

Consultation Document

Regulation of Advanced Therapy Products

Department of Health

3 April 2018

Abbreviations

ATMP	Advanced Therapy Medicinal Product (EU)
ATP	Advanced Therapy Product
CTT	Cell and Tissue-based Therapeutic (Singapore)
DH	Department of Health
EU	European Union
FHB	Food and Health Bureau
GCP	Good Clinical Practice
GDP	Good Distribution Practice
GMP	Good Manufacturing Practice
GTP	Good Tissue Practice
GVP	Good Pharmacovigilance Practice
IND	Investigational New Drug
PPB	The Pharmacy and Poisons Board of Hong Kong
PPO	Pharmacy and Poisons Ordinance
PPR	Pharmacy and Poisons Regulations
RMAT	Regenerative Medicine Advanced Therapy (US)
Task Force	Task Force on Regulation of Advanced Therapeutic Products in Hong Kong
US	United States
Working Group	Working Group on Regulation of Premises Processing Health Products for Advanced Therapies

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Executive Summary

In 2017, the Government has set up a Task Force on Regulation of Advanced Therapeutic Products in Hong Kong to advise the Government in formulating the regulatory framework for cell and tissue-based products.

Taking reference to the regulations of cells and tissues for human use in overseas jurisdictions, the Government proposes that regulation of cell and tissue-based products should be risk-based and to regulate Advanced Therapy Products or ATPs as pharmaceutical products. Amendments to the Pharmacy and Poisons Ordinance are necessary.

This Consultation Document sets out the proposal to include the definitions of ATPs, under the definition of pharmaceutical products in the Pharmacy and Poisons Ordinance. Requirements on product registration, licensing of manufacturers and distributors, import/export control, approval for clinical trials, labelling, record keeping and adverse event reporting would apply for these products.

Having regard to the unique nature of ATPs, in order to provide sufficient protection to patients, in addition to the above requirements which are applicable to all pharmaceutical products, the following specific requirements are proposed –

- Manufacturers are required to comply with guideline/standard on control of cells and tissues for ATPs production and relevant Good Manufacturing Practice guide. Manufacturing would include preparation of ATPs for the purpose of clinical trials or treatment of a particular patient.
- The unique donation identifiers/ product codes and patient identifiers should be labeled on the ATPs in formats specified by the regulatory authority.
- Manufacturers and distributors of ATPs are required to keep additional information such as storage, transport, and the medical practitioner who is responsible for the use of the product to ensure

sufficient monitoring and traceability. These records are required to be kept for 30 years.

The Task Force will continue to discuss the regulation of low-risk cells and tissues. Guidelines will be prepared and promulgated before relevant legislation is in place.

Members of the public and stakeholders are invited to send in your views on this Consultation Document within the two-month consultation period. Taking into account the views received during the exercise, the legislative proposals will be finalized.

Chapter 1 Introduction

1.1 The development of advanced therapy products (ATPs) is one of the fastest moving areas in the medical field at present. They are innovative medical products based on genes, cells and tissues. ATPs may have great medical potential and the science is rapidly evolving. As such, some of the therapeutic uses of ATP are still under research and yet to be proven. For the same reason, information in their long-term side effects and complications is limited. Due to the nature and risks involved, a regulatory framework is needed to effectively recognize and control their research and therapeutic use so as to safeguard public health.

1.2 In 2012, the Food and Health Bureau (FHB) set up the Steering Committee on Review of Regulation of Private Healthcare Facilities with four working groups to conduct in-depth study on four priority areas. One of these working groups, namely the Working Group on Regulation of Premises Processing Health Products for Advanced Therapies¹, issued a report² in 2014 which made the following five recommendations:

- (1) Cells, tissues and health products for advanced therapies for both medical treatments and clinical trials should be regulated with a regulatory framework to ensure public health and safety. All processes on cells, tissues and health products for advanced therapies for human application including donation, procurement, testing, processing, preservation, storage, and distribution should be subject to regulation.
- (2) Cells, tissues and health products for advanced therapies should be regulated according to their risks as determined by the extent of manipulation and the intended use of such products.

¹ Terms of reference and Membership of the Working Group are set out in Annex A of this Consultation Document.

