or exported.

(6) In paragraph (5), "unused clinical research material" means any clinical research material referred to in paragraph (1) which is not used in the clinical research for which the material was obtained (including where the material cannot or can no longer be used in the research).

Division 2 — Keeping of records

Records of manufacture

8. A manufacturer of, and a person who assembles, any clinical research material must keep records of the manufacture, assembly and testing of the material undertaken by or on behalf of the manufacturer or person.

Records of receipt and supply

9.—(1) A person who supplies any clinical research material (including a manufacturer, a person who assembles or an importer of the material, who supplies the material) must keep records relating to every receipt (where applicable) and every supply by the person of

the material, in order to permit proper evaluation to be made of the accountability and traceability of the material.

(2) The records referred to in paragraph (1) include all of the following:

(*a*) the proprietary name or description of the clinical research material;

(*b*) the identification number of the clinical research material (including the control number, lot number, batch number or serial number);

(*c*) where applicable, details of each receipt of the clinical research material by the person (whether as a result of an import by, or a supply to, the person), namely —

(i) the date on which the material was received;

(ii) the quantity of the material received; and

(iii) the name and address of the person from whom the material was received;

(*d*) details of each supply of the clinical research material by the person, namely —

(i) the date on which the material was supplied;

(ii) the quantity of the material supplied; and

(iii) the name and address of the person to whom the material was supplied.

Records of dealings with clinical research materials

10.—(1) A sponsor must keep records relating to all clinical research materials that are put to some other use, disposed of or exported, as the case may be, under regulation 7, in order to permit proper evaluation to be made of the accountability and traceability of the material.

(2) The records referred to in paragraph (1) include all of the following:

(*a*) the proprietary name or description of the clinical research material;

(*b*) the identification number of the clinical research material (including the control number, lot number, batch number or serial number);

(*c*) the date on which the clinical research material was put to some other use, disposed of or exported;

(*d*) the quantity of the clinical research material put to some other use, disposed of or exported;

(*e*) the name and address of the person responsible for the putting to some other use, disposal or export, of the clinical research material.

Production of and time for keeping of records

11.—(1) A person who is required to keep any record under this Division must —

(*a*) keep the records for the applicable period specified in paragraph (2) or (3); and

(*b*) produce the records for inspection when required by the Authority at any reasonable time during the applicable period.

(2) For records relating to any manufacture, assembly and testing of clinical research material, the applicable period is the longer of the following periods:

(*a*) one year after the expiry date of the material;

(*b*) 5 years after the date of such manufacture, assembly and testing.

(3) For records relating to the receipt and supply of, or the putting to some other use, disposal or export, of clinical research material, the applicable period is as follows:

(*a*) where the clinical research is not a regulated clinical trial, the period of 2 years after the supply, putting to some other use, export or disposal, as the case may be;

(*b*) where the clinical research is a regulated clinical trial, for the period for which records of the trial must be kept under

regulation 23(2)(*c*) of the Medicines (Clinical Trials) Regulations 2016 (G.N. No. S 335/2016) or regulation 23(2)(*c*) of the Health Products (Clinical Trials) Regulations 2016 (G.N. No. S 331/2016), as the case may be.

Division 3 — Reports to Authority

Notifications of unexpected serious adverse drug reactions

12.—(1) Where, during any clinical research that is not a regulated clinical trial, any USADR occurs in a subject that results in death or is life-threatening, then the sponsor must ensure that —

(*a*) all relevant information about the USADR is —

(i) recorded; and

(ii) reported to the Authority as soon as possible and in any event not later than 7 days after the sponsor first becomes aware of the event; and

(*b*) any additional relevant information about the USADR is —

(i) recorded; and

(ii) sent to the Authority within 8 days of the record referred to in sub-paragraph (i).

(2) Where, during any clinical research that is not a regulated clinical trial, any USADR that is not referred to in paragraph (1) occurs in a subject, the sponsor must ensure that all relevant information about the reaction is —

(*a*) recorded; and

(*b*) reported to the Authority as soon as possible and in any event not later than 15 days after the sponsor first becomes aware of the event.

(3) In this regulation —

"investigator's brochure" means a document of an investigator of any clinical research that is not a regulated clinical trial, containing a summary of the clinical and non-clinical data relating to the clinical research material relevant to the study of the material in subjects;

"serious adverse drug reaction" has the same meaning as in regulation 2(1) of the Medicines (Clinical Trials) Regulations 2016 (G.N. No. S 335/2016);

"USADR" means an unexpected serious adverse drug reaction in a subject following the administration of any clinical research material to the subject, the nature and severity of which is not consistent with the information about the material set out —

(*a*) in the case of clinical research material in respect of which a product licence has been issued, in the product information leaflet or the investigator's brochure relating to the material; and

(*b*) in the case of any other clinical research material, in the investigator's brochure relating to the material.

