No. S 000

HEALTH PRODUCTS ACT
(CHAPTER 122D)

HEALTH PRODUCTS (THERAPEUTIC PRODUCTS AS CLINICAL RESEARCH MATERIALS) REGULATIONS 2015

ARRANGEMENT OF REGULATIONS

In exercise of the powers conferred by sections 45, 71 and 72 of the Health Products Act, the Health Sciences Authority, with the approval of the Minister for Health, makes the following Regulations:

PART 1

GENERAL

Citation and commencement

1. These Regulations may be cited as the Health Products (Therapeutic Products as Clinical Research Materials) Regulations 2015 and come into operation on 2015.

Definitions

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

"administration", in relation to any clinical research material, means giving or applying the material to a human being —

(*a*) whether orally, by injection or by introduction into the body in any other way, or by external application, whether by direct contact with the body or not; and

(*b*) whether in its existing state or after it has been dissolved or dispersed in, or diluted or mixed with, some other substance used as a vehicle;

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

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

"clinical research material" means any therapeutic product or placebo that is manufactured, 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, as the test or as a reference in the research;

"codeine cough preparation" means a therapeutic product that —

(*a*) is in liquid form;

(*b*) contains codeine; and

(*c*) is intended by the person who manufactured the product for the treatment of cough;

"institutional review board" means an institutional review board appointed under the Human Biomedical Research Act 2015 (Act 29 of 2015);

"in-store pharmaceutical officer" means —

(*a*) a qualified pharmacist engaged or employed to provide pharmacy services at or from a licensed retail pharmacy; or

(*b*) a person acting under the supervision of the qualified pharmacist when providing pharmacy services at or from the licensed retail pharmacy;

"licensed retail pharmacy" means the premises specified in a pharmacy licence;

"pharmacy licence" means a licence issued under the Health Products (Licensing of Retail Pharmacies) Regulations 2015 (G.N. No. S __/2015);

"pharmacy-only medicine" means a registered health product that is entered into the Register of Health Products under the classification of "pharmacy-only medicine", and does not include any prescription-only medicine;

"prescription-only medicine" means a registered health product that is entered into the Register of Health Products under the classification of "prescription-only medicine", and does not include any pharmacy-only medicine;

"psychotropic substance" means a substance specified in the First Schedule to the Health Products (Therapeutic Products) Regulations 2015 (G.N. No. S __/2015);

"qualified pharmacist" means a person who —

(*a*) is registered as a pharmacist under the Pharmacists Registration Act (Cap. 230);

(*b*) holds a valid practising certificate granted under section 23 of that Act; and

(*c*) is in active practice, as defined in regulation 2 of the Pharmacists Registration (Practising Certificates) Regulations 2008 (G.N. No. S 438/2008);

"qualified practitioner" means —

(*a*) a registered medical practitioner under the Medical Registration Act (Cap. 174); or

(*b*) a registered dentist under the Dental Registration Act (Cap. 76) whose name appears in the first division of the Register of Dentists maintained and kept under section 13(1)(*a*) of that Act;

"regulated clinical trial" means any clinical research that is —

(*a*) 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 2015 (G.N. No. S __/2015); or

(*b*) issued with a certificate under regulation 5 of the Medicines (Clinical Trials) Regulations 2015 (G.N. No. S ____/2015);

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

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

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

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

"therapeutic product" means a health product categorised as a therapeutic product in the First Schedule to the Act.

(2) For the purposes of these Regulations, a prescription is valid only if the prescription —

(*a*) is written and signed by a qualified practitioner;

(*b*) contains all of the following particulars:

(i) the date of the prescription;

(ii) the name and address of the qualified practitioner giving it;

(iii) the name, contact details and identity card or other identification document number of the subject;

(iv) the name and total amount of the prescribed clinical research material to be supplied to, and the dose to be taken by, the subject;

(v) where the qualified practitioner giving the prescription intends for the prescription to be repeated, an indication of the number of times, and the time period between which, the prescribed clinical research material may be supplied;

(vi) where the prescription is given by a dentist, a declaration by the dentist that the prescription is "for dental treatment only".

PART 2

EXCEPTIONS FOR MANUFACTURE, IMPORT AND SUPPLY OF CLINICAL RESEARCH MATERIALS

Exceptions from Act

3.—(1) Section 12(1) of the Act does not apply to the manufacture of any clinical research material.

(2) Subject to regulations 4 and 5, section 13(1) of the Act does not apply to the import of any clinical research material.

(3) Subject to regulations 6 and 7, section 14(1) of the Act does not apply to the supply by wholesale of any clinical research material.

(4) Subject to regulation 7, section 15(1) of the Act does not apply to the supply of any clinical research material.

