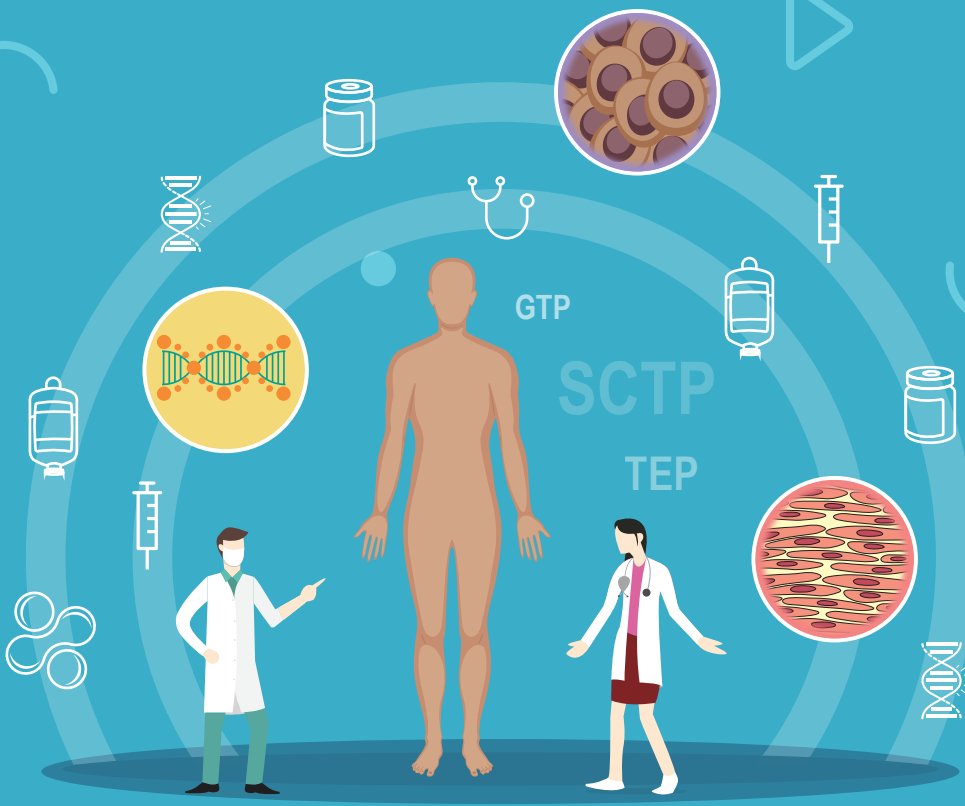
Regulatory Update on Advanced Therapy Products

(for Healthcare Professionals)



Drug Office
Department of Health

On 24 July 2020, the Pharmacy and Poisons (Amendment) Ordinance ("Amendment Ordinance") was published in the Gazette. The Amendment Ordinance seeks to strengthen the existing Pharmacy and Poisons Ordinance (Cap. 138) on regulation of advanced therapy products (ATPs).

This booklet provides a general overview of the regulation of ATPs after the amendment of the Pharmacy and Poisons Ordinance for healthcare professionals. The provisions of the Amendment Ordinance will come into operation on 1 August 2021.

For the full legislation, please refer to the Laws of Hong Kong.

Regulation of Advanced Therapy Products in Hong Kong

Advanced Therapy Products (ATPs) are innovative medical products based on genes, cells or tissues. The rapid scientific advancement in the research and development of ATPs offers great medical potential for benefiting patients. At the same time, due to their complicated nature, the risks and long-term side effects of ATPs need to be carefully managed.

In view of the high risks of ATPs, the government introduced a clear regulatory framework on the research and therapeutic use of ATPs in order to safeguard public health and facilitate their development.

The Pharmacy and Poisons (Amendment) Ordinance 2020

A Bill to regulate ATPs was passed by the Legislative Council on 17 July 2020 and published in the Gazette as the Pharmacy and Poisons (Amendment) Ordinance 2020 ("Amendment Ordinance") on 24 July 2020.