² Available at

http://www.hpdo.gov.hk/doc/fhsd/Report_on_WG3_of_Regulation_of_Premises_Advanced_Therapies_2014_e.pdf

- (3) Introduction of a new legislation with an overarching authority to effectively regulate cells, tissues and health products for advanced therapies through a comprehensive set of regulatory controls including licensing requirements for premises, accreditation of premises, compliance with guidelines, adverse event reporting, designation of Person-in-Charge, staffing requirement and training, import and export control, and registration of health products for advanced therapies.
- (4) Premises processing cells and tissues for research purposes other than application to human body, for diagnosis of a patient in the course of medical treatment by registered professionals or where cells and tissues are used as an autologous graft within the same surgical procedure by registered professionals without any banking process should be exempted from the regulatory controls for advanced therapies.
- (5) Implementation of interim measures on the processing of cells, tissues and health products for advanced therapies to enhance public health before the new legislation takes effect.

1.3 The Government considered that a prudent approach should be adopted in carrying forward the recommendations of the Working Group and opined that more time and efforts are required to look into each aspect of the proposed regulation so that details of implementation could be worked out in consultation with stakeholders concerned.

1.4 As interim measures, the Department of Health (DH) published two sets of educational information³, one on cord blood banking and one on cell therapy, for consumers in early 2016. Another two sets of information on the same topics for industry and researchers were also prepared and published in May 2017.

1.5 To advise the Government in the formulation of the regulatory framework for ATPs and related matters, the Task Force on Regulation of

³ Available at: www.advancedtherapyinfo.gov.hk

Advanced Therapeutic Products in Hong Kong (Task Force), with membership comprising relevant experts, was set up in December 2017. Annex B listed the terms of reference and membership of the Task Force.

1.6 This document is prepared taking into account the expert advice of the Task Force to facilitate gathering public views on the proposed regulation of ATPs.

Chapter 2 Regulatory Framework in other Jurisdictions

2.1 The regulatory frameworks for ATP in the United States (US), the European Union (EU), Singapore, Japan and Korea have been reviewed. It was noticed that there is a high degree of convergence in the general regulatory framework for ATP among these jurisdictions.

Risk-based Approach

2.2 A risk-based approach has been adopted in all reviewed jurisdictions. ATPs refer to products containing cells and tissues that have been subject to more than minimal manipulation⁴ (referred as substantial manipulation in some jurisdictions) or are intended for non-homologous use⁵. They are considered as high-risk and generally regulated within the more stringent framework of medicinal products and/or medical devices. Combined products (combination of ATP and medical device) and gene therapy products are also considered as “high-risk” and subject to more stringent controls.

2.3 On the other hand, cells or tissues that have been subject to minimal manipulation only and are intended for homologous use are usually considered as “low-risk” cell and tissue therapies and regulated under a separate regulatory framework.

2.4 In general, the following categories are excluded from the regulation of ATPs:

- (a) Human organ intended for transplantation

⁴ Manipulations of cells or tissues that do not alter the biological characteristics, physiological functions or structural properties of the cells or tissues are usually considered as minimal manipulations.

⁵ Homologous use means the repair, reconstruction, replacement or supplementation of a recipient’s cells or tissues with a product that performs the same basic functions in the recipient as in the donor.

- (b) Any product that is a whole blood or blood components⁶ intended for treating blood disorders and that has not been subject to substantial manipulations; and is intended solely for homologous use; or is not intended for aesthetic procedures
- (c) Substances used in dental surgery for filling dental cavities
- (d) Bandages and other surgical dressing for sterilizing purpose
- (e) Reproductive medicines/ reproductive assistance medical care
- (f) Products containing or consisting exclusively of non-viable human or animal cells and/or tissues, which do not contain any viable cells or tissues and which do not act principally by pharmacological, immunological or metabolic action

2.5 However, the exact scope of advanced therapies regulation may differ in different jurisdictions. Annex C lists out the scope of regulation in studied jurisdictions.

2.6 It is noted that the ATP regulation frameworks in all the reviewed jurisdictions only cover products for human use. No appropriate reference models for the regulation of ATPs for animals could be found.

Pre-marketing Approval

2.7 Due to the risk and nature of ATPs, ATPs regulated under the framework of medicinal products and/or medical devices in overseas are subject to pre-marketing evaluation and authorisation. In order to obtain marketing authorisation, safety, efficacy and quality of the products should be demonstrated.