Notification of import of clinical research material

4.—(1) Regulation 3(2) applies to the import of a clinical research material only if the person who imports (called an importer in these Regulations) the material gives the Authority notice of the import before importing the material.

(2) The notice must be given in the form and manner, and within the time, specified on the Authority's website.

(3) This regulation does not apply to any clinical research material which satisfies all of the following requirements:

(*a*) before [*date of commencement of these Regulations*], the clinical research material was a medicinal product under the Medicines Act (Cap. 176) whose import was permitted by the Authority for a period of time, in connection with any clinical trial regulated under the Medicines (Clinical Trials) Regulations (Cap. 176, Rg 3);

(*b*) the clinical research material is imported within that period.

Approval for import of consignments of clinical research materials containing psychotropic substances

5.—(1) Despite regulation 3(2), an importer must not import any clinical research material that contains any psychotropic substance, except under and in accordance with a prior approval of the Authority for every consignment of the material to be imported.

(2) An application for an approval under paragraph (1) must —

(*a*) be made in the form and manner, and within the time, specified on the Authority's website; and

(*b*) by accompanied by such particulars, information, documents and samples as the Authority may require.

(3) Upon receiving an application under this regulation, the Authority may approve the application or refuse to approve the application.

(4) The Authority may subject its approval to such conditions as the Authority thinks necessary and may, from time to time, by notice in writing to the person granted the approval —

(*a*) modify or remove any condition of the approval; or

(*b*) impose any new condition on the approval.

(5) The conditions referred to in paragraph (4) may include a condition limiting the quantity which may be imported in the consignment under the approval, and different limits may be imposed under different approvals.

(6) The Authority may, at any time, suspend or revoke any approval.

(7) To avoid doubt, this regulation applies in addition to regulation 4.

Approval for export of consignments of certain clinical research materials

6.—(1) This regulation applies to any clinical research material manufactured by, imported by or supplied to a person, which —

(*a*) contains any psychotropic substance; or

(*b*) is a codeine cough preparation.

(2) Despite regulation 3(3), the person must not export the clinical research material except under and in accordance with a prior approval of the Authority for every consignment of the material to be exported.

(3) An application for an approval under paragraph (2) must —

(*a*) be made in the form and manner, and within the time, specified on the Authority's website; and

(*b*) by accompanied by such particulars, information, documents and samples as the Authority may require.

(4) Upon receiving an application under this regulation, the Authority may approve the application or refuse to approve the application.

(5) The Authority may subject its approval to such conditions as the Authority thinks necessary and may, from time to time, by notice in writing to the person granted the approval —

(*a*) modify or remove any condition of the approval; or

(*b*) impose any new condition on the approval.

(6) The Authority may, at any time, suspend or revoke any approval.

Notification of supply of clinical research material by manufacturer

7.—(1) Regulation 3(3) and (4) applies to a supply of clinical research material by a person who manufactures (called a manufacturer in these Regulations) the material only if the manufacturer gives the Authority notice of the supply before the manufacturer supplies the material.

(2) The notice must be given in the form and manner, and within the time specified, on the Authority's website.

(3) This regulation does not apply if the manufacture of the clinical research material being supplied comprises solely of the packaging or labelling of the material.

PART 3

MANUFACTURE AND IMPORT OF CLINICAL RESEARCH MATERIALS

Manufacture and import of clinical research materials

8. A person who is 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 the material.

PART 4

SUPPLIES OF CLINICAL RESEARCH MATERIALS

Supply only as clinical research material

9.—(1) A person who manufactures, imports or is supplied with any clinical research material under regulation 3(1), (2), (3) or (4)

must only supply the material for the purpose of being used in clinical research by way of administration to a subject 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 paragraph (1) 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*) these Regulations cease to apply to the clinical research material; and

(*b*) nothing in these Regulations prevents any applicable law relating to therapeutic products from applying to the clinical research material.

Supply to subject of codeine cough preparations

10.—(1) This regulation applies to a supply of codeine cough preparation to a subject other than by way of administration, in any clinical research that is not a regulated clinical trial.

(2) A person must not make the supply unless —

(*a*) the person is a qualified practitioner or a qualified pharmacist; and

(*b*) the person complies with all of the following requirements:

(i) the person does not supply more than a total of 240ml of any one or more codeine cough preparations to any one subject on any one occasion;

(ii) the person does not supply any codeine cough preparation to the same subject more than once within a period of 4 days (including Sundays and public holidays); and

(iii) the person provides professional counselling on the use of codeine cough preparations on each occasion of supply.

