INFORMATION NOTE

Regulation of the Transplantation of Human Organs and Tissue Products in Selected Overseas Jurisdictions

1. Background

1.1 The purpose of this information note is to provide the Bills Committee on Human Organ Transplant (Amendment) Bill 2001 with information regarding the regulation of human organs and tissue products for transplantation in the United States of America (US) and the United Kingdom (UK). In particular, it focuses on how the relevant authorities:

(a) define and regulate human organs and tissue products for transplantation; and

(b) handle commercialization, distribution and appeals of human organs and tissue products.

1.2 The US is chosen for our study because it has a well-established system to regulate the transplantation of human organs and tissue products. The UK is chosen because its health authority is in the process of reviewing and revamping the regulatory framework to supplement the inadequacies of the current legislation.

2. United States of America

2.1 The US has separate regulatory systems for the transplantation of organs and tissue products.

Organ Transplant

Regulatory Authority

2.2 The Division of Transplantation under the Health Resources and Services Administration (HRSA), an agency of the Department of Human Health Services (HHS), is responsible for developing polices for and regulating organ transplantation.

Legislation

2.3 The National Organ Transplant Act of 1984 (NOTA), as amended, provides the framework for a national health care policy for organ transplantation, known as the Organ Procurement and Transplantation of Network (OPTN). Administered by a non-profit organization, OPTN is created to ensure that critically-ill and medically-qualified patients have equitable access to organs, to assure the safe and efficient recovery use of scarce vital organs, and to collect and track information on all transplants and transplant patients.

2.4 Title 42, Code of Federal Regulations, Part 121 (42 CFR 121) was enacted in 2000 by HHS to prescribe the operation of OPTN and to help achieve equitable and medically effective use of donated human organs.

Definition

2.5 Under 42 CFR 121, a human organ is defined as a "*human kidney, liver, heart, lung, or pancreas.*"[1]

Regulatory Framework

2.6 Under 42 CFR 121, the OPTN Board of Directors is responsible for providing the Secretary of HHS (the Secretary) with policies that it recommends to be enforceable, including policies on processing, allocation and distribution of organs intended for transplantation. Although the Secretary has not approved any of the OPTN policies so far, OPTN members[2] generally comply with these policies on a voluntary basis.[3]

Commercialization

2.7 Under NOTA, it is unlawful for any person to knowingly acquire, receive, or otherwise transfer any human organ[4] for valuable consideration for use in human transplantation.

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1 Questions have been raised on whether the definition should be expanded to include intestine, stomach, or a collection of human cells that perform a vital function of an organ. HHS is currently reviewing the request.

2 OPTN membership includes transplant centers, organ procurement organizations, tissue typing laboratories, voluntary health organizations and related medical and professional organizations.

3 Information provided by HRSA.

4 Under 42 US Code (USC) 274e(c) of NOTA, the term "*human organ*" is defined as the "*human (including fetal) kidney, liver, heart, lung, pancreas, bone marrow, cornea, eye, bone, and skin or any subpart there of…*". This definition is different from the one under 42 CFR 121 and is only applicable to criminal prohibition contained in that particular section. Information provided by HRSA.

Distribution

2.8 Under OPTN, organs are distributed fairly among patients who need them, using medical criteria instead of wealth basis.[5] OPTN develops policies concerning organ procurement and transplantation and maintains a national computerized list of patients waiting for organ transplantation.

2.9 Under 42 CFR 121, the Advisory Committee on Organ Transplantation (ACOT) is created to provide independent review of the proposed OPTN policies and advice to HHS concerning organ allocation policies, and to ensure that the system of organ transplantation is grounded on the best available medical science and is as effective and equitable as possible.[6]

Mechanism to Handle Appeals Against Definition of Human Organ

2.10 There is no specific statutory or regulatory mechanism to handle appeals against the definition of human organ under 42 CFR 121 and 42 USC 274. Nonetheless, interested parties can submit to the Secretary critical comments relating to the OPTN policies.[7]

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5 According to an independent study conducted by the Institute of Medicine (IOM) in 1999, OPTN was operating suboptimally due to a lack of standardization across the nation. OPTN was heavily weighted to the local use of organs instead of making organs available on a broader regional or national basis for patients with the greatest medical need. In other words, donated organs had always been first allocated to medically qualified candidates locally, then regionally and then nationally. The criteria used in listing the patients who needed transplantation varied from one transplant center to another, as did the criteria use to determine the medical status of a patient. As a result of both the local preference in allocation and the lack of standard medical criteria, waiting times for organs were much longer in some geographic areas than in others.