⁶ Blood-derived products, e.g. clotting factors, albumin, immunoglobulin, are considered as pharmaceutical products.

2.8 Similar to other medicinal products, ATPs may be available to patients under compassionate use program, which is a program to allow registered medical practitioners to treat patients with unapproved products if there are clinical needs. Specific “exemption” scheme may also be in place in certain jurisdictions to allow the use of unlicensed ATPs for the treatment of particular patients, such as the ‘Hospital exemption” scheme and “Specials” scheme in the United Kingdom⁷. This is to protect patients so that they will not be deprived access to required treatments that are not marketed due to marketing or commercial considerations.

Clinical Trial

2.9 Clinical trials of ATPs for the purpose of obtaining marketing authorisation are regulated in a way similar to that in medicinal products in overseas jurisdictions. Sponsors are required to apply to the authority for clinical trial authorisation or certificate or as Investigational New Drug (IND) before conducting clinical trials. There is also specific guidance for ATPs clinical trials highlighting the additional dossier requirements and other requirements, such as donor testing and screening procedures.

2.10 ATPs used in the clinical trials must be manufactured under Good Manufacturing Practice (GMP). The sponsors and investigators must also comply with Good Clinical Practice (GCP) and other applicable good practice guidelines, such as Good Tissue Practice (GTP), Good Distribution Practice (GDP) and Good Pharmacovigilance Practice (GVP), if specified.

Manufacturing

⁷ In UK, there is a specific exemption (hospital exemption) for advanced therapies which are prepared on a non-routine basis and used within UK hospitals for the treatment of individual patient. There is also a more general exemption (special exemption) for medicinal products (including ATPs) which are used as unlicensed medicines and which may only be supplied in order to meet the special needs of an individual patient in response to a bona fide unsolicited request from the treating physician. In both cases, the advanced therapies do not need marketing authorization but the processing facilities require GMP Licence.

2.11 Licensing of manufacture establishment is required in all reviewed jurisdictions. The licensed manufacturers must comply with GMP, which often contain jurisdiction-specific elements, and subject to periodic GMP inspections. There are also additional manufacturing and quality requirements (e.g. mandatory donor screening and testing procedures) to control the specific risks that originate from using viable human or animal source material, and product specific requirements on product characterisation, traceability, record keeping and lot-release requirements. In addition, reporting on the manufacturing process changes and serious adverse events are often a mandatory requirement. If the ATPs are combined with medical devices, requirements for medical devices should also be met.

Post-marketing Requirements

2.12 The post-marketing requirements for ATPs for most reviewed jurisdictions are similar to those for medicinal products, i.e. risk management plan, adverse events reporting and pharmacovigilance system. EU requires that records relating to ATPs must be kept for a minimum of 30 years after expiry of the products.

Chapter 3 Proposed Regulations for Advanced Therapy Products

Risk-based Approach

3.1 Having studied the regulatory frameworks for advanced therapies in various overseas jurisdictions, the Government proposes to adopt a similar approach to designate high-risk cell and tissue-based products as ATPs and be regulated as pharmaceutical products under the Pharmacy and Poisons Ordinance (PPO) (Cap. 138). Low-risk cells and tissues therapies will be regulated under a separate regulatory framework. Chapters 3 and 4 lay out the proposed regulations and way forward.

Regulatory framework for ATPs

3.2 To protect the public health and to be in line with international practice, the following elements would be included in the proposed regulatory framework:

Area 1 - To provide a definition for “Advanced Therapy Product”

3.3 Due to the complexity of ATPs and the differentiation in the nature and uses between low-risk and high-risk cells and tissues therapies, a precise definition for ATPs is required to clearly define the scope for regulation.

3.4 It is noted that the definitions of ATPs varies across different jurisdictions. To be in line with international practice, it is proposed to adopt the EU definition for ATP, which provides a comprehensive and precise scope for ATP (known as advanced therapy medicinal products (ATMP) in EU Legislation). The reason for adopting the EU definition is because the definition of medicinal products in EU Legislation has also been adopted in defining pharmaceutical product in PPO.

3.5 Based on the EU definition, ATP refers to any of the following products intended for human use:

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

3.6 In addition, ‘combined advanced therapy product’, i.e. an ATP incorporate one or more medical devices, is also regulated as pharmaceutical product because whatever the role of the medical device, the principal mode of action of the combination product rests with the pharmacological, immunological or metabolic action of the cells or tissues.

