DEPARTMENT OF HEALTH
HEALTH TECHNOLOGY AND ADVISORY DIVISION

Guidance Notes on Application for Exemption of Regulated Products under the Human Organ Transplant Ordinance (Chapter 465)

I. Purpose

This document is to provide guidance to persons who apply for exemption of regulated products under the Human Organ Transplant Ordinance (Chapter 465) ("HOT Ordinance") about the legal requirements, application procedures and post-approval matters.

II. Background

2. The HOT Ordinance is to prohibit commercial dealings in human organs intended for transplanting, to restrict the transplanting of human organs between living persons and the transplanting of imported human organs. Section 4 of the Ordinance sets out the conditions where a person is guilty of an offence if, in Hong Kong, he is involved in the commercial dealings of an organ which has been or is to be removed from a dead or living person, whether in Hong Kong or elsewhere, and is intended to be transplanted into another person, whether in Hong Kong or elsewhere.

3. With advances in medical technology, commercial products made from human tissues (such as skin and bone derived products) are available overseas for transplant purposes. These products, however, fall under the definition of "organ" under section 2 of the HOT Ordinance, and commercial dealings of them are prohibited.

4. The HOT Ordinance was therefore amended in 2004. Part 7 of the amended Ordinance provides for the Director of Health ("Director") a mechanism to exempt these commercial products (referred to as "regulated products") from the application of the Ordinance. The amended Ordinance has come into operation on 1 September 2011.

III. Definition of regulated products

5. According to section 7A(1) of the HOT Ordinance, a regulated product means a product containing any structured arrangement of tissues that –

(a) falls within paragraph (a)(iii) of the definition of "organ" in section 2 of the Ordinance:

> "Organ" means any structured arrangement of tissues forming part of any human bodily part which consists of a structured arrangement of tissues; and if wholly removed, cannot be regenerated by the body; or any structured arrangement of tissues forming part of any human bodily part specified in the Schedule of the Ordinance, that is blood (including cord blood) and bone marrow; and

(b) has been subjected to processing:

> "Processing", in relation to any structured arrangement of tissues, means any activity performed on the tissues which alters the biological characteristics, function or integrity of the tissues, but does not include recovering or preparing the tissues, preserving the tissues for storage, or removing the tissues from storage.

IV. Criteria for exemption

6. According to section 7A(3) of the HOT Ordinance, the Director may, on application, exempt a regulated product from the application of the Ordinance if he is satisfied –

(a) that using the product for transplant purposes is safe and has no adverse impact on public health;

(b) either that the donor of the tissues concerned has given his consent to the removal of the tissues for the purpose of producing the product without coercion or the offer of inducement, or that the tissues are removed for the therapy of the donor;

(c) that no payment has been made, or is intended to be made to that donor for his supplying the tissues from his body;
(d) that all applicable laws of the place where the tissues were obtained or processed have been complied with in obtaining and processing the tissues; and
(e) that the circumstances and manner in which the tissues are obtained and processed are not affected by any matter that the Director may consider to be objectionable.

7. As regards the exemption criteria under section 7A(3)(a) of the Ordinance, the Director will consider, inter alia, whether adequate measures have been taken to address the potential health risks of the product to recipients and the public (see Table 1 below), and whether the product has been approved for marketing by regulatory authorities in other jurisdictions.

Table 1

	Risks of regulated products	Measures to address the risks[1]
(a)	The risk of transmitting diseases from donors to recipients (in particular, infectious diseases such as HIV, hepatitis B, hepatitis C, prion diseases, syphilis and HTLV-I/II)	Proper donor screening and testing
(b)	The risk of microbial contamination and cross-contamination of products during processing and storage	Compliance with Good Tissue Practice (GTP) or equivalent in tissue procurement and tissue processing

[1] The safety requirements of regulated products are set out with reference to the regulatory requirements for human tissue products in overseas jurisdictions including the United States ("US"), the European Union ("EU"), Canada and Australia.

	Risks of regulated products	Measures to address the risks[1]
(c)	For products that are derived from substantial processing of human organs or tissues, or that are intended for non-homologous[2] use, the safety, quality and efficacy of products for transplant	Non-clinical and clinical studies to substantiate the safety and, where appropriate, efficacy of the product; and Compliance with Good Manufacturing Practice (GMP) in product manufacturing
(d)	For (a) to (c) above	Implementation of a track and trace system that allows tracking of individual products from donors to end users*, or preferably to recipients, and tracing from end users or recipients to donors; and A system in place to identify, investigate and report serious adverse events[3] and reactions[4]

* End users refer to registered medical practitioners under the Medical Registration Ordinance (Chapter 161), registered dentists under the Dentists Registration Ordinance (Chapter 156), and healthcare institutions.