6 ACOT, established following the recommendation of IOM, is to provide the Secretary with third party independent comments on OPTN polices and other matters related to transplantation. The Committee is composed of non-governmental members from diverse backgrounds, such as public health care policy, biostatistics, immunology, health economics, bioethics and law.

7 Information provided by HRSA.

Tissue Transplant

Regulatory Authority

2.11 The Center for Biologics Evaluation and Research (CBER) under the Food and Drug Administration (FDA), an agency of HHS, is responsible for developing policies for and regulating the transplantation of human cells and tissue products.

Legislation

2.12 The regulation of human cells, tissues, cellular or tissue-based products (HCT/P's) for transplantation is prescribed by Title 21, Code of Federal Regulations, Parts 1270 and 1271 (21 CFR 1270 and 1271), under the authority of section 361 of the Public Health Service Act.

Definition

2.13 Under 21 CFR 1271[8], HCT/P's refer to "*articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. Examples of HCT/P's include, but not limited to, ligament, bone allograft, skin allograft, dura mater, heart valve, cornea, hematopoietic stem cells derived from peripheral and cord blood, manipulated autologous chondrocytes, epithelial cells on a synthetic matrix, semen, and other reproductive tissues.*"[9]

[8] This section of the Regulation (21 CFR 1271.3(d)(2)) became effective on 21 January 2003.

[9] The following articles are not considered HCT/P's:

1. vascularized human organs;
2. whole blood or blood components or blood derivative products;
3. secreted or extracted human products, such as milk and collagen; except that semen is considered an HCT/P;
4. minimally manipulated bone marrow for homologous use and not combined with a drug or a device;
5. ancillary products used in the manufacture of HCT/P;
6. cells, tissues, and organs derived from animals other than humans; and
7. in vitro diagnostic products.

Regulatory Framework

2.14 In the early 1990's, the Centers for Disease Control and Prevention reported that human immuno-deficiency virus (HIV) had been transmitted through the transplantation of human tissues. Reports suggested that unsafe tissues were being imported into the US for transplantation into humans, thus prompting FDA to set up a regulatory framework for HCT/P's to address the public health needs, to monitor industry developments and to assure an adequate supply of safe and functional products for transplantation.

2.15 In order to effectively monitor industry developments, under 21 CFR 1271, manufacturers of HCT/P's are required to register and list their products with CBER, and to submit regular updates to create an official inventory of establishments. This rule applies to tissue *establishments*[10] that are engaged in the recovery, screening, testing, processing, storage, or distribution of human tissues intended for transplantation.

2.16 In addition, to prevent the transmission of communicable diseases via transplantation of human tissues, FDA is in the process of proposing new regulations for donor suitability and good tissue practice for manufacturers of HCT/P's.[11]

(a) Donor Suitability

2.17 The determination of whether or not a donor is suitable would be made by a *responsible person*[12] and based on donor screening and testing. Donor screening involves the review of *relevant medical records*[13] of the donor to detect clinical evidence of communicable diseases. Donor testing refers to performing laboratory tests on a specimen collected from the donor, generally a blood sample, to determine whether the donor has been exposed or is infected with a communicable disease agent.

2.18 A donor may be determined suitable only if the results of the laboratory tests are negative or non-reactive and screening shows the donor to be free from clinical evidence of infection.

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[10] The term "*establishment*" refers to a place of business under one management, at one physical location, that engages in the manufacture of HCT/P's. This includes any individual, partnership, corporation, association, or other legal entity that engages in the manufacture of HCT/P's. Examples are tissue banks, tissue processors, hospitals, clinics, testing laboratories and medical examiners' offices.