3.7 The proposed definition for ATP and some related definitions are set out in Annex D. One should note that the current proposal covers advanced therapy products intended for use in human but not animal, as ATP for animal use are yet to be regulated in overseas jurisdictions.

Area 2 - To ensure the quality and safety of cells and tissues that used for the production of ATPs

3.8 The quality and safety of the source cells or tissues are very crucial for ensuring the quality and safety of ATP. Quality and safety standards for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells would be set.

3.9 In addition, when donation of human cells or tissues is involved, the donation should be voluntary and unpaid. Anonymity of both donor and recipient, and altruism of the donor and solidarity between donor and recipient should be observed.

Area 3 - To require all facilities that produce ATPs to obtain a licence and comply with prescribed standards

3.10 Due to the high-risk and complex nature of ATPs, the facilities that produce ATPs should be regulated through a licensing system. They should fully comply with GMP and other standards as set by the regulatory authority, including those facilities (even facilities within the hospital) that produce ATPs on a non-routine basis for the treatment of an individual patient or for the purpose of conducting clinical trial⁸.

3.11 It is noted that some overseas jurisdictions promulgate separate GMP guide for the production of ATPs. The regulatory authority will review these standards and provide appropriate guidelines for local trade.

Area 4 – To require ATPs to obtain approval prior to import/export, marketing and clinical trial

3.12 Currently, the Pharmacy and Poisons Regulations (PPR) (Cap. 138A) provides that pharmaceutical products must fulfil the criteria of safety, efficacy and quality, and be registered with the Pharmacy and Poisons Board of Hong Kong (PPB) before it could be marketed. Exemption applies to the possession and use of pharmaceutical product for the purpose of treatment by a registered medical practitioner or a registered dentist of a particular patient.

3.13 The PPR also provides that a person must not conduct a clinical trial on human being except in accordance with a clinical trial certificate issued to the person. In addition, the Import and Export Ordinance provides that import and export of pharmaceutical products must under and in accordance with an import licence or export licence.

⁸ Manufacturing of other pharmaceutical products for the purpose of conducting clinical trial should also be licensed.

3.14 As with all other pharmaceutical products, the above regulations and requirements should also apply to ATPs.

Area 5 - To provide specific labelling requirements for ATPs

3.15 Due to the unique nature of ATPs, an adequate system to ensure the traceability via record maintenance and an appropriate labelling system should be established. This would also make it possible to verify compliance with quality and safety standards if necessary and at the same time protect the anonymity of both the donor and patient. Information such as unique donation or donor identifiers and product codes should be labelled on the immediate packaging of ATPs. For autologous products, unique patient identifiers and a statement like “for autologous use only” should be labelled as well to avoid mixing up.

Area 6 - To provide specific record keeping requirements for ATPs

3.16 Enhanced record keeping requirement facilitates the long-term safety and efficacy monitoring of ATPs, product tracing and recall. Taking reference from the EU, the Government proposes to require the manufacturers and/or product registration holders to keep record on all starting and raw materials, production process, packaging, storage, transport, and the medical practitioner who is responsible for the use of the product.

3.17 ATP is a recent development and the scientific development in the field evolves very rapidly. There is little information on its safety and efficacy thus a longer record keeping requirement to ensure sufficient monitoring and tracing is required. The above record should be kept for at least 30 years after the expiry date of the product. Special provisions should also be in place to deal with situations like insolvency or transfer of the licence.

Area 7 - To require suppliers of ATPs to report adverse events related to the use of ATPs

3.18 As the experience of using ATPs is still very limited, it is important for the manufacturers and/or registration holders of ATPs to monitor the efficacy and adverse reactions of ATPs after use. Risk management plan should be in place and the suppliers should also report serious adverse reactions related to the use of ATPs to the regulatory authority within a specified time frame. Similar requirements are in place (as registration and licensing conditions) for suppliers of pharmaceutical products.

Chapter 4 Proposal to Amend the Pharmacy and Poisons Ordinance

4.1 In Hong Kong, the PPO is the key ordinance that regulates pharmaceutical products or medicines. The PPO and its Regulations set out the requirements for product registration, licensing of the manufacturing facilities, compliance with the GMP Guide, clinical trial authorisation, supply and distribution of pharmaceutical products. Based on the above rationales and to be in line with international practice, it is proposed that ATPs be regulated as pharmaceutical products under the PPO, which would be amended to cater for the unique nature of ATPs.

