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REPORT

MEETING ON WHO GUIDING PRINCIPLES ON HUMAN ORGAN TRANSPLANTATION

Convened by:

WORLD HEALTH ORGANIZATION
REGIONAL OFFICE FOR THE WESTERN PACIFIC

Kuala Lumpur, Malaysia
8 to 10 June 2009

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NOTE

The views expressed in this report are those of the participants of the Meeting on WHO Guiding Principles on Human Organ Transplantation and do not necessarily reflect the policy of the World Health Organization.

This report has been prepared by the World Health Organization Regional Office for the Western Pacific for governments of Member States in the Region and for those who participated in the Meeting on WHO Guiding Principles on Human Organ Transplantation which was held in Kuala Lumpur, Malaysia from 8 to 10 June 2009.

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SUMMARY

A regional meeting on human organ transplantation was organized in Kuala Lumpur, Malaysia, from 08 to 10 June 2009. Nineteen participants from ten countries of the WHO Western Pacific Region participated. Apologies were received from Australia, New Zealand and Japan. There were eight temporary advisers and two observers who attended the meeting. The WHO secretariat had representatives from the WHO Regional Office for the Western Pacific and WHO headquarters.

The objectives of the meeting were:

(1) to review the status of organ, tissue and cell transplantation in the Region;

(2) to orient participants on principles, objectives and application of WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation;

(3) to identify gaps and draft recommendations for good practices including legislation and ethics in organ transplantation in the Region; and,

(4) to be updated on tissue banking and xenotransplantation.

The participants reviewed and unanimously endorsed the updated WHO Guiding Principles on Cell, Tissue and Organ Transplantation and described these as critical fundamental components of a template on which the national policies and programmes can be built.

Countries shared experiences in the status and development of organ, tissue and cell transplantation policies, plans and legislation. The participants agreed to incorporate the necessary actions to improve the management of the transplantation programmes in their respective countries. International experts spoke of the importance of having legislation; the definition of death and the factors that can help in the establishment of a successful deceased donor programme and the role of scientific and professional societies. Xenotransplantation, tissue banking, hemopoietic cell transplantation, the role of regulatory authorities and the utility versus equity of healthcare resources were some of the important topics presented. The genesis and success of the Spanish model (of the deceased donor programme) was shared and a learning experience for all.

The participants were divided into working groups and they discussed the WHO Guiding Principles as applied to organ donors, physicians and health facilities and health systems. The meeting was successful in achieving its objectives. Major recommendations are given in the report.

1. INTRODUCTION

1.1 Background information

Transplantation of various human organs, tissues and cells to prolong and improve our quality of life has increased worldwide in the recent past. Globally, about 68 000 kidney, 19 000 liver and 5 000 heart transplantations take place every year. Data from 2007 shows that the estimated number of kidney transplants were around 11 000, performed in about 400 centres in the Western Pacific Region. Almost 50% of kidney donors in the Western Pacific Region are live unrelated donors and the number of heart and liver transplants in the Region is also increasing.

The shortage of available organs and the huge gap between supply and demand have prompted many countries to develop procedures and systems to increase supply, but at the same time, have also led to unethical practices like commercial trafficking of human organs, particularly from living, unrelated donors. The inadequate number of donors is a major challenge and public awareness of the dangers of commercial trade and trafficking of human organs has become highly essential.

WHO/HQ developed the "Guiding Principles on Human Organ Transplantation" in 1991 to assist national authorities in developing robust national programmes for organ transplantaion. Since then, these Guiding Principles have been utilized by more than 50 countries in developing their national policies and plans.

The World Health Assembly, through resolution WHA 57.18, requested WHO to continue examining and collecting global data on the practices, safety, quality, efficacy and epidemiology of allogeneic transplantation and on ethical issues, including living donation, and to update the "Guiding Principles on Human Cell, Tissue and Organ Transplantation."

With all these developments taking place, it was considered the right time to disseminate the revised “Guiding Principles” in the Western Pacific Region so that legislations, ethical practices and technologies on organ transplantation can be addressed and improved. A regional meeting was organized in Kuala Lumpur, Malaysia, from 08 to10 June 2009, to address these issues , disseminate the revised Guiding principles and to review the current status of tissue banking and xenotransplantation.

1.2 Objectives

The objectives of the workshop were:

(1) to review the status of organ, tissue and cell transplantation in the Region;

(2) to orient participants on principles, objectives and application of WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation;

(3) to identify gaps and draft recommendations for good practices including legislation and ethics in organ transplantation in the Region; and,

(4) to be updated on tissue banking and xenotransplantation.

1.3 Participants

Participants were invited from Member States that have some facility for transplantation. Nineteen participants attended from the following countries: China, Fiji, Hong Kong (China), Malaysia, Mongolia, the Philippines, the Republic of Korea, Singapore and Viet Nam.

There were also eight temporary advisers, three observers and a WHO secretariat team from Geneva (HQ) and the Western Pacific Regional Office (Annex 1).

1.4 Organization and content

The programme for the meeting included sessions on the (1) the deceased donor programme; (2) legal framework for oversight of transplantation; (3) Istanbul declaration;(4) tissue banking; (5) the role of regulatory authorities;(6) hemopoietic cell transplantation;(7) role of scientific and professional societies in donation and transplantation activities; and (8) safety and availability of transplantation services.

Each session consisted of one or more presentations, followed by questions, discussion and exchange of views and experiences in plenary sessions.

The workshop agenda and programme of work (timetable) are in Annex 2. The participants were provided with some background materials related to the subjects. A complete set of all presentations and additional background documents were incorporated into a CD-ROM and given to each participant.

