HEALTH PRODUCTS (CLINICAL TRIALS) (AMENDMENT) REGULATIONS 2021

S.L. 179 of 2021

Presented to Parliament pursuant to section 72(5) of the Health Products Act.
Ordered by Parliament to lie upon the Table:

10 March 2021

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HEALTH PRODUCTS ACT (CHAPTER 122D)

HEALTH PRODUCTS (CLINICAL TRIALS) (AMENDMENT) REGULATIONS 2021

In exercise of the powers conferred by section 72(1) of the Health Products Act, the Health Sciences Authority, with the approval of the Minister for Health, makes the following Regulations:

Citation and commencement

1. These Regulations are the Health Products (Clinical Trials) (Amendment) Regulations 2021 and come into operation on 1 March 2021.

Amendment of regulation 2

2. Regulation 2(1) of the Health Products (Clinical Trials) Regulations 2016 (G.N. No. S 331/2016) (called in these Regulations the principal Regulations) is amended —

(*a*) by inserting, immediately before the definition of "adult", the following definition:

" "active substance", in relation to a CTGT product, means a substance that —

(*a*) is usable in the manufacture of the CTGT product as an active constituent; and

(*b*) achieves its intended action by pharmacological, immunological, physiological, metabolic or physical means;";

(*b*) by deleting the definition of "appropriate non-proprietary name" and substituting the following definitions:

"" "applicable CTGT product" means a CTGT product that is treated as a Class 2 CTGT product under the Health Products (Cell, Tissue and Gene Therapy Products) Regulations 2021 (G.N. No. S 104/2021);

"appropriate non-proprietary name", in relation to an active ingredient of a therapeutic product or an active substance in an applicable CTGT product, means —

(*a*) the name or a synonym of the active ingredient or the active substance (as the case may be) described in the relevant monograph appearing in the latest edition of any specified publication; or

(*b*) in any other case, its international non-proprietary name or the accepted scientific name or other name descriptive of the true nature of the active ingredient or the active substance, as the case may be;";

(*c*) by deleting the definition of "auxiliary therapeutic product" and substituting the following definitions:

"" "auxiliary product" means a therapeutic product or an applicable CTGT product used for the needs of a clinical trial as described in the protocol, but not as an investigational product;

"CTGT product" means a health product categorised as a cell, tissue or gene therapy product in the First Schedule to the Act;";

(*d*) by inserting, immediately after the definition of "institutional review board", the following definition:

"“international non-proprietary name”, for an active ingredient of a therapeutic product or an active substance in an applicable CTGT product, means a name which has been selected by the World Health Organization as a recommended international non-proprietary name for the active ingredient or active substance, as the case may be;”;

(*e*) by deleting the definition of “investigational therapeutic product” and substituting the following definition:

"“investigational product” means —

(*a*) a therapeutic product;

(*b*) an applicable CTGT product; or

(*c*) a placebo,

that is to be tested or used as a reference in a clinical trial;”;

(*f*) by inserting, immediately after the words “registered therapeutic products” in the definition of “observational trial”, the words “or registered applicable CTGT products (as the case may be)”;

(*g*) by deleting the definition of “proprietary name” and substituting the following definition:

"“proprietary name” means a word or words used in connection with the supply of a therapeutic product or CTGT product for the purpose of indicating that the therapeutic product or CTGT product (as the case may be) is the product of a particular person who manufactures, selects the name of, certifies or deals with that therapeutic product or CTGT product, or offers it for supply;”;

(*h*) by inserting, immediately after the definition of “serious adverse event”, the following definition:

" "specified publication" means any of the following:

(*a*) the British Pharmacopoeia;

(*b*) the European Pharmacopoeia;

(*c*) the United States Pharmacopoeia and the National Formulary;

(*d*) any other publication that is specified on the Authority's website;"; and

(*i*) by inserting, immediately after the definition of "therapeutic product", the following definition:

" "traceability", in relation to an applicable CTGT product, means —

(*a*) the ability to locate and identify the CTGT product and its starting and raw materials at any point in time during its manufacture, import, supply or administration, including the sourcing, procurement, processing, testing, packaging, storage, transport, delivery and disposal of the CTGT product;

(*b*) the ability to identify the donor and tissue bank, blood bank or manufacturing facility that receives, processes or stores any cells or tissue that the CTGT product contains;

(*c*) the ability to locate and identify all data relating to any raw material or other substance that comes into contact with any cells or tissue that the CTGT product contains; and

(*d*) the ability to identify the person who receives the CTGT product at a licensed healthcare institution or a

licensed retail pharmacy at which the CTGT product is administered, dispensed or supplied to a subject;".