[11] The proposed rules are published in Federal Registers 64 FR 52696 (30 September 1999) and 66 FR 1508 (8 January 2001). FDA is currently compiling views on these proposed rules before announcing the final version of the related rules.

[12] A responsible person means a person who is authorized to perform designated functions for which he or she is trained and qualified.

[13] Relevant medical records means a collection of documents that includes a current donor medical history interview, a current report of the physical assessment of a cadaveric donor or the physical examination of a living donor, laboratory test results, and coroner and autopsy reports if applicable.

(b) Good Tissue Practice for Manufacturers of HCT/P's

2.19 The proposed regulation requires manufacturers to take precautions against the transmission of communicable diseases by following appropriate manufacturing practices, such as cleaning of facilities and equipment, record-keeping of procedures to prevent products mix-ups, and controls over labelling and processing to prevent contamination and to preserve tissue function and integrity. Proposed actions include:

(i) Each establishment would be required to establish and maintain procedures for all significant steps that it performs in the manufacture of HCP/T's. FDA is not prescribing the contents of particular procedures, but is allowing establishments to develop procedures that suit their particular operations as long as the procedures are designed to prevent circumstances that increase the risk of the transmission of communicable diseases;

(ii) Any facility used in the manufacture of HCT/P's must be of suitable size, construction, and location to facilitate cleaning, maintenance, and proper operations. The facility is to be maintained in a good state with adequate lighting, ventilation, plumbing and drainage in place; and

(iii) The establishment would be required to establish environmental monitoring and control to provide proper conditions for operations. These include temperature and humidity controls, ventilation and air filtration, cleaning and disinfecting of rooms and equipment to ensure aseptic processing operations, and environmental monitoring for organisms.

Commercialization

2.20 Corneas and skin are covered under the ruling of NOTA in the case of criminal prohibition.[14] However, there is no other legislation in place to prohibit commercial dealings of other tissues.[15]

Distribution

2.21 Unlike organs, there is no federal government system regulating the allocation of tissues. Professional organizations, such as the American Association of Tissue Banks, operate a voluntary "National Tissue Network" to provide allograft tissues to meet patient needs.[16]

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14 See Note 4.
15 Information provided by CBER.
16 Ibid.

Mechanism to Handle Appeals Against Definition of Tissue Products

2.22 The Tissue Reference Group (TRG) is established under CBER to serve as the forum for resolving any disagreements that arise with regard to the application of definitions.[17] In the cases where interpretations of the legislation differ or additional guidance is desirable, TRG provides a single reference point and makes recommendations to Directors of CBER regarding the regulation of specific HCT/P's.

2.23 TRG is composed of:

(a) three representatives from CBER;

(b) three representatives from the Center for Devices and Radiological Health; and

(c) a liaison from the Office of the Chief Mediator and Ombudsman (OCMO) of FDA.

2.24 If a product regulated under 21 CFR 1271 falls under the jurisdiction of more than one agency, e.g., a combination device and biological product, OCMO may step in to assist in resolving disputes after considering TRG's recommendations.

[17] In addition, TRG is responsible for responding to inquiries from the cellular and tissue product industry, identifying the need for further scientific or policy development, and interacting with the Office of the Chief Mediator and Ombudsman of FDA on product designation requests.

3. The United Kingdom

Regulatory Authority

3.1 The Department of Health (DoH) is responsible for developing policies for and regulating the transplantation of both human organs and tissue products.

Legislation

3.2 The two key laws that govern organ and tissue transplantation are:

(a) Human Tissue Act 1961 which allows organs and tissues to be used for therapeutic purposes. However, this Act does not contain a regulatory framework, nor does it explicitly require consent to be given for the removal, retention and use of human tissues; and

(b) Human Organ Transplants Act 1989 (HOTA) which prohibits any commercial dealings in human organs for transplant. Under the provisions of this Act, the Unrelated Live Transplant Regulatory Authority (ULTRA) is established to review any proposed transplantation of an organ from a live donor genetically unrelated to the recipient.

