For discussion on
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Legislative Council Panel on Health Services

Proposals for Regulation of Advanced Therapy Products

PURPOSE

This paper seeks Members' comments on the proposals for the regulation of Advanced Therapy Products (ATPs).

NEED FOR REGULATION

2. ATPs are innovative medical products based on genes, cells and 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.

3. There is at present no dedicated regulatory framework for ATPs in Hong Kong. In view of the high risks of ATPs, the Government considers it necessary to introduce a clear regulatory framework on the research and therapeutic use of ATPs in order to safeguard public health and facilitate their development.

4. In 2014, the Working Group on Regulation of Premises processing Health Products for Advanced Therapies (the Working Group)[1] recommended that ATPs should be regulated according to their risks. Subsequently, the Task Force on Regulation of Advanced Therapy Products in Hong Kong (the Task Force)[2] was set up in December 2017 to advise the Government in the formulation of the regulatory framework for ATPs

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[1] The Working Group was set up under the Steering Committee on Review of Regulation of Private Healthcare Facilities in 2012. It was chaired by Dr Homer Tso and comprised 25 members from academia in the fields of biotechnology and clinical research, relevant medical specialties and laboratory professions, trade and industry sector and consumer group.

[2] The Task Force is chaired by Professor CS Lau and comprises seven expert members.

and related matters. Following the recommendations of the Working Group and the Task Force, the Government proposed that high-risk cell and tissue therapy products and gene therapy products should be designated as ATPs and regulated as pharmaceutical products under the Pharmacy and Poisons Ordinance (PPO, Cap. 138). After thorough public consultation in early 2018, the 2018 Policy Address announced that the Government would introduce legislation to regulate ATPs.

LEGISLATIVE PROPOSAL

5. The Government intends to introduce a bill to amend the PPO and the Pharmacy and Poisons Regulations (PPR, Cap. 138A) (the Bill).

Definition of ATPs

6. With reference to the European Union (EU)[3], ATPs would be defined as **high-risk cell, tissue and gene therapy products for human use**. Cells or tissues that have been subject to substantial manipulation[4] and/or intended for non-homologous use[5] are considered as high-risk. Under the proposed definition, ATPs means any of the following products intended for human use –

(a) a **gene therapy product**, for example, genetically engineered immune cells for the treatment of certain types of cancer;

(b) a **somatic cell therapy product**, for example, cultured stem cells from fat tissue for the treatment of chronic inflammation of the gut; and

(c) a **tissue engineered product**, for example, cultured corneal epithelial cells for the treatment of burns of the eyes.

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[3] The existing definition of pharmaceutical products under PPO is modelled on the EU definition. Adopting the EU definition of ATPs could facilitate the integration of new regulatory requirements to the existing regulatory regime under PPO. The EU definition is also widely accepted internationally.

[4] Manipulations of cells or tissues that alter the biological characteristics, physiological functions or structural properties of the cells or tissues are considered as substantial manipulation.

[5] Non-homologous use means the use of cells or tissues in the recipient is not for the same essential functions as that in the donor.

7. We propose that ATPs should form a specific subset of pharmaceutical products under the existing PPO. As such, requirements for pharmaceutical products under the PPO and other relevant ordinances will apply to ATPs. These include registration prior to marketing, prior approval for clinical trials, licensing of manufacturers and distributors, import/export control, etc.

Licensing requirements for manufacturers of ATP

8. Due to the high-risk and complex nature of ATPs, we propose that facilities that manufacture ATPs should obtain a license under PPO. Suitable amendments would be made to the definition of "manufacture" under PPO to stipulate the relevant requirements. In line with the existing requirement for approving clinical trial certificate for pharmaceutical products, facilities which produce pharmaceutical products, including ATPs, for clinical trial should also be licensed under PPO.

9. Under the above proposal, all licensed manufacturers of ATPs, similar to those of current pharmaceutical products, are required to comply with the Good Manufacturing Practices (GMP) of the Pharmaceutical Inspection Co-operation Scheme, which is an international standard for production of pharmaceutical products. Detailed guidelines would be issued by the Department of Health to facilitate compliance by the trade. Licensed manufacturers of ATPs would also be subject to existing provisions in PPR which govern manufacturers of pharmaceutical products. Meanwhile, in view of the special nature of ATPs, special requirements on licensed manufacturers of ATPs as listed in paragraphs 10 to 15 below would be included in the Bill to ensure the safety, quality and efficacy of their products.