(3) Paragraph (2) applies despite anything in a prescription given to the subject by the qualified practitioner of the clinical research who is in charge of the care of the subject.

Supply to subject other than by administration of prescription-only or pharmacy-only medicine

11.—(1) This regulation applies to a supply of prescription-only medicine or pharmacy-only medicine to a subject other than by way of administration, in any clinical research that is not a regulated clinical trial.

(2) A person must not make the supply unless —

(*a*) the person is specified in the first column of Part 1 of the First Schedule; and

(*b*) the person makes the supply in the circumstances specified against the person in the second column of Part 1 of the First Schedule.

Supply to subject by administration of prescription-only medicine

12. A person must not administer any prescription-only medicine to a subject unless —

(*a*) the person is a qualified practitioner; or

(*b*) the person administers the material in accordance with the instructions of a qualified practitioner.

Supply of clinical research material properly labelled

13.—(1) Subject to paragraph (2), a person must not supply any clinical research material if the material is not labelled in accordance with regulation 26 of the Health Products (Clinical Trials) Regulations 2015 (G.N. No. S __/2015), modified as follows:

(*a*) a reference to an investigational therapeutic product in that regulation is to be read as a reference to a clinical research material that is the clinical research material to be tested or used as a reference in the clinical research;

(*b*) a reference to an auxiliary therapeutic product in that regulation is to be read as the clinical research material used for the needs of the clinical research as described in the protocol, but not as the material to be tested or used as a reference in the research;

(*c*) a reference to a clinical trial in that regulation is to be read as a reference to a clinical research; and

(*d*) a reference to a clinical trial reference code in that regulation is to be read as a reference to a clinical research reference.

(2) Regulation 26(1)(*d*) and (2)(*a*), (*e*), (*f*) and (*g*) of the Health Products (Clinical Trials) Regulations 2015 does not apply where the supply is by way of wholesale.

PART 5

DUTIES RELATING TO CLINICAL RESEARCH MATERIALS

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

Dealing with clinical research materials

14.—(1) This regulation applies to any clinical research material manufactured in, imported into, or supplied in, Singapore under regulation 3.

(2) Without prejudice to regulation 9, 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 by way of administration to a subject 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*) these Regulations cease to apply to the clinical research material; and

(*b*) nothing in these Regulations prevents any applicable law relating to therapeutic products from applying to the clinical research material.

(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 (subject to regulation 6 in relation to any material that contains any psychotropic substance) exported.

(6) In paragraph (5), "unused clinical research material" means the 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

15. A manufacturer of any clinical research material must keep records of the manufacture, assembly and testing of the material.

Records of receipt and supply

16.—(1) A person who supplies any clinical research material (including a manufacturer 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 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.

(3) In addition to any records required to be kept under this regulation, where the clinical research material is pharmacy-only medicine that is supplied to a subject, the person making the supply must also keep records of all of the following:

(*a*) the contact details and identity card or other identification document number of the subject;

(*b*) the strength of the material supplied; and

(*c*) the dosage, and the frequency and purpose of the treatment for which the supply is made.

(4) In addition to any records required to be kept under this regulation, where the clinical research material is supplied to a subject against a valid prescription given by a qualified practitioner, the person making the supply must also keep records of all of the following:

(*a*) the contact details and identity card or other identification document number of the subject; and

(*b*) if the material is supplied by a qualified pharmacist or a person acting under the supervision of a qualified pharmacist, the name and the address of the qualified practitioner who signed the prescription.

(5) The records referred to in paragraphs (3) and (4) must be made on the day of the event to which the records relate or, if that is not reasonably practicable, the next day.

Records of dealings with clinical research materials

17.—(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 14, 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

18.—(1) A person who is required to keep any record referred to in 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 the manufacture of clinical research material, the applicable period is the longer of the following periods:

(*a*) 1 year after the expiry date of the clinical research material;

(*b*) 5 years after the date of manufacture of the clinical research material.

(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, disposal or export, 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 Health Products (Clinical Trials) Regulations 2015 (G.N. No. S XX/2015) or regulation XX of the Medicines (Clinical Trials) Regulations 2015 (G.N. No. S XX/2015), as the case may be.

Division 3 — Reports to Authority

Notifications of unexpected serious adverse drug reactions

19.—(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 Health Products (Clinical Trials) Regulations 2015 (G.N. No. Sxx/2015);

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

(*a*) in the case of material that is a registered health product, in the product information leaflet or the investigator's brochure relating to the material; and

(*b*) in the case of material that is not a registered health product, in the investigator's brochure relating to the material.

Recall of clinical research material

20.—(1) For the purposes of section 44(1) of the Act, where any person intends to recall any clinical research material which the person manufactured, imported or supplied pursuant to 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.