1.5 Opening remarks

On behalf of Dr Shin Young-soo, WHO Regional Director for the Western Pacific Region, Dr Han Tieru, WHO Representative for Malaysia, Brunei Darussalam and Singapore, welcomed the participants and read out the Regional Director's message. Dr Shin thanked Malaysia for supporting WHO's efforts to introduce and implement the WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation.

He reiterated in his speech that this meeting was an excellent venue which provided an opportunity for Member States to share experiences and develop future plans for strengthening their organ, tissue and cell transplantation programmes and to ensure effective service delivery. He said that improvements in medical technology, particularly in relation to organ and tissue rejection, have enhanced the cost-effectiveness and utility of transplantation and has enhanced the quality of life. This, however, has also led to an increase in the demand for organs which exceeds their supply, presenting a challenge to health authorities and potential unethical practices. Several Member States report the availability of legal frameworks on transplantation of human organs, however, commercialization and trafficking in human organs continues.

Dr Shin acknowledged that the revised WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation addresses these issues and encouraged Member States to incorporate these in their national regulations and practices pertaining to transplantation.

The meeting was inaugurated by the Director General of Health, Malaysia, Tan Sri Dato' Seri Dr Hj. Mohd. Ismail Bin Mericain. He welcomed the participants and thanked WHO and the Malaysian Society of Transplantation for organizing this meeting in Kuala Lumpur with the support of Ministry of Health, Malaysia. He spoke about the moral dilemmas being faced in the allocation of organs to recipients, the problem of shortage of organs available for

transplantation, commercialization of organ donation and the emerging concerns regarding transplant tourism.

He acknowledged that the rapidly changing socio-economic development in Malaysia had led to changes in the health care needs and expectations of the people, now facing the challenges of "new public health problems." However, the Government of Malaysia was committed to developing, providing, monitoring and improving health care services for the good of the people. Transplantation services started in Malaysia in the 1970s with corneal transplantations and at present, there are facilities for kidney, liver and lung transplantation in the country, with every effort being made to ensure that that these services are the best in the world. To support a national transplant programme, the national organ, tissue and cell transplantation policy was formulated in 2007.

The Director General highlighted the important proclamation of the ethical principles and practices adopted by Malaysia on transplantations and said that Malaysia fully supported the "Declaration of Istanbul on Organ trafficking and transplant tourism." He emphasized the importance of regional cooperation in this emerging and important area and offered technical support from Malaysia to all the Member States of the Region.

1.6 Appointment of Chairperson and Vice-Chairperson

The workshop elected Dr Tan Chwee Choon from Malaysia as the Chairperson and Dr Ahn Curie, Director, Seoul National University Hospital Transplantation Research Center, Republic of Korea as the Co-Chairperson.

2. PROCEEDINGS

The meeting included:

- the presentation of country reports to review the current status of transplantation activities in respective countries;
- presentations and discussions on the fundamental issues addressed by the revised WHO Guiding Principles;
- an update on xenotransplantation and tissue-transplantation; and,
- the identification of a way forward.

2.1 Transplantation activities by WHO

Dr Luc Noel, WHO/HQ, Geneva, gave a presentation on the evolution of the World Health Assembly (WHA) resolutions as related to organ transplantations. In 1987, the WHA expressed concern at the trade for profit in human organs among living human beings and affirmed that such trade is inconsistent with the most basic human values and contravenes the Universal Declaration of Human Rights and the spirit of the WHO Constitution. It requested that WHO, through Resolution WHA40.13, would develop guiding principles for human organ transplants. Accordingly, in 1991, WHO developed the Guiding Principles with the following key elements:

1) preference for deceased over living organ donors;
2) preference for genetically related over unrelated living donors;
3) preconditions in all cases:
   (a) informed consent by a competent person
   (b) free of undue influence or pressure
4) non-commercialization (no sale or purchase, no payment for organ, no profit from organ); and,
5) fair distribution of organs (equitable access to a common resource.)

In 2004, the issues and challenges in organ transplantation were discussed at the World Health Assembly and Member States were urged to implement effective national oversight of procurement, processing and transplantation of human cells, tissues and organs, including ensuring accountability for human material for transplantation and its traceability. WHA also urged them to take measures to protect the poorest and vulnerable groups from "transplant tourism" and the sale of tissues and organs, including attention to the wider problem of international trafficking in human tissues and organs. WHO was asked to update its Guiding Principles of 1991 and ensure global harmonization of practices (including safety, quality, efficacy and ethics.)

Accordingly, WHO undertook an extensive process of consultation in the form of several global and regional meetings with multiple partners. These included health authorities (policy makers, national transplantation coordinators and national regulatory authority); scientific and professional societies; ethicists and lawyers; patients (both donors and recipients); and, finally, representatives of civil society from every region of the globe and level of development. The process led to updating the WHO Guiding Principles which pertain to the following 11 key elements:

(1) consent for deceased donor's donation;
(2) clear definition and determination death;
(3) consent from deceased, and live donors;

(4) protection of minors and incompetent persons;
(5) no sale or purchase of organs, tissues and cells;
(6) altruistic promotion of donation, no advertising or brokering;
(7) responsibility on origin of transplant;
(8) justifiable professional fees;
(9) allocation rules;
(10) quality, safety, efficacy of procedures and transplants; and,
(11) transparency and confidentiality.

2.2 Global overview of human cell, tissue and organ transplantation

Ms Mar Carmona, WHO/HQ, Geneva, presented data from the *2007 Global Knowledge Base on Transplantation* and *Global Database on Donation and Transplantation* and also data pertaining to the countries of the Western Pacific Region.