4.2 The definition of pharmaceutical product in the PPO was mainly adopted from the EU Legislation (known as medicinal products). Pharmaceutical products or medicines means any substance or combination of substances –

- (a) presented as having properties for treating or preventing disease in human beings or animals; or
- (b) that may be used in, or administered to, human beings or animals, either with a view to –
 - (i) restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action; or
 - (ii) making a medical diagnosis

4.3 The above definition of pharmaceutical products did not make reference specifically to ATP. While ATPs developed so far fall under the definition of pharmaceutical products under the PPO, given the potential for further development, it would be prudent to examine the requirements to clarify in our law that pharmaceutical products cover ATP for avoidance of doubts.

4.4 It is proposed to amend the definition of pharmaceutical products under section 2 of the PPO to include ATP (i.e. those definitions presented in Annex D). With the amendment to the definition of pharmaceutical products, requirements for these products under the PPO and other relevant ordinances would be applied. These include registration prior to marketing, licensing of manufacturers and distributors, import/export control, prior approval for clinical trials, i.e. Areas 3 and 4 mentioned in Chapter 3. Current exemption under the PPR to possess and use pharmaceutical product for the purpose of treatment by a registered medical practitioner or a registered dentist of a particular patient continues to apply.

4.5 It is also required to make modifications to provide for additional requirements having regard to the unique nature of ATPs as set out in Chapter 3 above in order to provide sufficient protection to patients and to ensure the quality of ATPs prepared for human use.

4.6 The control of cells and tissues for the production of ATPs (Area 2) involves the regulation of standards for the donation, procurement, testing, processing, preservation, storage and distribution of cells and tissues. It is proposed that such control to be implemented via licensing conditions for manufacturers. Guidelines and standards would be prepared and promulgated to local trade from time to time to ensure responsiveness to latest international development and practice.

4.7 The current PPR provides that manufacturers and distributors of pharmaceutical products must obtain relevant licences. Licensed manufacturers are also required to fully comply with GMP guide. Due to the risks and complex nature in the manipulation and preparation of ATP, it is proposed to amend the definition of manufacture to ensure that anyone who manipulate and prepare ATPs for the purpose of clinical trials or for the purpose of treatment of a particular patient requires a licence and to fully comply with GMP guide.

4.8 To include additional labelling requirements (Area 5) for ATPs, it is proposed to amend section 31 of the PPR. The unique donation

identifiers/ product codes and patient identifiers should be labeled in formats specified by the PPB.

4.9 It is also proposed to amend sections 35 and 39 of the PPR to include additional record keeping requirements (Area 6) for manufacturers and distributors of ATPs. Additional information on storage, transport, and the medical practitioner who is responsible for the use of the product should be recorded. These pieces of information, together with other records required for manufacturing and distributing pharmaceutical products, should be kept for at least 30 years after the expiry date of the product. Provisions on handling of the records during situations like insolvency or transfer of licence would be added.

4.10 Area 7, i.e. requirements on adverse reactions reporting, is already in place for pharmaceutical products as registration and licensing conditions. The existing regulations would also apply to ATPs upon the amendment of the definition of pharmaceutical products.

4.11 The above proposals are summarized in the following table:

Regulation area	Proposed action
1 Definitions for ATPs	Amend section 2 of PPO
2 Regulation of cells and tissues for ATPs	To be included as licensing conditions
3 Licensure requirements for manufacturers of ATPs	Amend section 2 of PPO
4 Prior approval for import/export, marketing and clinical trials	Already covered by regulations for pharmaceutical products. No amendment needed
5 Labelling requirements for ATPs	Amend section 31 of PPR
6 Record keeping requirements for ATPs	Amend sections 35 and 39 of PPR
7 Reporting of adverse reactions	Already covered by regulations for pharmaceutical products. No action needed

Chapter 5 Regulation of Low-risk Cells and Tissues

5.1 The regulation of low-risk cells and tissues would be the next stage of work of the Government.

5.2 In certain overseas jurisdictions, premises that collect, procure, handle, process, test, store and distribute cells and tissues for human use are required to be licensed. The licence holders are required to fully comply with specific guidelines, e.g. GTP. Although no prior approval is needed before marketing and distributing low-risk cells and tissues, record-keeping, labelling and adverse reactions monitoring requirements and import/export control are usually in place to ensure safety of these products.