Recall of clinical research material

13.—(1) Where any person intends to recall any clinical research material which the person manufactured, assembled, imported or supplied under regulation 3, the person must immediately, but in any case no later than 24 hours before the start of the intended recall, notify the Authority of the intended recall and the reasons for the recall.

(2) The notice in paragraph (1) must be made in such form and manner as the Authority may require.

(3) Where the Authority has been notified of the intended recall of any clinical research material under paragraph (1), the Authority may by notice in writing require the person to do either or both of the following:

(*a*) investigate the matter occasioning the recall of the clinical research material and provide a report of the findings of the investigation;

(*b*) take such other measures as the Authority thinks necessary.

(4) A person to whom a notice in paragraph (3) is given must comply with the notice at the person's own cost and within the time specified in the notice or, if no time is specified in the notice, within a reasonable time after the date of the notice.

PART 6

MISCELLANEOUS

Offences

14.—(1) A person shall be guilty of an offence if the person —

(*a*) contravenes regulation 4(1) or (2), 5(1), 7(2), (3)(*b*) or (5), 8, 9(1), 10(1), 11(1), 12(1) or (2) or 13(1) or (4); or

(*b*) for the purposes of giving any notice or report to the Authority under these Regulations, furnishes the Authority with any particulars, information or document which the person knows is false or misleading.

(2) A person who is guilty of an offence under paragraph (1) shall be liable on conviction to a fine not exceeding $5,000 or to imprisonment for a term not exceeding 2 years or to both.

FIRST SCHEDULE

Regulations 2 and 3(1)

EXCLUDED MEDICINAL PRODUCTS

1. Homeopathic medicine, being any substance used in the system of therapeutics in which a disease is treated by the use of minute amounts of one or more substances which, in their undiluted forms, are capable of producing in a healthy human being symptoms similar to those of the disease being treated.

2. Medicated oil and balm, being any external medicated embrocation, medicated cream, ointment or inhalant —

(*a*) which is used mainly for soothing purposes; and

(*b*) which contains one or more of the following substances as an active ingredient or as active ingredients:

(i) any essential oil;

(ii) any fixed oil derived from a plant;

(iii) methyl salicylate;

(iv) menthol;

(v) camphor;

(vi) peppermint.

FIRST SCHEDULE — *continued*

3. Quasi-medicinal product, being any of the following:

(*a*) any anti-dandruff preparation;

(*b*) any medicated cosmetic product for the treatment of pimples or acne, except any preparation containing etretinate or 13-cis-retinoic acid;

(*c*) any medicated soap;

(*d*) any sweet for relieving coughs or throat irritations;

(*e*) any medicated plaster;

(*f*) any sunscreen or suntan preparation;

(*g*) any medicated beverage;

(*h*) any vitamin or nutritional preparation from any plant, animal or mineral, or any combination thereof;

(*i*) any medicated toothpaste.

4. Traditional medicine, being any medicinal product consisting of one or more substances derived from any plant, animal or mineral, or any combination thereof, but does not include the following:

(*a*) any medicinal product to be administered by injection into a human body;

(*b*) any vaccine to be administered to a human being;

(*c*) any product derived from human blood;

(*d*) any item specified in the Poisons List in the Schedule to the Poisons Act (Cap. 234);

(*e*) any Chinese proprietary medicine.

5. Herbal remedy, being any medicinal product consisting of a substance produced by subjecting a plant or plants to drying, crushing or other process or of a mixture whose ingredients are 2 or more substances so produced, or of a combination of such mixture with water or such other inert substances as the licensing authority may specify.

6. Medicinal products that are raw materials used as ingredients in the preparation or manufacture of any medicinal product.

SECOND SCHEDULE

Regulation 6(2)

LABELLING REQUIREMENTS

1.—(1) Clinical research materials supplied on or after 1 November 2017 must be labelled with information for all of the following purposes:

(*a*) to ensure protection of the subject and traceability;

(*b*) to enable identification of the material and the trial;

(*c*) to facilitate proper use and storage of the material;

(*d*) to ensure the reliability and robustness of data generated in the trial.