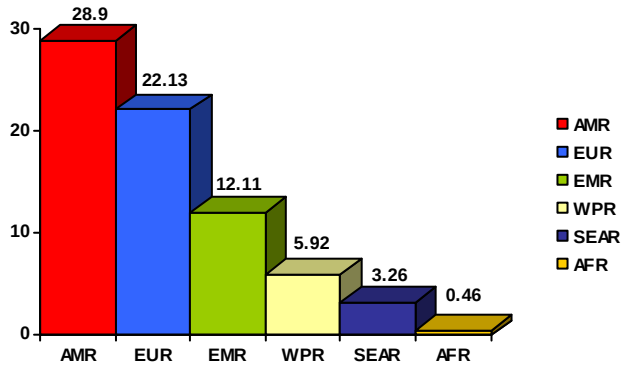
WHO has collected data through a structured questionnaire from all Member States. The current Global Database compiles organ activity data from 97 countries, representing nearly 80% of the global population. Of these, 94 countries have an organizational and legislative framework for organ transplantation. While 74% of the countries have an official body for overseeing and coordinating donation and transplantation, 82% have specific legislation on organ transplantation. The global estimates of organs transplanted during 2007 indicate that around 100 000 solid organ transplantations take place every year (Figure 1).

Figure 1: Global estimates of organs transplanted during 2007

Kidney	Liver	Heart	Lung	Pancreas
68 273	19 882	5181	3245	2797

Kidneys constitute the majority of transplanted organs. The estimation of kidney transplantations per million population (ppm) in different WHO Regions is shown in Figure 2.

Figure 2: Estimations on kidney transplantation (LD and DD**) (pmp) per region*



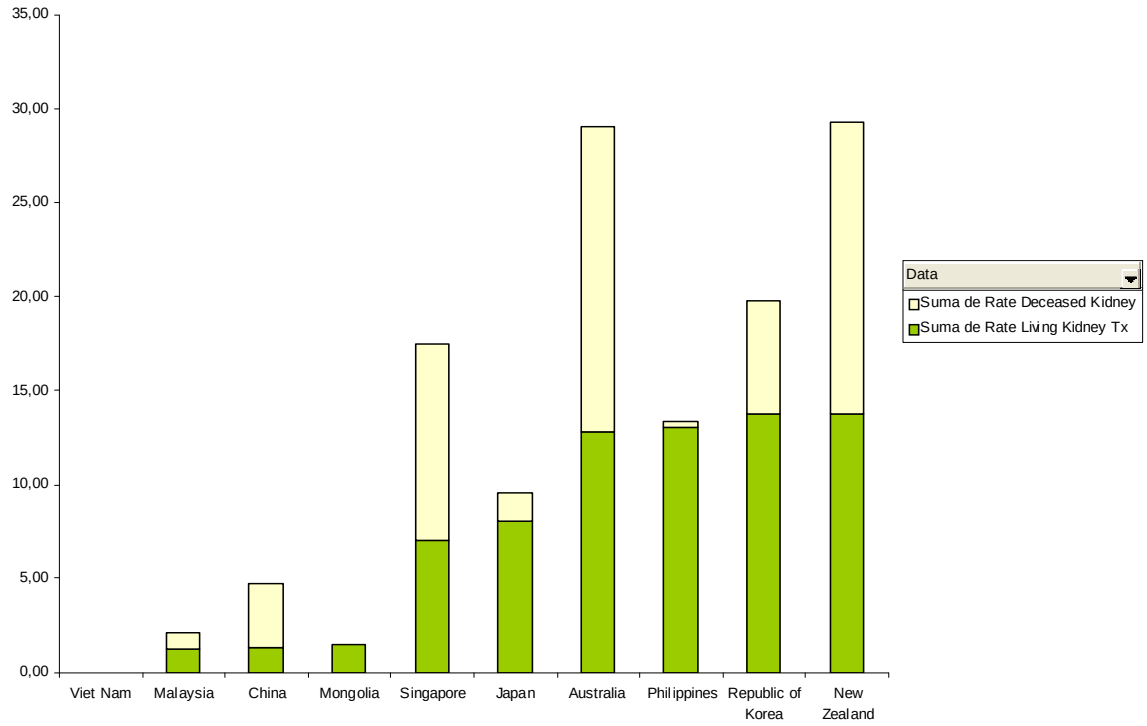
* Source; 2007 Global Knowledge Base on Transplantation
Global Database on Donation and Transplantation
** LD: Living Donors; DD: Deceased Donors

2.3 Status of transplantation in the Western Pacific Region

Dr Gayatri Ghadiok, WHO Western Pacific Regional office, Manila, provided an overview of the status of transplantation in the Western Pacific Region of WHO. Organ, tissue and cell transplantation is in varying stages of development in the Region. Transplantations take place for

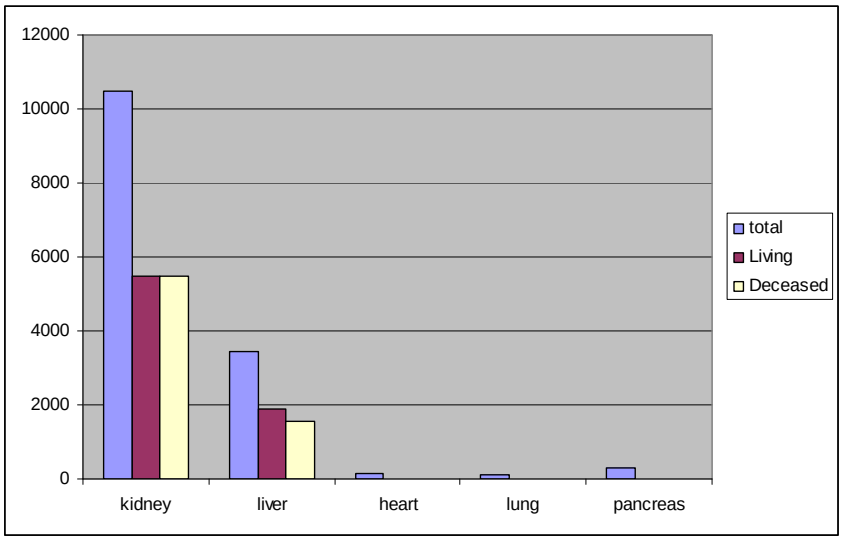
organs (kidney, lung, liver, heart, spleen, small bowel); tissues (cornea, skin, bone, tendon, ligaments, islets of Langerhans, parathyroid, iliac artery and vein, pulmonary valves); cells (hematopoietic stem cells, spleen cells and mesenchymal stem cells). The estimated numbers of annual transplantations in the Region are: greater than 10 000 kidneys; greater than 3000 livers; approximately 150 hearts, greater than 100 lungs and greater than 250 pancreases. Donations for kidney and liver transplants are approximately 50% from living and 50% from deceased donors. It is thought, however, that the number for kidney deceased donors is underestimated.