5.2 Examples of low-risk cell and tissue therapies include blood transfusion, cord blood banking for therapeutic uses, cornea transplant and bone marrow transplant. While certain therapeutic products made from human organ are subject to the regulation of the Human Organ Transplant Ordinance (Cap. 465), regulation of these low-risk cells and tissues will need further assessments and consultation in formulating a regulatory regime. The Task Force will continue to work on this regulatory regime. Guidelines and standards will be prepared and promulgated before relevant legislation is in place.

Chapter 6 Invitation of Views

6.1 You are invited to provide your views on the proposed amendments to the PPO as set out in details in Chapters 3 and 4. Please send your views on the Consultation Document on or before **2 June 2018** through mail, facsimile or email to the Drug Office of the Department of Health, details as below:

Address: Drug Office,
Department of Health,
Room 1856, 18/F,
Wu Chung House,
213 Queen's Road East
Wanchai, Hong Kong

Fax: 2834 5117

E-mail: pharmgeneral@dh.gov.hk

6.2 The views received from this public consultation exercise will be consolidated and analysed and be considered when the legislative proposal is finalised. Amendment Bills to the Legislative Council for consideration in 2019.

6.3 It is optional for you to supply your personal data in providing views on this Consultation document. Any personal data provided with a submission may be transferred to the relevant Government bureaux and departments for purposes directly related to this consultation exercise. The Government bureaux and departments receiving the data are bound by such purposes in their subsequent use of such data.

6.4 The names and views of individuals and organisations which put forth submissions in response to this Consultation Document may be published for public viewing after conclusion of the public consultation

exercise. The Government may, either in discussion with others (whether privately or publicly), or in any subsequent report, attribute comments submitted in response to this Consultation Document.

6.5 To safeguard your data privacy, we will remove your relevant data (if provided), such as residential/return address, e-mail address, identity card number, telephone number, facsimile number and signature, where provided, when publishing your views.

6.6 Please indicate if you do not want your views to be published or if you wish to remain anonymous when your views are published. Unless otherwise specified, all responses will be treated as public information and may be publicized in the future.

6.7 Any persons providing personal data to the Government in the submission will have rights of access and correction with respect to such personal data. Requests for data access and correction of personal data should be made in writing to:

Address: Senior Executive Officer (Drug)

Drug Office,

Department of Health,

Room 1856, 18/F,

Wu Chung House,

213 Queen's Road East

Wanchai, Hong Kong

Fax: 2834 5117

E-mail: pharmgeneral@dh.gov.hk

Working Group on Regulation of Premises Processing Health Products for Advanced Therapies

Terms of Reference and Membership

Terms of Reference

- To define and come up with the range of health products for advanced therapies that could be conducted in laboratory/ambulatory setting; and
- To examine whether and how to impose regulatory control on premises where health products for advanced therapies are stored and/or processed having regard to the latest development in medical practice and technology, as well as overseas regulations and international best practices applicable to local circumstances.

Membership

Chairperson

Dr Homer TSO

Members

Steering Committee members

Ms Jasminia Kristine CHEUNG

Mr Andy LAU

Director of Health (or representative)

Chief Executive, Hospital Authority (or representative)

Head of Healthcare Planning and Development Office, Food and Health Bureau (or representative)

Co-opted members

Mr CHAN Wing-kwong
Mr CHANG Hsiu-kang
Dr Celine CHENG
Ms Bella HO Shiu-wun
Dr LAM Tak-sum
Mr Arthur LAU
Professor Kenneth LEE Ka-ho
Professor LEE Shui-shan
Dr LEE Cheuk-kwong
Professor Ronald Adolphus LI
Mr Alex LI Wai-chun
Dr Sian NG Chor-shan
Dr Cecilia PANG Wai-bing
Dr Jonathan SHAM Shun-tong
Dr Dominic TSANG Ngai-chong
Professor TSE Hung-fat
Professor Ian WONG Chi-kei
Dr Raymond WONG Siu-ming
Dr WONG Yiu-chung
Professor Albert YU Cheung-hoi

Task Force on Regulation of Advanced Therapeutic Products in Hong Kong

Terms of Reference and Membership

Terms of Reference

- To examine and to advise the Government on setting up a regulatory regime for cell and tissue-based therapy and health products for advanced therapies in Hong Kong;
- To advise the Government on the approach for stakeholder consultation and engagement; and
- To advise the Government on the preparation of good practice guidelines for handling cells and tissues for human application.