(2) Without limiting the generality of sub-paragraph (1), every investigational CRM that is not licensed, every licensed investigational CRM which does not satisfy the requirements in sub-paragraph (5), and every auxiliary CRM that is not licensed must be labelled with all of the following information:

(*a*) the words "For clinical research use only" or similar wordings;

(*b*) a clinical research reference allowing identification of the trial, site, investigator and sponsor;

(*c*) the research subject identification number or treatment number and, where relevant, visit number;

(*d*) the name, address and telephone number of the main contact for —

(i) information on the clinical research material;

(ii) information on the research; and

(iii) emergency unblinding;

(*e*) the name of the substance used in the clinical research material and its strength or potency, as well as, in the case of blinded trials, the name of the comparator or placebo;

(*f*) the pharmaceutical form, route of administration and quantity of dosage units of the clinical research material;

(*g*) the directions for use of the clinical research material (which may be a reference to a leaflet or other explanatory document intended for use by the subject or person administering the material);

(*h*) the batch or code number identifying the contents and packaging operation of the clinical research material;

(*i*) the period of use (which may be an expiry date or a retest date), in month and year format and in a manner that avoids any confusion as to which is the month and which is the year;

SECOND SCHEDULE — *continued*

(*j*) the storage conditions.

(3) Without limiting the generality of sub-paragraph (1), every licensed investigational CRM which satisfies the requirements of sub-paragraph (5) must be labelled with all of the following information:

(*a*) the words "For clinical research use only" or similar wordings;

(*b*) a clinical research reference allowing identification of the trial, site, investigator and sponsor;

(*c*) the name of the person to whom the clinical research material is to be administered or the research subject identification number;

(*d*) the name, address and any identification number or logo of the licensed healthcare institution or trial site where the clinical research material is supplied or dispensed;

(*e*) the name of the clinical research material, being the proprietary name and the appropriate non-proprietary name of the active ingredient in the clinical research material;

(*f*) where the appropriate non-proprietary name is included on the label of the product, the appropriate quantitative particulars of any active ingredient of the clinical research material;

(*g*) the directions for use of the clinical research material;

(*h*) an appropriate control number, such as a serial number, batch number or lot number;

(*i*) the expiry date of the clinical research material;

(*j*) the date that the clinical research material is dispensed;

(*k*) where the clinical research material is registered, the registration number assigned to the product by the Authority.

(4) Without limiting the generality of sub-paragraph (1), every licensed auxiliary CRM must be labelled with all of the following information:

(*a*) the name of the person to whom the clinical research material is to be administered or the research subject identification number;

(*b*) the name, address and any identification number or logo of the licensed healthcare institution or trial site where the clinical research material is supplied or dispensed;

(*c*) the name of the clinical research material, being the proprietary name and the appropriate non-proprietary name of the active ingredient in the clinical research material;

SECOND SCHEDULE — *continued*

(*d*) where the appropriate non-proprietary name is included on the label of the product, the appropriate quantitative particulars of any active ingredient of the clinical research material;

(*e*) the directions for use of the clinical research material;

(*f*) an appropriate control number, such as a serial number, batch number or lot number;

(*g*) the expiry date of the clinical research material;

(*h*) the date that the clinical research material is dispensed;

(*i*) where the clinical research material is registered, the registration number assigned to the product by the Authority.

(5) The requirements for the purpose of sub-paragraphs (2) and (3) in relation to any investigational CRM are all of the following:

(*a*) the material is not used in the clinical trial in a blinded fashion;

(*b*) the material is not repackaged for use in the trial;

(*c*) the material is used in accordance with the terms of its registration (if registered).

(6) The information referred to in sub-paragraphs (2), (3) and (4) must be in English, and must be clearly legible and unambiguous.

(7) The address and telephone number referred to in sub-paragraph (2)(*d*) need not appear on the label if the subjects are given a leaflet or card providing such information and instructed to keep the leaflet or card in their possession at all times.

(8) The information referred to in sub-paragraph (2)(*b*), (*c*), (*d*) and (*f*) to (*i*) need not appear on the label if they are available by any other means, so long as —

(*a*) sub-paragraph (1) is complied with; and

(*b*) the reasons for the omission are set out in the protocol or such other document as the Authority may allow.

(9) Sub-paragraphs (1)(*d*), (2)(*a*) to (*d*) and (*g*), (3)(*a*) to (*d*), (*g*) and (*j*) and (4)(*a*), (*b*), (*e*) and (*h*) do not apply where the supply is by wholesale.

2. Clinical research materials supplied before 1 November 2017 must —

(*a*) be labelled in accordance with paragraph 1; or

(*b*) have the following particulars written on its container:

(i) the proprietary name, reference number or other identification mark of each item of such material;

SECOND SCHEDULE — *continued*

(ii) the name and address of the manufacturer;

(iii) the production batch number of the material;

(iv) the name or other identification mark of the subject for whom the material is intended;

(v) the date of manufacture and the expiry date of the material;

(vi) the storage conditions appropriate for each item of material as may be indicated by the manufacturer; and

(vii) the words "This product shall only be used under strict medical surveillance" or "This product shall only be used under strict dental surveillance", as the case may be.

Made on 13 July 2016.

CHAN HENG KEE
Permanent Secretary,
Ministry of Health,
Singapore.

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