Figure 3: Comparison between kidney transplants from DD and from LD (rate: pmp)



Number of organ transplants in Western Pacific Region (2007)*

* Source: 2007 Global Knowledge Base on Transplantation
Global Database on Donation and Transplantation



More than 400 health facilities in the Region are currently performing solid organ transplantation; 25% of which are in the private sector. A need for strong partnership between the public and private sectors is called for, along with a uniform and effective regulatory oversight. Of the 10 countries which presented data, only eight (China, Hong Kong China, Malaysia, Mongolia, the Philippines, the Republic of Korea, Singapore and Viet Nam) have national transplantation activities. Brunei Darussalam and Fiji do not have transplantation facilities in-country and patients from these two countries go overseas for organ donation and transplantation.

All eight countries undertaking organ transplantation in the Region have national regulations in place. All these countries are strengthening national activities and are at varying stages of implementation of national plans. National registries for donors and recipients do exist in six of the countries and national networks are being proposed in the national plans. Community awareness is being recognized as an important component of the programme with active support from the NGO sector.

Xenotransplantation occurs in the form of basic research in three countries—China, Mongolia, and the Republic of Korea.

The major issues that are being faced in the Western Pacific Region pertain to:

- National framework: Advocacy and programme planning
  - Low focus on tissue and cell transplantation
  - Lack of a national coordinating agency
  - No clear definition /determination of brain death

- Access: Health system
  - Availability of organs from deceased donors
  - Allocation review process
  - Transparency of procurement and transplantation

- Ethics and regulations
  - Compensation vs. reimbursement
  - Powers of the ethics committee

- Quality Systems
  - Safety and quality of practices
  - Traceability of donor organs, tissues
  - Lack of laboratory coordination

- Community awareness and participation
  - Community acceptance of transplant tourism and payment for organs
  - Media interaction

2.4 Country reports

2.4.1 Brunei Darussalam

Brunei Darussalam is a small country with a population of less than 400 000. There are no formal cell, tissue and organ transplantation activities in the country. However, they are actively looking at developing a Human Organ Transplant Act with strong collaboration from ASEAN countries. Brunei Darussalam has recently undertaken a feasibility study to look into establishing a kidney transplant programme and hopes to implement this programme by 2010.

Presently, all patients requiring an organ transplant are referred to appropriate centres abroad and these patients are subject to rules and regulations of the country they obtain their transplants. National regulations for Brunei Darussalam are yet to be established. Regulations of the country where live related transplants are done comply with international standards, however, for unrelated donors, there is no government control in place. Until 2009, a total of 32 patients for kidney, one for liver and 18 for corneal transplants were referred overseas for transplantation.

The need for a transplant is decided by the treating physician. Informed consent from the donor is mandatory after psychological assessment and ensuring that there is no evidence of pressure/coercion for money transactions/incentives. All pre-transplant medical screening for the donor is performed by the physician taking care of the recipient. The patient has to make arrangements for the donor who accompanies the patient abroad.

Community participation is important and a recent survey on community awareness was conducted which showed that there is acceptance of renal transplants. However, there are significant cultural and religious barriers still to be overcome.

2.4.2 China

China has a successful national transplantation programme under the Ministry of Health. Facilities for the transplantation of the following organs (kidney, liver, heart, lung, pancreas, spleen, small intestine); tissues (cornea, islet of Langerhans, parathyroid gland); cells (hematopoietic stem cells and spleen cells) are available in the country. The national Ministry of Health has established two registry centres in 2008: the Chinese Scientific Registry of Kidney Transplantation and the China Liver Transplant Registry. One-hundred sixty-four hospitals are qualified to perform transplants and this permission is granted and approved by the Ministry of Health's committee on the clinical application of technologies of human organ transplantation and the human organ transplant branch of Chinese medical association.

The salient features of the national programme and registry of donors and recipients are that the two national registries (kidney and liver) are registered and networked with the organ transplantation centres. There is continuing scientific evaluation, publications and advice on the management of human organ transplantation to ensure the quality and security of transplantation and provide scientific evidence to policy-makers.

The national regulations for transplantation evolved in two steps. In 2006, the regulations applied to the management of clinical application of human organ transplantation to regulate the practice of medical institutions and practitioners. In 2007, the regulations defined the liabilities of illegal removal, trade and transplantation of organs (liver, kidney, lung and heart). These regulations are effective and adequate and under the committee on the clinical application of technologies and ethics of human organ transplantation. These regulations oppose transplant tourism where trans-border organ transplantation is banned (2006) and the expert/import of organs, tissues or cells is prohibited.

Selection criteria for a potential donor are carefully scrutinized. Only those that are capable of competently making their own decision and are willing/free of any undue influence are selected. They are given a thorough explanation of the probable risks and benefits before donation, informed and voluntary consent of the living donor is taken, professional care is ensured, and follow-up is well organized.