[2] "Homologous use" means the product performing the same basic functions in the recipient as in the donor, while "non-homologous use" means the product performing different basic functions.

[3] "Serious adverse event" means any untoward occurrence associated with the procurement, testing, processing, storage and distribution of exempted regulated products (or the starting human materials as appropriate) which might lead to the transmission of a communicable disease, to death or life-threatening, disabling or incapacitating conditions for patients, or might result in or prolong hospitalisation or morbidity.

[4] "Serious adverse reaction" means any unintended response, including a communicable disease, in the recipient associated with the human application of exempted regulated products that is fatal, life-threatening, disabling, incapacitating or which results in or prolongs hospitalisation or morbidity.

V. Application procedures

a) Applicant

8. According to section 7B(1) of the HOT Ordinance, a person may apply for an exemption in respect of a regulated product by submitting an application to the Director in a form specified by the Director.

b) Application documents

9. A completed application form along with the appendices to the application form (Appendix A: Marketing Approval Status of Regulated Product outside Hong Kong; and Appendix B: List of All Facilities Involved in the Tissue Procurement and Tissue Processing/Product Manufacturing Steps) and the following supporting documents are required to submit to demonstrate that the exemption criteria under section 7A(3) of the HOT Ordinance are met. The Director may require the applicant to provide additional information and documents as are necessary to determine the application.

Administrative documents

i. A copy of the HKID card or passport of the applicant; or for a company applicant, a copy of the business registration certificate of the company or equivalent document;
ii. An authorisation letter from the applying company designating a representative ("authorised representative") to make the application and handle related matters on behalf of the company;
iii. A letter from the manufacturer to authorise the applicant to apply for an exemption unless the applicant is the manufacturer of the product;
iv. A documentary proof of marketing approval (e.g. free sale certificate) by the regulatory authority in the US, EU, Canada or Australia, or in a country with equivalent product assessment standards;
v. A documentary proof of compliance with GTP, GMP or equivalent standard for each of the facilities listed in Appendix B to the application form involved in tissue

procurement, tissue processing and/or product manufacturing steps;

vi. A documentary proof from the manufacturer certifying that in accordance with section 7A(3)(b) to (d) of the HOT Ordinance, in obtaining tissues from donors and in processing the tissues for the purpose of producing regulated products to be supplied in Hong Kong:
   - the donor of the tissues concerned has given his consent to the removal of the tissues for the purpose of producing the product without coercion or the offer of inducement, or that the tissues are removed for the therapy of the donor;
   - no payment has been made, or is intended to be made to that donor for his supplying the tissues from his body; and
   - all applicable laws of the place where the tissues were obtained or processed have been complied with in obtaining and processing the tissues.

Technical documents

i. Product assessment reports issued by overseas regulatory authorities (if available);
ii. A technical dossier to provide the following information:

Organ/tissue donation:

- The policy of the manufacturer and the laws of the place/country where human organ/tissue is procured governing obtaining consent and payment to donation;

Donor screening and testing:

- Criteria for selection or exclusion of donors including a list of examinations and laboratory tests required for donor evaluation;

Evaluation of product safety, quality and efficacy:

- Overview of the product development;
- Overview of the manufacturing processes and controls, and other quality aspects relating to the manufacturing of the product;
- Summary of non-clinical and clinical studies substantiating the safety and, if applicable, efficacy of

the product.

Others

i. Photographs of the regulated product (including the sales pack, inner container or package, and the tissue product itself) – labels on all sides of the packaging should be clearly shown in the photographs;
ii. Labels and package inserts for use in Hong Kong – which should be the same as the ones approved by the overseas regulatory authority;
iii. A sample of the outer package of the sales unit of the regulated product, or its drawing, with a designated space for displaying the exemption number (i.e. HK-RPEx No.: XXXXXX);
iv. Description of the track and trace systems of the manufacturer and the applicant that allow tracking of individual products from donors to end users or recipients, and tracing from end users or recipients to donors.

c) Submission of application

10. The applicants are encouraged to fill out and submit the application online. The online form requires digital signature by either digital certificate or "iAM Smart". Please visit the websites at https://www.gov.hk/en/residents/communication/infosec/cybersecurity/digitalcert.htm and https://www.iamsmart.gov.hk/en/ for further information about digital certificate and "iAM Smart". The online form is accessible at https://www.dh.gov.hk/english/useful/useful_forms/useful_forms_Exemption.html.