The Amendment Ordinance seeks to strengthen the existing Pharmacy and Poisons Ordinance (Cap. 138) (PPO) on regulation of ATPs.

After the Amendment Ordinance comes into operation, ATPs will fall under the definition of pharmaceutical product and will be regulated as a specific subset of pharmaceutical products in Hong Kong. Regulatory requirements for pharmaceutical products under the existing PPO, the Pharmacy and Poisons Regulations (Cap. 138A) (PPR) and other relevant ordinances, will apply to ATPs. These include registration prior to marketing, prior approval for clinical trials, licensing of the manufacturers and distributors, and import and export control.

Due to the complicated nature of ATPs and the lack of clinical experience in their usage, the risks and long-term side effects of ATPs need to be carefully monitored and managed. In some situations, the safety and quality issues of an ATP may only be identified after it has been administered to the patients. An effective and efficient traceability system covering from donation, through processing, to the end use is essential to allow determination of which ATP and patient could potentially be affected for the necessary patient follow-up or recall of the affected ATPs. Therefore, the Amendment Ordinance stipulates extra requirements on labelling and record keeping specific to ATPs in order to enhance traceability of these products.

Some key features of the Amendment Ordinance are highlighted below:

(1) Definition of ATP

Under the Amendment Ordinance, ATP means any of the following products that is for human use:

- a gene therapy product
- a somatic cell therapy product
- a tissue engineered product

Gene therapy product (GTP)

GTP is a recombinant nucleic acid containing product used in human with a view to delivering its therapeutic, prophylactic or diagnostic effect through regulating, repairing, replacing, adding or deleting a genetic sequence.

Example: A product containing recombinant viral vectors for delivering a copy of missing gene to the human body for the treatment of a genetic disorder.

Somatic cell therapy product (SCTP)

SCTP is a cell- or tissue-containing product used in human for the purpose of treating, preventing or diagnosing a disease, or restoring, correcting or modifying a physiological function. Not all cell- or tissue-containing products are SCTPs. The cells or tissues that an SCTP contains have to meet one or both of the following criteria –

1. Having been manipulated to alter their biological characteristics, physiological function or structural properties (i.e. substantial manipulation)
2. Being used for functions different from the essential functions in their donor (i.e. non-homologous use)

What is substantial manipulation?

Substantial manipulation refers to a product preparation process which would alter the biological characteristics, physiological function or structural properties of the cells or tissues that the product contains or consists of.

According to the Amendment Ordinance, manipulation processes, in relation to cells or tissues, like cutting, grinding, shaping, centrifugation, soaking in antibiotic or antimicrobial solutions, sterilization, irradiation, cell separation, concentration or purification, filtering, lyophilization, freezing, cryopreservation and vitrification, are not considered as substantial manipulation.

Other preparation processes are generally considered as substantial manipulation.

Example: A product containing immune cells (such as T cells, NK cells, CIK cells and dendritic cells) which have undergone cell expansion and are used for cancer treatment.

Tissue engineered product (TEP)

TEP is a cell- or tissue-containing product used in human with a view to regenerating, repairing or replacing a human tissue. As in SCTP, the cells and tissues that a TEP contains have to meet one or both of the criteria - having been subject to substantial manipulation and/or intending for non-homologous use.

Example: A product containing cultured corneal epithelial cells for regenerating (or repairing) the cornea tissue damaged by burns.

(2) Licensing Requirements for Manufacturers of ATP

All local facilities, including hospitals and private healthcare facilities, that substantially manipulate cells or tissues for human use must obtain the licence to manufacture issued under the PPO.

Licensed manufacturers of ATP, similar to those of current pharmaceutical product, will be required to comply with the Pharmaceutical Inspection Co-operation Scheme Good Manufacturing Practices ("PIC/S GMP") standard, which is an international standard for production of pharmaceutical products, and the Code of Practice promulgated by the Pharmacy and Poisons Board of Hong Kong.

Please note that manufacture of pharmaceutical products/ATPs without a licence is an offence. The maximum penalty is a fine of $100,000 and two years' imprisonment.