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

(3) For the purpose of section 44(2) of the Act, where the Authority has been notified of the intended recall of any clinical research material under paragraph (1), the Authority may by written notice 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.

PART 6

MISCELLANEOUS

Certificate of manufacturing standard of clinical research materials

21.—(1) The Authority may, on the application of a manufacturer of any clinical research material and upon assessment of satisfactory conformity with a Good Manufacturing Practice Standard, issue a GMP certificate to the manufacturer subject to such terms and conditions as the Authority thinks fit.

(2) Every GMP Certificate issued is valid for a period specified in the certificate, being not longer than 3 years from the date of assessment of satisfactory conformity with a Good Manufacturing Practice Standard.

(3) An application for a GMP Certificate must —

(*a*) be made in the form and manner specified on the Authority's website; and

(*b*) be accompanied by the relevant fee specified in the Second Schedule.

(4) In this regulation —

"Good Manufacturing Practice Standard" means the Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme Guide to Good Manufacturing Practice for Medicinal Products or such other good manufacturing practice standard approved by the Authority;

"GMP Certificate" means a certificate issued by the Authority to certify compliance with the Good Manufacturing Practice Standard.

Enforcement requirements

22.—(1) An enforcement officer may conduct routine inspections of —

(*a*) any premises that are being used for the manufacture, supply or storage of any clinical research material; and

(*b*) any conveyances that are being used for the transport of any clinical research material.

(2) An enforcement officer conducting a routine inspection under paragraph (1) may —

(*a*) require any person having possession or control of any clinical research material that is found during the inspection to furnish, without charge, a sample of such material for the Authority's examination; and the person must comply with the requirement; and

(*b*) take or cause to be taken any photograph of —

(i) the premises or conveyances referred to in paragraph (1); or

(ii) any property or material found on the premises or in the conveyances.

Offences

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

(*a*) contravenes regulation 4(1), 5(1), 6(2), 7(1), 8, 9(1), 10(2), 11(2), 12, 13(1), 14(2), (3)(*b*) or (5), 15, 16(1), (3), (4) or (5), 17(1), 18(1), 19(1) or (2) or 22(2)(*a*); or

(*b*) for the purposes of making an application or 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, or any sample which the person knows is altered or adulterated.

(2) A person who is guilty of an offence under paragraph (1) shall be liable on conviction to a fine not exceeding $20,000 or to imprisonment for a term not exceeding 12 months or to both.

FIRST SCHEDULE

Regulation 11(2)

PART 1

SUPPLY TO SUBJECT OF CERTAIN THERAPEUTIC PRODUCTS

	First column	*Second column*
S/No.	*Person who may supply*	*Circumstances of supply*
1.	For prescription-only medicine	
	(*a*) A qualified practitioner, or a person acting in accordance with the instructions of a qualified practitioner	The supply is to a subject under the care of the qualified practitioner
	(*b*) An in-store pharmaceutical officer providing pharmacy services at or from a licensed retail pharmacy	(i) The supply is in accordance with a valid prescription given by a qualified practitioner; or (ii) the supply is of prescription-only medicine specified in the list of prescription-only medicines exempted for limited sale and supply under all of the following conditions: (A) the medicine is labelled to show a maximum daily dose not exceeding that specified in the list; (B) the medicine is supplied in a quantity that does not exceed the maximum supply specified in the list;

S/No.	*First column* *Person who may supply*	*Second column* *Circumstances of supply*
		(C) the medicine is supplied to a subject who is of or above any minimum age specified in the list;
		(D) the in-store pharmaceutical officer keeps a record of the supply of the medicine under regulation 16(4).
2.	For pharmacy-only medicine:	
	(*a*) A qualified practitioner, or a person acting in accordance with the instructions of a qualified practitioner	The supply is to a subject under the care of the qualified practitioner
	(*b*) An in-store pharmaceutical officer engaged or employed by the holder of a pharmacy licence for the licensed retail pharmacy	The supply is made at or from the licensed retail pharmacy.

PART 2

INTERPRETATION

1. For the purposes of item 1(*c*) in Part 1, "list of prescription-only medicine exempted for limited sale and supply" or "list" means the list, as published on the Authority's website, of therapeutic products classified as prescription-only medicines that may be supplied by an in-store pharmaceutical officer at [or from] a licensed retail pharmacy without the need for a valid prescription.

SECOND SCHEDULE

Regulation 21(2)

FEES

S/No.	*Description of fee*	*Amount of fee*
1.	Application fee for each of the following:	
	(*a*) a GMP Certificate	$6,000
	(*b*) any additional GMP Certificate where no further assessment is required	$200.