



MINISTRY OF HEALTH
SINGAPORE

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MOH Circular No. 21/2021

18 February 2021

Licensees of Hospitals, Medical, and Dental Clinics

ADDENDUM TO MOH DIRECTIVE NO. 6/2020 ON THE USE OF CELL, TISSUE AND GENE THERAPY PRODUCTS MANUFACTURED IN-HOUSE BY HEALTHCARE INSTITUTIONS

We refer to Directive No. 6/2020 on the Use of Cell, Tissue and Gene Therapy Products Manufactured In-house by Healthcare Institutions (“the Directive”) which was issued on 13 November 2020 and came into effect on 1 February 2021. This circular seeks to inform all licensees of hospitals, medical and dental clinics that there is a change in the applicable Regulations which govern Class 2 cell, tissue and gene therapy products (CTGTPs) manufactured in-house for use in research.

2. In view that the Health Products Act (Amendment of First Schedule) Order 2021 has come into effect on 1 March 2021, **the Medicines (Clinical Trials) Regulations no longer apply to in-house manufactured Class 2 CTGTPs used in research.** As CTGTPs are now specified and defined as a distinct category of products under the Health Products Act, **all Class 2 CTGTPs used in research will be subject to the Health Products (Clinical Trials) Regulations instead.** Please find appended a revised Annex A of the Directive, with the aforementioned change indicated in red.

3. In line with the date from which the controls for CTGTPs are effectively brought under the Health Products Act, these changes to the Directive will take effect from **1 March 2021**.

4. For any queries or further clarifications, please email eLis@moh.gov.sg. Thank you.

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Revised Annex A of the Directive

Use of In-House Manufactured CTGTPs in Research

1. The applicable legislation for HCLs and practitioners offering an in-house manufactured CTGTP in the research setting depends on the type of CTGTP:

- (a) Human Biomedical Research Act for Class 1 CTGTPs (lower risk), which contain human cells/tissue that are:
 - i. no more than minimally manipulated;¹
 - ii. intended for homologous use (i.e. used² for the same function as its original function and administered at the same anatomical site or histological environment in the recipient as in the donor); and
 - iii. not combined or used in conjunction with a therapeutic product or medical device; or
- (b) **Health Products (Clinical Trials) Regulations** for Class 2 CTGTPs (higher risk) i.e. CTGTPs that contain:
 - i. animal cells or tissue;
 - ii. recombinant nucleic acids; or
 - iii. human cells or tissue that are not Class 1 CTGTP.

Use of In-house Manufactured CTGTPs as Innovative Salvage Therapy

2. Outside of the research setting, section B6 of the SMC ECEG sets out the conditions under which medical practitioners may offer an untested practice as innovative salvage therapy.

3. In the context of in-house manufactured CTGTPs that fall under this category, the following conditions would apply:

- (a) Conventional therapy has proven to be unhelpful and it is a desperate or dire situation;
- (b) There must be professional consensus on the use of the in-house manufactured CTGTP in the particular clinical situation; and
- (c) Consent from the patients must be obtained, if they are able to give it.³

¹ CTGTPs that have been processed by any of, or any combination of, the following methods, are deemed to be “minimally manipulated”: cutting or sizing; grinding; shaping; centrifugation; soaking in an antibiotic or antimicrobial solution; sterilisation or irradiation; cell separation, concentration or purification; filtration; lyophilisation; freezing; cryopreservation; or vitrification – such that the biological characteristics or functions of the cell(s) or the structural properties of the tissue (as the case may be) are not altered.

² This refers to the repair, reconstruction, replacement, or supplementation of the recipient’s cells.

³ Where applicable, consent shall in addition or instead be obtained from the patient’s legal guardian, as the case may be.

Summary of Relevant Requirements for HCl's Using In-House Manufactured CTGTPs