(3) Approval for Clinical Trials

Under regulation 36B of the PPR, a Certificate for Clinical Trial is required for the purpose of conducting a clinical trial on human beings. This regulation applies to all pharmaceutical products which will include ATPs. The sponsor, sponsor-investigator or principal investigator of a clinical trial of an ATP will have to apply for the certificate before conducting the trial.

(4) Import and Export Control

Under the Import and Export Ordinance (Cap. 60), every importation/exportation of pharmaceutical product must be covered by an import/export licence. The import and export control will apply to ATPs.

Please note that import or export of a pharmaceutical product without a valid licence is a criminal offence. The maximum penalty is a fine of $500,000 and two years' imprisonment.

Other Points to Note related to ATPs

(1) Record Keeping

In order to allow prompt and complete tracing of ATP treatment to patients for quality or safety reasons, it is important for the healthcare professionals to keep and maintain a system for records containing sufficient information, such as identifier of patient, and name and batch number of the applied ATP.

According to the Amendment Ordinance, the licensed manufacturers and wholesale dealers will have to keep the ATP records for 30 years. To be in line with this record keeping requirement, healthcare professionals are recommended to keep the ATP records for 30 years after the use of the products, if feasible. This duration of record keeping can be determined by healthcare professionals taking into account individual circumstances of the case as appropriate.

(2) Adverse Drug Reaction Reporting

Adverse drug reaction (ADR) reporting is an integral element of drug safety surveillance and pharmacovigilance. Due to the novelty, complexity and technical specificity of ATP, it may raise some new and unexplored risks and safety concerns which require special attention.

Healthcare professionals are encouraged to report suspected ADR of their patients to the Drug Office.

(3) Acquisition and Provision of ATP

To assure that ATPs (as pharmaceutical products) are supplied from legitimate source and under proper logistic management, healthcare professionals are

advised to only procure and obtain the products from licensed wholesale dealers, licensed manufacturers or authorized sellers of poisons.

Also, the ATPs supplied by these licensed dealers should be registered with the Pharmacy and Poisons Board in accordance with regulation 36 of the PPR. Information on registered ATPs (under pharmaceutical products) and licensed dealers is available at the website of the Drug Office.

Procedures involving the transplant of cell- or tissue-containing ATPs to patients (including autologous transplant) are Scheduled Medical Procedures under the Private Healthcare Facilities Ordinance (Cap. 633) (PHFO) and should only be performed in hospitals or day procedure centres with relevant licence in force. For further details, please refer to the website of the Office for Regulation of Private Healthcare Facilities, Department of Health. For the definition of Scheduled Medical Procedures, please refer to section 2 of and Schedule 3 to the PHFO.

Relevant Legislation and Guidelines

Besides the abovementioned ordinances, other Ordinances and Regulations may be relevant to healthcare professionals when handling ATPs. They include, but not limited to:

- Human Organ Transplant Ordinance (Cap. 465)
- Human Reproductive Technology Ordinance (Cap. 561)
- Prevention and Control of Disease Regulation (Cap. 599A)
- Public Health and Municipal Services Ordinance (Cap. 132)
- Undesirable Medical Advertisements Ordinance (Cap. 231)

For details of the legislations and guidance documents on ATPs, please see **Useful Information**.

In addition, healthcare professionals should observe their relevant codes of professional conduct and guidelines prior to the provision of ATP treatments.

USEFUL INFORMATION

Laws of Hong Kong
www.elegislation.gov.hk

Pharmacy and Poisons (Amendment) Ordinance 2020
www.gld.gov.hk/egazette/pdf/20202430/es12020243019.pdf

Office for Regulation of Private Healthcare Facilities, Department of Health
www.orphf.gov.hk

Guidance documents on regulation of ATPs
(The guidance documents will be regularly updated.)
www.drugoffice.gov.hk/eps/do/en/pharmaceutical_trade/atp_regulation.html

Drug Office
Department of Health
www.drugoffice.gov.hk

June 2021