The Red Cross Society of China has been designated as the national human organ donation organization and oversees the present network of organ banks. However, a national network is being planned in the next three to five years. This would include a donation registry and an organ

sharing and allocation system. The Red Cross Society of China has also set up special institution and volunteer groups for organ donation and plans to expand this through education and encouragement of local communities.

Data for 2007-2008 shows that nearly 11 000 transplantations have taken place in China, with kidney transplants being the highest number followed by liver transplants. Less than 50% of kidneys and more than 75% of livers come from deceased donors. The survival rates for both kidney and liver donors is 100% , while for recipients survival rates are 96% and 89%, respectively.

2.4.3 Fiji

There is currently no formal organ, tissue and cell transplantation programme or services in Fiji. There is also no legislation, regulation or health policy governing transplantation operations or services. Patients who can afford it travel abroad for transplantation needs. The incidence of diabetes mellitus is high in the adult population and most cases of end-stage renal disease travel to India for kidney transplantation.

A national registry is maintained at the central level and systems and processes are developed to ensure that reports are updated and accurate.

Organ transplantation will eventually be provided in Fiji. There is a need to put in place appropriate legislation and health policies to provide the framework for the service. There is also a need for regional collaboration and networking with neighbouring Pacific island countries who share the same concerns as Fiji on organ, tissue and cell transplantation.

Fiji has plans to develop a national registry and develop and adopt legislation and regulations for donations and transplantation at the national level.

2.4.4 Hong Kong, China

Health care services for a population of approximately 7 million are provided by both public and private sectors. Hospital service is provided mostly by the public sector and all public hospitals are under the management of the Hospital Authority, a statutory organization mainly funded by the Government. In 2008, 456 transplant operations were performed. The majority of these were kidney transplants (78) and liver transplants (72). Others were heart, lung, cornea, sclera, skin, bone, small bowel, etc. The percentage of deceased donors as the source of organs was around 80% for kidney and around 40% for liver.

There is no formal territory-wide transplantation network programme in Hong Kong. Nevertheless, most of the transplantation activities are carried out in the hospitals under the management of the Hospital Authority. There are four renal transplantation centres, one liver transplantation centre and one heart and lung transplantation centre in the Hospital Authority. There is single waiting list for each type of the organs mentioned above. The Hospital Authority operates two skin banks, two bone banks and one eye bank.

The Human Organ Transplant Ordinance was put into full operation in 1998. The Ordinance provides the legal basis for prohibition of commercial dealings in human organs intended for transplanting, restriction of the transplanting of human organs between living persons, restriction of the transplanting of imported human organs, and statutory requirementsfor reporting all transplant operations. The law does not cover donation and transplantation of cells such as those derived from bone marrow. There is also a computerized registry of potential organ donors for citizens to register their wish to donate organs as specified by them after death. Transplant coordinators of the

Hospital Authority can access the register to check the intention to donate organs by the deceased persons.

The Government partners with health professionals and NGOs to promote awareness and acceptance of organ donation among the public, and especially the need for potential donors to express their wish to their family members. Informed consent from the donor, or from the deceased person's relatives, is required for organ removal.

2.4.5 Republic of Korea

Organ transplantation started in Korea in 1966 with corneal transplants, with the programme steadily expanding and the numbers gradually increasing. Data from 2007 shows that transplantation occurs inside the country for organs (kidney, liver, heart, pancreas, bone marrow, small intestine); tissues (cornea, heart valve, skin, bone, blood vessels); cells (hematopoietic stem cells, islets and mesenchymal stem cells). Kidney transplantations account for approximately 1000 cases with an estimated 30% donors being deceased donors, whereas liver transplants number around 750 and about 80% livers are from live related donors. There are 67 institutions performing transplants in the country and the majority are in the private sector (57).

There is a national programme and registry for donors and recipients for transplantation. The legislation of organ transplantation law was first set up in 1999 (prohibition of organ sharing) and has evolved by 2002 to include the definition of organ and process for judging brain death. The law permits transplantation of organs on patients from abroad and also allows the export/import of tissues only but not solid organs.

Informed consent from living donors is mandatory and in the case of unrelated donors, the consent has to go through an ethics committee. However, for deceased donors, consent from family members is necessary before harvesting of organs. The Korean Network of Organ Sharing (KONOS) and Korea Organ Donation Agency (KODA) are two national programmes which play a strong role in donor recruitment and also issue donor cards to individuals. They are assisted by close to 30 NGOs in their activities.

2.4.6 Malaysia

The transplantation programme in Malaysia started in 1975 with kidney transplants and by 2006, liver and lung transplants had been successfully carried out in the country. Data from 2007 shows that nearly 50% of kidney and liver donors are deceased donors. Majority of the transplantation centres are public hospitals with a few private institutions also having the facilities.

Malaysia has seen improvements in its national transplantation programme with the restructuring of its organizational structure, resulting in a more streamlined and accountable framework. It has in place the Human Tissues Act (1974) which, however, addresses only cadaveric organ, tissue and cell removal. This Act is currently under revision in order to include the definition of death and provisions prohibiting commercialism. In addition, there is a need for a comprehensive act to address issues of live donation, transparency, traceability and surveillance.

In 2007, the national organ, tissue, and cell transplantation policy was formulated by various stakeholders. This policy provides governance for both private and public sectors as well as national ethical guidelines on organ transplantation.

The national transplant registry (established in 2004) provides various information and outcome data on organ, tissue, and cell transplant recipients. However, Malaysia has yet to establish a live donor registry.

2.4.7 Mongolia

Organ, tissue, and cell transplantation was established in Mongolia in 2006 and takes place only in the government supported State Central clinical hospital. The transplantation law was approved in 2000 and a transplantation policy established in 2001. This was followed by the development of the national clinical guidelines on kidney transplantation (including ethical issues) in 2006.