Current Development

3.3 In January 2001, the Chief Medical Officer of DoH reported that organs and tissues were often removed, retained and used without the consent of the patients or their relatives. This led to a big public outcry and a review of the legislation governing the practice of organ and tissue transplantation.[18] To address the uncertainties and ambiguities of the current policy, DoH issued a consultation report on the law of human organs in England and Wales in July 2002.[19] It has solicited responses from the public and professional staff to prepare a complete regulatory framework to provide guidance for the removal, retention, processing and use of human organs and tissues from living people and those who have died.

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[18] During the inquiry into the management of the care of children at Bristol Royal Infirmary and Alder Hey Children's Hospital in Liverpool, it was discovered that children's hearts and other organs had been removed and, in many cases, without parental consent. When hospital post-mortems were carried out, consent forms were signed but there was little information on what tissues or organs would be taken. There is no defined legal limit to the amount of "tissue" that can be retained (i.e. no barrier to retaining whole organs or body parts). The revelation of organ retention has led to the present review of the legislation.

[19] The consultation period ended on 14 October 2002. The title of the consultation report is *Human Bodies, Human Choices. The Law on Human Organs and Tissue in England and Wales. A Consultation Report.* Department of Health, July 2002.

Definition

3.4 According to HOTA, an organ is defined as "*any part of a human body consisting of a structured arrangement of tissues which, if wholly removed, cannot be replicated by the body*".

3.5 At present, there is no clear definition of what constitutes a "tissue" as the term is not defined in law. DoH is soliciting views on the exact wording to be used in the new legislation to describe "organ" and "tissue" to avoid ambiguity.

Regulatory Framework

3.6 The present legal framework for the removal, retention and use of human organs and tissues contains many uncertainties. DoH aims to establish a non-statutory regulatory body to monitor compliance among human organ and tissue banks. It is in the process of drafting a new legislation to provide:

(a) a statutory basis for regulating all aspects of obtaining, storage, use and disposal of all organs and tissues:

- the review establishes guidelines on what can be removed from a human body, the purposes for which organs and tissues might be retained or used, and how the remaining tissues should be disposed of respectfully.

(b) a detailed exposition of who can give consent to taking and using organs and tissues for therapeutic, research, and educational purposes:

- the review establishes a code of practice for obtaining explicit consent from a patient and examines definitional issues concerning who the "next of kin" is if the patient lacks the capacity to give consent.

(c) a system of controls on the importation of body parts:

- the review establishes a code of practice to ensure that body parts are obtained ethically, the appropriate consents have been obtained, and they have been subject to screening to minimize the risk of infection.

Commercialization

3.7 Under HOTA, it is a criminal offence to:

(a) deal commercially in human organs from deceased or living organs that are intended for use in transplantation;

(b) advertise the buying or selling of organs; or

(c) withhold information required by law about transplant operations.

3.8 At present, tissues such as hair and nails are excluded from the scope of the Council of Europe Convention on Human Rights and Biomedicine[20] which prohibits financial gain from "the human body and its parts". Such materials are regarded as discarded tissues with the view taken that their sale is not an affront to human dignity.

3.9 DoH is soliciting views on whether there are any justifiable basis that human tissues or materials should be excluded from the new legislation.

Distribution

3.10 The United Kingdom Transplant is a Special Health Authority under DoH that provides centralized support for transplantation of human organs and tissue products. It maintains a national waiting list, a national transplant database, and a 24-hour operating office to organize the retrieval, allocation and transport of organs and tissues. Its advisory committees decide on the organ allocation arrangements such that each organ goes to the most suitable recipient.

Mechanisms to Handle Appeals Against Definition of Organs and Tissue Products

3.11 Depending on the nature of appeal, oversight of transplantation is provided in specified areas by the Retained Organs Commissions, ULTRA, HM Inspector of Anatomy and the Human Fertilisation and Embryology Authority respectively.

3.12 DoH is soliciting views on whether there should be a regulatory body or bodies to handle appeals against the definition of organs and tissue products and to provide guidance on compliance with the new legislation.

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[20] Established in 1997, the Council of Europe Convention on Human Rights and Biomeidicine is an international organization which sets out general principles of human rights protection in the field of biomedicine. The UK, being a member state of the Council of Europe, is required to abide by its ruling.

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