11. For submission by post or by hand, the applicant should print and sign on the PDF application form with company chop (if applicable). The signed PDF form together with other application documents (see paragraph 9) should be submitted during office hours to the Department of Health (DH) at the following address:

Address
Health Technology and Advisory Division
Department of Health
21/F, Wu Chung House,
213 Queen's Road East, Wanchai, Hong Kong
(Re: Application for exemption of regulated products)

Office hours
Mondays to Fridays*: 9:00 a.m. to 1:00 p.m.; and
2:00 p.m. to 5:30 p.m.
* Except public holidays

Enquiries
Phone: (852) 2961 8944
Fax: (852) 2127 7329
E-mail: hot_rpe@dh.gov.hk

VI. Offence

12. According to section 7B(7) of the HOT Ordinance, any person who, in an application for exemption of regulated product, provides information that he knows to be false or misleading in a material respect, or recklessly provides information that is false or misleading in a material respect, commits an offence and is liable on conviction to a fine at level 5 and to imprisonment for 3 months.

VII. Determination of application for exemption

13. The Director may decide to approve the application and grant the exemption, or to reject the application. The applicant will be given a written notice of the decision by registered post. If the application is rejected, a statement setting out the reasons for such decision will be included in the notice.

14. In approving the application for exemption, the Director may specify the extent of the HOT Ordinance which shall not be applicable to a

regulated product. The Director may also (a) limit the validity of the exemption to a specified period; (b) grant the exemption only to the applicant, a specified person or a specified class of persons; or (c) grant the exemption subject to such conditions as the Director considers appropriate.

a) Extent of exemption

15. The Director may decide to exempt the regulated product from the application of all parts or part(s) of the HOT Ordinance. Sections 4 to 7 of the Ordinance are particularly relevant and the applicants are advised to refer to these provisions for details.

b) Exemption conditions

16. The Director may impose conditions on the exemption granted. On the breach of the condition(s) imposed, the Director may revoke, vary or suspend the exemption concerned.

c) Validity of exemption

17. The validity period of an exemption depends on the validity period of marketing approval obtained in overseas countries, which will be up to 5 years. The applicant shall submit another application for exemption at least 3 months before the expiry of the exemption if the applicant wishes the regulated product to continue to be exempted.

VIII. <u>Revocation, variation or suspension of exemption</u>

18. At any time after an exemption has been granted, the Director may, on such grounds as he considers appropriate –

(a) revoke the exemption so that it shall have no effect from such date as he may determine;
(b) vary the exemption in such manner as he may determine; or
(c) suspend the exemption so that it shall have no effect for such period or until compliance with such conditions as he may determine.

19. The Director will give the person to whom the exemption is granted a written notice of any of the decisions in paragraph 18 by registered post. The notice will include a statement setting out the reasons for the decision.

IX. Register of exemptions

20. The register of exemptions containing details of the exemptions granted, revoked, varied or suspended is available for inspection by the public, free of charge, during business hours at the office of the DH by appointment. An electronic version of the register is available at the DH website (http://www.dh.gov.hk/english/useful/hot_exemption.html).

X. Appeal against a decision of the Director in relation to the exemption

21. According to section 7F of the HOT Ordinance and in turn section 4 of the HOT (Appeal Board) Regulation (Chapter 465 sub. leg. B), a person aggrieved by a decision of the Director under section 7C or 7D of the HOT Ordinance[5] may appeal to the Appeal Board by giving the secretary of the Appeal Board a notice of appeal. The notice of appeal must be given within 30 days after the date of the notice of the decision given by the Director under that section of the HOT Ordinance. It must be in writing and in the specified form. For details, please contact the secretary to the Appeal Board at:

Address:	Secretary Appeal Board (Exemption of Regulated Products) Health Bureau 19/F, East Wing Central Government Offices 2 Tim Mei Avenue, Tamar Hong Kong
Office hours -	9:00 a.m. to 1:00 p.m.; and 2:00 p.m. to 5:00 p.m.

[5] The Director's decision under section 7C or 7D of the HOT Ordinance is a decision to approve or reject an application for exemption or to revoke, vary or suspend an exemption already granted.

Mondays to Fridays (except public holidays):	
Phone:	(852) 3509 8959
Fax:	(852) 2840 0467

XI. Other relevant legislation

22. Applicants are reminded to comply with other relevant legislation which may include but are not limited to the Prevention and Control of Disease Ordinance (Chapter 599) for import of biological materials; the Pharmacy and Poisons (P&P) Ordinance (Chapter 138) for registration of pharmaceutical products; and the Import and Export Ordinance (Chapter 60) for import and export of prohibited articles – prohibited articles include pharmaceutical products under the P&P Ordinance.

XII. Disclaimer

23. The decision of the Director to exempt a regulated product and inclusion of such product into the register of exemptions must not be regarded as an official advice, recommendation or warranty, or a substitute for advice or opinions from appropriate health professionals on using such product for patient treatment.

24. Neither the DH nor any of its employees or agents shall in any circumstances whatsoever be liable or responsible for any loss or damage whatsoever arising out of or in connection with the use of any exempted regulated products, the use of any of the information contained in or retrieved from the register of exemptions, or any errors or omissions in such register.