The national organ transplantation programme is supported by the Ministry of Health with financial support from Korea and the United Kingdom for the "Kidney transplantation project." The government of Mongolia covers 80% of all costs associated with kidney transplant surgery and fully covers cost of immunosuppressive treatment for all recipients. The donor law states that it is obligatory to take informed consent from all living related donors and from next of kin for deceased donors.

Data from 2007 shows that a total of 37 kidney transplants took place, which included four patients who went overseas for their kidney transplants. However, with the implementation of the transplantation programme, the number of patients going overseas for transplant surgery has decreased.

The network of organ banks includes cooperation with the eye bank in Seattle, USA. The priority now is to establish a nationwide network on organ procurement, and promotion of donation. The Mongolian Transplantation Society (MTS) is increasingly involved in raising community awareness for different transplant-related activities.

2.4.8 The Philippines

The Philippines has facilities for kidney, liver and corneal transplantation only. The number of kidney transplants that took place in 2007 was approximately 1000. This number includes the transplants on foreigners that were allowed then. Subsequently, in 2008, the law was changed and foreigners were not allowed to receive organs from non-related Filipino donors. As a result, the total number of transplants that took place in the country in 2008 dropped to about 650. The majority (greater than 90%) of the donors are living non-related donors and deceased donors constitute only 10%.

There is a national policy on kidney transplantation from living non-related donors via an administrative order (2002) which sets guidelines and ethical principles for donation and conduct of transplantation from such donors. The order also prohibits the sale and purchase of kidneys. The Philippine organ donation program was established under the national center for disease prevention and control and sets the rules and regulations governing hospitals engaged in kidney transplantation.

Administration orders to address the following are still in draft form:

- Guidelines on donor allocation from deceased and living donor and donor/candidate waiting list
- Ethical guidelines on living non-related donors
- Donor follow-up and monitoring
- Deceased organ donation and transplantation

There are several legislative measures on organ donation being discussed currently in the House of Representatives in the Philippines. These include the National Regulations for Transplantation (current laws).

(a) RA 7170: Organ Donation Act (Covers voluntary cadaver donations)

(b) RA 9208: Anti-Trafficking in Person Act of 2003 (Prohibits sale and trafficking of organs)

(c) RA 7885: An Act to Promote Corneal Transplantation

There are also several pending House Bills that include:

(a) Bill 5930: An Act to Regulate Organ Transplantation and Appropriating Funds Thereof

((b) Bill 6210: An Act Regulating the Donation and Transplantation of Human Organs and Tissues from Living and Deceased Donors

(c) Bill 3374: An Act Regulating Living Non-Related Organ Donation

(d) Bill 6011: An Act Promoting Organ Donation Awareness

Deliberation is ongoing particularly on the following issues:

- Presumed versus voluntary consent
- Definition of valuable consideration
- Presumed consent

2.4.9 Singapore

The national organ transplant programme in Singapore started in 1970 and is operated currently by the national organ transplant unit which has the following responsibilities:

- coordinating the deceased organ donation programme;
- maintaining national registry of organ donors and recipients; and,
- managing the national organ waiting list.

Facilities for kidney, liver, lungs, heart, corneas, skin, bone, and bone marrow transplants are available in both public and private hospitals. The data from 2007 shows that there was nearly equal distribution of live related, live unrelated and deceased donors for kidney transplantation. Nearly half of the donors for liver transplants were live related donors.

National regulations have been implemented since 1970 and its salient features include:

- regulation of deceased and live organ donation;
- live organ donations need to be approved by a transplant ethics committee;
- transplantation of organs on patients from abroad is allowed but regulated; and,
- transfer of organs /cells across the border is allowed but regulated.

Informed consent under the Human Organ Transplant Act (HOTA) is essential for live donations. For cadaveric organ donation, it is presumed consent under HOTA. In addition, under the Medical Therapy, Education, Research Act (MTERA), individuals (including foreigners) can pledge additional organs for transplant, education or research.

Singapore is committed to and undertaking major initiatives to promote ethical organ donations. Major legislative initiatives include the following:

- removal for age-limit of deceased organ donation under presumed consent;
- allowing for paired donations;
- reimbursement to donor for reasonable and verifiable costs incurred and associated with the donation; and,
- increased penalties for organ trading.

There is a high level of community awareness due to the national programme and also through NGOs and involvement of other institutions. In addition, efforts are under way to maximize the potential for deceased donation, to ensure the welfare of living donors and public education.

2.4.10 Viet Nam

The organ transplant programme in Viet Nam started in 1992 and facilities for transplantations are available for organs (kidney, liver), tissue (cornea, skin, bone) and stem cells for blood, skin and cornea. Heart transplants are in the trial phase. The number of kidneys and livers transplanted (1992-2008) so far are nearly 100% from live related donors. Institutions that perform these transplants are mainly government institutions with a few private ones dealing with corneal transplants only.

There is no national organ transplantation programme yet, but plans are underway to develop a national coordinating centre for organ transplantation. Meanwhile, the law on organ and tissue transplantation was approved and implemented since 2007. This law addresses the donation, removal, transplantation of organs, tissues and cells from deceased donors. There are however, no national guidelines on ethics in transplantation. The law bans all kinds of commercial transactions in the transplantation of organs, tissues and cells. It does, however, permit transplants of organs on patients from abroad, but qualifies that the donors must be related to the patients receiving the transplant or be volunteer donors.

Viet Nam has one tissue bank and one eye bank, but there are no organ banks and network of organ banks. Raising community awareness and advocacy with the national authorities for a national organ transplant programme is on the cards.