Membership

Chairman

Professor LAU Chak Sing

Members

Professor Barbara CHAN

Professor Godfrey CHAN

Dr LEE Cheuk Kwong

Ms Kim LEE

Professor Kathy LUI

Dr Cecilia PANG

Professor POON Wai Sang

Definitions of Advanced Therapies in Different Jurisdictions

European Union

In EU, advanced therapies include Advanced Therapy Medicinal Product (ATMP) and Combined Advanced Therapy Medicinal Product.

Advanced Therapy Medicinal Product

Advanced Therapy Medicinal Product (ATMP) means any of the following medicinal products for human use:

- (a) A gene therapy medicinal product⁹;
- (b) A somatic cell therapy medicinal product¹⁰;
- (c) A tissue engineered product¹¹.

⁹ Gene therapy medicinal product means a biological medicinal product which has the following characteristics:

- (a) It contains an active substance which contains or consists of a recombinant nucleic acid used in or administered to human beings with a view to regulating, repairing, replacing, adding or deleting a genetic sequence;
- (b) Its therapeutic prophylactic or diagnostic effect relates directly to the recombinant nucleic acid sequence it contains, or to the product of genetic expression of this sequence.

Gene therapy medicinal products shall not include vaccines against infectious diseases.

¹⁰ Somatic cell therapy medicinal product means a biological medicinal product which has the following characteristics:

- (a) Contains or consists of cells or tissues that have been subject to substantial manipulation so that biological characteristics, physiological functions or structural properties relevant for the intended clinical use have been altered, or of cells or tissues that are not intended to be used for the same essential function(s) in the recipient and the donor;
- (b) Is presented as having properties for, or is used in or administered to human beings with a view to treating, preventing or diagnosing a disease through the pharmacological, immunological or metabolic action of its cells or tissues.

For the purposes of point (a), the manipulations that are not considered as substantial manipulations include cutting, grinding, shaping, centrifugation, soaking in antibiotic or antimicrobial solutions, sterilization, irradiation, cell separation, concentration or purification, filtering, lyophilization, freezing, cryopreservation and vitrification.

¹¹ Tissue engineered product means a product that:

- (a) Contains or consists of engineered cells or tissues, and

Combined Advanced Therapy Medicinal Product

Combined advanced therapy medicinal product means an advanced therapy medicinal product that fulfils the following conditions:

- (a) It must incorporate, as an integral part of the product, one or more medical devices under EU Directive 93/42/EEC or one or more active implantable medical devices under EU Directive 90/385/EEC, and
- (b) Its cellular or tissue part must contain viable cells or tissues, or
- (c) Its cellular or tissue part containing non-viable cells or tissues must be liable to act upon the human body with action that can be considered primary to that of the devices referred to.

United States

In US, gene, cell or tissue-based products that are more-than-minimally manipulated, or for non-homologous use, or have a systemic effect or depend on its metabolic activity (except for autologous cells, allogeneic cells for 1st or 2nd degree relatives and reproductive cells) are regulated as biologic products.

The products may also be a combination of a biologic product and a device (combination product).

Regenerative Medicine Advanced Therapy Designation

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- (b) Is presented as having properties for, or is used in or administered to human beings with a view to regenerating, repairing or replacing a human tissue.

A tissue engineered product may contain cells or tissues of human or animal origin, or both. The cells or tissues may be viable or non-viable. It may also contain additional substances, such as cellular products, bio-molecules, bio-materials, chemical substances, scaffolds or matrices.

Products containing or consisting exclusively of non-viable human or animal cells and/or tissues, which do not contain any viable cells or tissues and which do not act principally by pharmacological, immunological or metabolic action, shall be excluded from this definition.

In addition, there are separate approval pathways if granted the “regenerative medicine advanced therapy (RMAT) designation”, which means –

- (a) The drug is a regenerative medicine therapy, which is defined as a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, except for those regulated solely under Section 361 of the Public Health Service Act and part 1271 of Title 21, Code of Federal Regulations;
- (b) The drug is intended to treat, modify, reverse, or cure a serious or life-threatening disease or condition; and
- (c) Preliminary clinical evidence indicates that the drug has the potential to address unmet medical needs for such disease or condition.