Deletion and substitution of regulation 3

3. Regulation 3 of the principal Regulations is deleted and the following regulation substituted therefor:

"**Scope of Regulations**

3. These Regulations apply to all clinical trials of the following products that are not observational trials:

(*a*) therapeutic products;

(*b*) applicable CTGT products.".

Amendment of regulation 23

4. Regulation 23 of the principal Regulations is amended —

(*a*) by deleting the word "and" at the end of paragraph (1)(*a*);

(*b*) by deleting the full-stop at the end of sub-paragraph (*b*) of paragraph (1) and substituting the word "; and", and by inserting immediately thereafter the following sub-paragraph:

"(*c*) in the case of an investigational product that is an applicable CTGT product, allow traceability of the product."; and

(*c*) by inserting, immediately after sub-paragraph (iv) of paragraph (2)(*c*), the following sub-paragraph:

"(iv*a*) where the record is of a clinical trial that involves an applicable CTGT product and relates to the traceability of that product — the expiry of 30 years after the expiry date of that product or any other shorter period that the Authority allows in a particular case;".

New regulation 23A

5. The principal Regulations are amended by inserting, immediately after regulation 23, the following regulation:

"**Traceability of applicable CTGT products used in clinical trials**

23A.—(1) The sponsor of a clinical trial that involves any applicable CTGT product must ensure that a system of traceability that complies with paragraph (2) is established and maintained.

(2) The system mentioned in paragraph (1) must at the minimum enable the traceability of the CTGT product and its starting and raw materials, including all substances that may come into contact with the cells or tissue it contains during any of the following processes:

(*a*) sourcing;

(*b*) procurement;

(*c*) processing;

(*d*) testing;

(*e*) packaging;

(*f*) storage;

(*g*) transport;

(*h*) delivery to the trial site where the CTGT product is used or administered;

(*i*) any other final reconciliation, disposal or destruction of the CTGT product.

(3) The principal investigator of a clinical trial that involves any applicable CTGT product must ensure that a system of traceability is established and maintained at the trial site such that the CTGT product may be linked to the subject who received it, and vice versa.

(4) The sponsor and principal investigator mentioned in paragraphs (1) and (3) must keep all data obtained from the

system of traceability for at least 30 years after the expiry date of the CTGT product or any other shorter period that the Authority allows in a particular case.".

Amendment of regulation 29

6. Regulation 29(1) of the principal Regulations is amended by inserting, immediately after the words "23(1) or (3)," in sub-paragraph (*a*), the words "23A(1), (3) or (4),".

Amendment of Second Schedule

7. The Second Schedule to the principal Regulations is amended —

(*a*) by deleting the word "traceability" in paragraph 1(1)(*a*) and substituting the words "product tracking";

(*b*) by inserting, immediately before the words "the name of the substance" in paragraph 1(2)(*e*), the words "in the case of a therapeutic product,";

(*c*) by inserting, immediately after sub-paragraph (*e*) of paragraph 1(2), the following sub-paragraph:

"(*ea*) in the case of an applicable CTGT product, the name of the CTGT product and a description, expressed qualitatively and quantitatively, of any active substance in the CTGT product, as well as, in the case of blinded trials, the name of the comparator or placebo;";

(*d*) by deleting the full-stop at the end of sub-paragraph (*j*) of paragraph 1(2) and substituting a semi-colon, and by inserting immediately thereafter the following sub-paragraphs:

"(*k*) in the case of an autologous applicable CTGT product, the unique patient identifier and the words "for autologous use only" or similar wordings;

(*l*) in the case of an applicable CTGT product, the list of excipients, including preservative systems (if applicable), for the CTGT product;

(*m*) in the case of an applicable CTGT product, any warning that is necessary for the CTGT product;

(*n*) in the case of an applicable CTGT product, any precaution relating to the disposal of any unused CTGT product or any waste derived from the CTGT product (where appropriate) and any available collection system for the unused CTGT product or waste.";

(*e*) by deleting the word "and" in paragraph 1(3)(*e*) and substituting the word "or";

(*f*) by inserting, immediately before the words "where the appropriate" in paragraph 1(3)(*f*), the words "in the case of a therapeutic product,";

(*g*) by inserting, immediately after sub-paragraph (*f*) of paragraph 1(3), the following sub-paragraph:

"(*fa*) in the case of an applicable CTGT product, the name of the CTGT product and a description, expressed qualitatively and quantitatively, of any active substance in the CTGT product;";

(*h*) by deleting the full-stop at the end of sub-paragraph (*k*) of paragraph 1(3) and substituting a semi-colon, and by inserting immediately thereafter the following sub-paragraphs:

"(*l*) the conditions under which the product must be stored;

(*m*) in the case of an autologous applicable CTGT product, the unique patient identifier and the words "for autologous use only" or similar wordings;