2.5 Plenary sessions

2.5.1 Systematizing the deceased donation process in different resourced environments

Professor Delmonico of Harvard Medical School, USA, shared the common factors that contribute to the challenges in systemizing a deceased donor programme, including experiences from India, Russia, Saudi Arabia and South Africa. Common contributory factors include: lack of/overburdened infrastructure with a failure on the part of the government to establish quality treatment at affordable costs for the vast majority; an inadequate number of ICU beds and laboratories for harvesting, transporting and transplanting organs; and, poor emergency care. Was it fair to ask the poor and unemployed to be part of a deceased donor programme when they cannot be the beneficiaries?

How does one define death? The National Conference of Commissioners on Uniform State Laws (USA) in 1980 formulated the Uniform Determination of Death Act (UDDA). The definition for death is irreversible cessation of circulatory and respiratory functions, or irreversible cessation of all functions of the entire brain, including the brain stem.

This definition was approved by the American Medical Association in 1980 and by the American Bar Association in 1981. Today all fifty states and the District of Columbia follow the UDDA as a legal standard of death.

Statistics from USA show a gradual increase in the number of organs available from deceased donors and the number of organs harvested from living donors gradually decreasing. However, potential brain-dead donors are still being lost to donation after cardiac death. Referring to studies from the Massachusetts General Hospital and data from the New England Organ Bank (NEOB), Professor Delmonico showed that medical/surgical interventions could alter progression to brain death when severe brain injury is managed aggressively, i.e., with the infusion of cooling, hypertonic saline, neurosurgical intervention, intracranial pressure monitoring and treatment and maintaining hypothermia.

A twelve-month review study (July 2007 – June 2008) showed how 3,248 heart-beating referrals ultimately resulted in only 46 deceased cardiac death (DCD) donors. One of the challenges is in the traditional definition of brain death which requires the complete absence of all functions of the entire brain. It is clear that a person is not dead unless his brain is dead. The time-honoured criteria of stoppage of the heartbeat and circulation are indicative of death only when they persist long enough for the brain to die." These factors contribute to the decreasing number of brain-dead donors; the increasing numbers of donation after cardiac death donors and the resultant decrease in the number of organ transplants.

Organs transplanted per donor (OTPD) is a function of the entire donation and transplantation system. Highest OTPD rates are found in well-developed hospitals with aggressive transplant programs, the underlying factors being clinical excellence, efficient systems and policies, and the will to excel.

The vision of NEOB includes investment in the future of a DCD programme. This includes sponsoring young scientists for training fellowships at premier US institutes, improving the DCD donor selection process (a predictive tool based on NEOB data is being validated) and having in place a centralized DCD organ resuscitation and functional improvement laboratory.

Current research includes the development of a novel donor lung strategy—the Normothermic ex vivo lung perfusion system. This system provides an opportunity to maintain the organ at physiologic temperatures and allows for a continuous evaluation of lung function.

Professor Delmonico alluded to the ethical axiom "adhere to the dead donor rule: the retrieval of organs for transplantation should not cause the death of a donor." His take-home message was to examine existing programmes that could be implemented despite constrained resources and environments that present obstacles of infrastructure.

2.5.2 Key components of a legal framework for human transplantation

Dr Peter Doyle of the United Kingdom discussed the importance of having legislation in transplantation. Transplantation is a complex issue and since a transplant requires the donation of the transplant material from one human (the donor), to another (the recipient), it is legally, ethically and organizationally one of the most complex branches of medicine. Transplant procedures pose risks for donors, as well as recipients.

This law protects the dignity and identity of every person and guarantees, without discrimination, respect for his or her integrity and other rights and fundamental freedoms with regard to transplantation of cells, tissues and organs of human origin. The law will regulate the

transplantation of cells, tissues and organs of human origin carried out for therapeutic purposes and provide for a system to ensure equitable access to transplantation services to patients.

A comprehensive legal framework must include adequate definitions of transplant terms and provide adequate powers to permit and regulate all aspects of transplantation. To be legally and ethically acceptable, transplantation laws must be consistent with international standards, e.g., WHO Guiding Principles. The model laws would provide adequate powers to permit and regulate all aspects of transplantation including:

(1) the establishment of national transplantation organizations;

(2) the donation of cells, tissues and organs from deceased (heart beating and non-heart beating) donors, as well as living donors. A few examples include:

(a) who can donate, where and how?
(b) determination of death
(c) donor screening
(d) organ retrieval and preservation
(e) matching and allocation

(3) the allocation and implantation of organs;

(4) the oversight/control of transplant services;

(5) the safety and quality of all procedures;

(6) information sharing /data protection and traceability;

(7) the strict control of import/export of cell, tissues and organs;

(8) the prevention commercialisation, abuse and trafficking and provide for strict penalties;

(9) outcomes and audit;

(10) follow-up of living donors/recipients;

(11) research; and,

(12) xenotransplantation.

Transplant services are complex, but there are serious legal and ethical concerns that should be addressed so that citizens have full confidence in transplantation activities in their countries.

2.5.3 The Istanbul Declaration and the role of professional bodies in maintaining ethical value

Professor Francis Delmonico, Director, Medical Affairs of The Transplantation Society (TTS) elaborated on the role of TTS to improve patient outcomes, competence and performance of TTS members and the international medical community, including:

- development and communication of the science and clinical practice;
- continuing education; and,
- guidance on ethical practice.

In collaboration with WHO, TTS has been providing technical support to the countries in support of the WHO guiding principles to accomplish:

- deceased organ donation;
- safety and monitoring of live donation; and,
- development of public policy.