Singapore

In Singapore, gene therapeutic products and cell- and tissue-based therapeutic (CTT) products are regulated as medicinal products. CTT products are defined as articles containing or consisting of autologous or allogeneic human cells or tissues that are used for or administered to, or intended to be used for or administered to human beings, for diagnosis, treatment or prevention of human diseases or conditions, but excludes –

- Any human organ intended for transplantation to replace a corresponding diseased organ;
- Any cell- and tissue-based therapeutic product that is a whole blood or blood components intended for treating blood disorders and that
 - (1) Has not been subject to substantial manipulation; and
 - (2) Is intended solely for homologous use; or

(3) Is not intended for aesthetic procedures.

Japan

In Japan, regenerative medical products are defined as processed live human/animal cells that are intended to be used –

(a) for either

- the reconstruction, repair, or formation of structures or functions of the human body or
- the treatment or prevention of human diseases, or

(b) for gene therapy.

Korea

In Korea, advanced therapies include cell therapy product and gene therapy product.

Cell Therapy Product

Cell therapy product means a medicinal product manufactured through physical, chemical, and/or biological manipulation, such as in vitro culture of autologous, allogeneic, or xenogeneic cells.

This does not apply to a case where a medical doctor performs minimal manipulation (e.g. simple separation, washing, freezing, thawing, and other manipulations, while maintaining biologic properties) that does not cause safety problems of the cells in the course of surgical operation or treatment at a medical centre.

Gene therapy product

Gene therapy product means a genetic material or a medicinal product containing such genetic material intended to be administered to human beings for treatment of disease.

Human tissue intended for transplantation is regulated under different Law.

Proposed Definitions of Advanced Therapy Product to be included in the Pharmacy and Poisons Ordinance

Advanced Therapy Product

“Advanced therapy product” means any of the following pharmaceutical products for human use:

- (a) A gene therapy product
- (b) A somatic cell therapy product
- (c) A tissue engineered product

Gene Therapy Product

“Gene therapy product” means a pharmaceutical product which has the following characteristics:

- (a) it contains an active substance which contains or consists of a recombinant nucleic acid used in or administered to human beings with a view to regulating, repairing, replacing, adding or deleting a genetic sequence;
- (b) its therapeutic, prophylactic or diagnostic effect relates directly to the recombinant nucleic acid sequence it contains, or to the product of genetic expression of this sequence.

“Gene therapy product” shall not include vaccines against infectious diseases.

Somatic Cell Therapy Product

“Somatic cell therapy product” means a pharmaceutical product which has the following characteristics:

- (a) contains or consists of cells or tissues that have been subject to substantial manipulation so that biological characteristics, physiological functions or structural properties relevant for the intended clinical use have been altered, or of cells or tissues that are not intended to be used for the same essential function(s) in the recipient and the donor;
- (b) is presented as having properties for, or is used in or administered to human beings with a view to treating, preventing or diagnosing a disease through the pharmacological, immunological or metabolic action of its cells or tissues.

For the purposes of point (a), the following manipulations shall not be considered as substantial manipulations:

- cutting
- grinding
- shaping
- centrifugation
- soaking in antibiotic or antimicrobial solutions
- sterilization
- irradiation
- cell separation
- concentration or purification
- filtering
- lyophilisation
- freezing
- cryopreservation
- vitrification

Tissue Engineered Product

“Tissue engineered product” means a pharmaceutical product that:

- (a) contains or consists of engineered cells or tissues, and
- (b) is presented as having properties for, or is used in or administered to human beings with a view to regenerating, repairing or replacing a human tissue.

excluding products containing or consisting exclusively of non-viable human or animal cells and/or tissues, which do not contain any viable cells or tissues and which do not act principally by pharmacological, immunological or metabolic action.

Combined Advanced Therapy Product

“Combined advanced therapy product” means an advanced therapy product that fulfils the following conditions:

- (a) it must incorporate, as an integral part of the product, one or more medical devices or one or more active implantable medical devices, and
- (b) (i) its cellular or tissue part must contain viable cells or tissues, or
(ii) its cellular or tissue part containing non-viable cells or tissues must be liable to act upon the human body with action that can be considered as primary to that of the devices referred to.