Labelling requirements

10. Under the Bill, we propose that ATP manufacturers should be required to label information on unique donation identifiers and product codes on the packaging of ATPs, on top of those information required for all pharmaceutical products. For autologous products (i.e. donor and recipient are the same person), unique patient identifiers and a statement like "for autologous use only" should be labelled to avoid mixing up with

other products. The formats of the unique donation identifiers, product codes and patient identifiers are to be specified by the Pharmacy and Poisons Board.

Record keeping for ATPs

11. Enhanced record keeping requirement is essential to the monitoring of long-term safety and efficacy of ATPs, product tracing and recall. On top of those particulars required for the record of all pharmaceutical products, we propose a requirement for the manufacturers and wholesale dealers supplying the ATPs to the end-users to record the medical practitioner or dentist who is responsible for the use of the product, records related to storage and transport, etc. Details will be specified in the respective guidelines.

12. ATPs are recent development and the scientific advancement in the field evolves rapidly. There is little information on its safety and efficacy, thus a longer record keeping requirement to ensure sufficient monitoring and tracing is required. With reference to overseas practices, we propose that the records mentioned in paragraph 11 in respect of ATPs should be kept for at least 30 years after the expiry date of the product. If the manufacturer or wholesale dealer of an ATP ceased to operate, the records should be transferred to the Pharmacy and Poisons Board.

Sample keeping and sales pack provision

13. The PPR provides that a licensed manufacturer must retain a control sample of each batch of finished products under conditions of storage suitable to that product for a period of not less than one year after the expiry date of the product. However, it is acknowledged internationally that such requirement is not always feasible in the case of ATPs due to scarcity of the materials or limited size of the batches of products. We propose that ATP manufacturers are only required to keep photographs which clearly present the required information of the finished products for a period of not less than one year after the expiry date of the products.

14. Under the PPR, representative specimen sales packs of the product or representative samples of the substance are required to be

provided for registration of pharmaceutical product. Considering the scarcity of materials for certain biological products and related ethical issue for providing such materials for regulatory purpose, we propose to amend the PPR to accept prototypes of the sale packs for all pharmaceutical products including ATPs, which are sufficient for regulatory purposes.

Collection of cells or tissues

15. Since the collection of cells or tissues may take place outside the manufacturer's premises, extra requirements in respect of ATPs, such as donor selection and testing, quality control of cells and tissues, record keeping, etc. will be imposed via licensing conditions of relevant ATP manufacturers.

Commencement Date

16. It is our intention to allow sufficient time for the industry to get prepared before the commencement of the Bill.

CONSULTATION WITH STAKEHOLDERS

17. We conducted a public consultation on the proposed regulatory framework from April to June 2018. During the consultation period, a total of 127 participants attended the three briefing sessions, and 28 written submissions were received. Respondents generally supported the proposal which could provide a clear regulatory framework for development of ATPs. Some requested for more guidelines on the GMP requirements, such as premises design and qualifications of authorised persons, for obtaining a manufacturer's licence. The views received have been summarised in the consultation report published in October 2018 and suitably incorporated in the legislative proposal.

18. The Food and Health Bureau and the Department of Health have been in close dialogue with relevant stakeholders in formulating the legislative proposal. Subsequent to the public consultation, we have further briefed the University of Hong Kong, the Chinese University of Hong Kong, the Hong Kong Science and Technology Parks Corporation, Hospital Authority, local biotechnology companies, local pharmaceutical

traders and healthcare professionals at 17 briefings, seminars, meetings and visits. We would continue our efforts on this front.

LEGISLATIVE TIMETABLE

19. We aim to introduce the Bill to the Legislative Council within this legislative year.

ADVICE SOUGHT

20. Members are invited to comment on the proposals in this paper.

Food and Health Bureau
Department of Health
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