(*n*) in the case of an applicable CTGT product, the list of excipients, including preservative systems (if applicable), for the CTGT product;

(*o*) in the case of an applicable CTGT product, any warning that is necessary for the CTGT product;

(*p*) in the case of an applicable CTGT product, any precaution relating to the disposal of any unused CTGT product or any waste derived from the CTGT product (where appropriate) and any available collection system for the unused CTGT product or waste.";

(*i*) by deleting the word "and" in paragraph 1(4)(*c*) and substituting the word "or";

(*j*) by inserting, immediately before the words "where the appropriate" in paragraph 1(4)(*d*), the words "in the case of a therapeutic product,";

(*k*) by inserting, immediately after sub-paragraph (*d*) of paragraph 1(4), the following sub-paragraph:

"(*da*) in the case of an applicable CTGT product, the name of the CTGT product and a description, expressed qualitatively and quantitatively, of any active substance in the CTGT product;";

(*l*) by deleting the full-stop at the end of sub-paragraph (*i*) of paragraph 1(4) and substituting a semi-colon, and by inserting immediately thereafter the following sub-paragraphs:

"(*j*) the conditions under which the product must be stored;

(*k*) in the case of an autologous applicable CTGT product, the unique patient identifier and the words "for autologous use only" or similar wordings;

(*l*) in the case of an applicable CTGT product, the list of excipients, including preservative systems (if applicable), for the CTGT product;

(*m*) in the case of an applicable CTGT product, any warning that is necessary for the CTGT product;

(*n*) in the case of an applicable CTGT product, any precaution relating to the disposal of any unused CTGT product or any waste derived from the CTGT product (where appropriate) and any available collection system for the unused CTGT product or waste.";

(*m*) by deleting the words "sub-paragraph (2)(*b*), (*c*), (*d*) and (*f*) to (*i*)" in paragraph 1(8) and substituting the words "sub-paragraphs (2)(*b*), (*c*), (*d*) and (*f*) to (*i*), (3)(*a*), (*b*), (*d*), (*g*), (*j*), (*k*) and (4)(*b*), (*e*), (*h*) and (*i*)";

(*n*) by inserting, immediately after sub-paragraph (8) of paragraph 1, the following sub-paragraph:

"(9) In this paragraph, "autologous", in relation to an applicable CTGT product, means a CTGT product that contains cells or tissue that are obtained only from the individual to whom the CTGT product is to be administered."; and

(*o*) by deleting paragraph 2.

Miscellaneous amendments

8. The principal Regulations are amended —

(*a*) by deleting the words "investigational therapeutic product" wherever they appear in the following provisions and substituting in each case the words "investigational product":

Regulation 2 (definitions of "adverse drug reaction", "adverse event", "clinical trial in an emergency situation", "investigator's brochure", "subject", "substantial amendment", "unexpected serious adverse drug reaction" or "USADR" and "window period")

Regulation 4(4)(*a*)(i)

Regulation 5(4)

Regulation 26(2) and (4)

Paragraph 4 of the First Schedule

Paragraph 1(1), (2), (3) and (5) of the Second Schedule;

(*b*) by deleting the words "THERAPEUTIC PRODUCTS" in the heading of Part 2 and substituting the words "THERAPEUTIC PRODUCTS OR APPLICABLE CTGT PRODUCTS";

(*c*) by deleting the words "*therapeutic products*" in the heading of Division 2 of Part 2 and substituting the words "*therapeutic products or applicable CTGT products*";

(*d*) by deleting the words "therapeutic product" in the following provisions and substituting in each case the words "therapeutic product or applicable CTGT product":

Regulation 7(1)(*b*)

Regulation 8(3)(*a*) and (*c*)(ii) and (iii)(C)

Regulation 9(3)(*a*) and (*c*)(ii) and (iii)(C)

Regulation 16(4)(*b*)(ii), (7)(*b*)(ii) and (8)(*a*) and (*b*)(iii)

Regulation 23(2)(*c*)(i);

(*e*) by deleting the words "investigational therapeutic products and auxiliary therapeutic products" in regulation 26(1) and (3) and substituting in each case the words "investigational products and auxiliary products";

(*f*) by deleting the words "auxiliary therapeutic product" in the following provisions and substituting in each case the words "auxiliary product":

Regulation 26(4) and the regulation heading

Paragraph 1(1), (2) and (4) of the Second Schedule;

(*g*) by deleting the words "Investigational therapeutic product" in the regulation heading of regulation 26 and substituting the words "Investigational product"; and

(*h*) by deleting the words "Investigational therapeutic products" in paragraph 12 of the First Schedule and substituting the words "Investigational products".

Made on 15 February 2021.

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Chairman,
Health Sciences Authority,
Singapore.

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