TTS also played a critical role in the development of the *Istanbul Declaration on Organ Trafficking and Transplant Tourism,* which aims to address the growing problems of organ sales, transplant tourism and trafficking in organ donors in the context of the global shortage of organs. It was the result of a summit meeting held in Istanbul and attended by more than 150 representatives of scientific and medical bodies from 78 countries, including government officials, social scientists, and ethicists. The Istanbul Declaration (reference: http://www.nscb.gov.ph/announce/2007/IstanbulDeclaration) states that:

- Organ trafficking and transplant tourism violate respect for human dignity and the principles of equity and justice and should be prohibited.
- Because transplant commercialism targets impoverished and otherwise vulnerable donors*, it inexorably leads to inequity and injustice and should be prohibited. (*minors, illiterate and impoverished persons, undocumented immigrants, prisoners and political or economic refugees.)

The following definitions were also adopted:

(1) *Organ trafficking*: the recruitment, transport, transfer, screening, harbouring or receipt of living or deceased persons or human organs by means of the threat or use of force or other forms of coercion, of abduction, of fraud, of deception, of the abuse of power or of a position of vulnerability or of the giving or receiving of payments or benefits to achieve the consent of another person having control over the potential donor, for the purpose of exploitation by the removal and/or transplant of organs.

(2) *Transplant commercialism*: a policy or practice in which an organ is treated as a commodity, including by being bought or sold.

(3) *Travel for transplantation*: the movement of organs, donors, recipients or transplant professionals across jurisdictional borders for transplantation.

(4) Travel for transplantation becomes *transplant tourism* if:

(a) it involves organ trafficking and/or transplant commercialism; or,

(b) the resources (organs, professionals and transplant centres) devoted to providing transplants to patients from outside the country interfere with the country's ability to provide transplant services for its own population.

The following principles were promulgated:

(1) National governments, working in collaboration with international and non-governmental organizations, should develop and implement comprehensive programmes for the screening, prevention and treatment of organ failure, which include:

- the advancement of clinical and basic science research;

- effective programmes, based on international guidelines, to treat and maintain patients with end-stage diseases, such as dialysis programmes for renal patients, to minimize morbidity and mortality, alongside transplant programmes for such diseases; and,

- organ transplantation as the preferred treatment for organ failure for medically suitable recipients.

(2) Comprehensive reimbursement of the actual, documented cost of donating an organ does not constitute a payment for an organ, but is rather part of the legitimate costs of treating the recipient.

Following the meeting, task forces have been formed that will implement the Istanbul Declaration and monitor the activities listed below:

(a) implementation at scientific congresses and engagement of the appropriate Ministry of Health;
(b) liaison with medical societies;
(c) addressing emerging threats; and
(d) development/funding of appropriate groups.

2.5.4 Organ donation from deceased donors: the Spanish experience

Dr Rafael Matesanz, Director, Spanish National Transplant Organization (ONT) is the national coordinator for transplantation activities in Spain. He described the evolution of the national programme from 1989 until today when Spain is considered the world leader in the deceased donor programme. They realized that the classic approaches to improve organ donation, among them changes of legislation, publicity campaigns, donor registries, donor cards/ driving licenses or other ways of promotion, were not making any difference. Under his leadership, they started an original, integrated approach designed to improve cadaveric organ donation, which resulted in the establishment of a national network of specifically trained, part-time, dedicated and strongly motivated hospital physicians in charge of the whole process of organ donation.

Since then, the number of donors has increased by 187% (from 550 in 1990 to 1577 in 2008,) and the donation rate for Spain is 14 – 342 donors per million population, by far the highest donor rate ever reached by a country. The programme initiated in Spain that dramatically improved cadaveric organ donation is known at the international level as the "Spanish Model" of organ donation. Dr Matesanz emphasized that the philosophy of the Spanish model is based on improved management.

Basic principles of the Spanish model include:

- adequate legal and technical background;
- transplant coordination networks at three levels: national, regional and hospital;
- special profile of the three levels of Transplant Care;
- hospital coordinators inside the hospitals. The human factor is the key to the success of the programme. They are all medical doctors (anaesthesiologists/ intensivists) dedicated to transplant activities;
- continuous brain death audit performed by the transplant coordinators;
- the central office of the National Transplantation Organization (ONT) acts as the support agency in charge of organ sharing, transport, waiting list management, transplant registries, statistics, general and specialized information and action which can improve the whole process of organ donation and transplantation;

- great effort in continuous medical training and education for new and old transplant coordinators financed and directed by the central health administration;
- hospital reimbursement by the regional or national health administrations; and,
- much attention to the mass media.

2.5.5 Xenotransplantation

Dr Peter Doyle from the United Kingdom introduced this subject. Animals could potentially provide a plentiful, readily available, high quality source of cells, tissues and organs for transplantation. Successful xenotransplantation has the potential to treat a wide range of serious diseases such as diabetes, heart and kidney disease. Genetic modification of source animals may enhance or increase the utility of xenogeneic products. Animals used in xenotransplantation should be from a closed herd, bred for the purpose and housed in a well-controlled, pathogen-free environment with high standards of animal welfare. Source animals should be extensively tested to ensure freedom from known pathogens with appropriate biosecurity and surveillance in place to ensure continued freedom from infectious disease.

Xenotransplantation is a complex process which carries risks, including graft rejection, inadequate graft function and transmission of recognized or unrecognized infectious diseases to the recipient. There is also the risk of developing serious or novel infections which could infect not just the transplant recipient but also close contacts or the wider human or animal populations.

Xenotransplantation should be regulated because of the complexity of the process, to reduce the risk of novel infections, especially when dealing with genetically modified animals, and to prevent the possibility of xenotourism. Because of these wider community risks, xenotransplantation clinical trials and procedures need to be effectively regulated. Regulation should have a legal basis with powers to ban unregulated procedures and enforce compliance with regulatory requirements. The regulatory system should be transparent, and must include scientific, ethical and risk assessment.

Proposers of xenotransplantation clinical trials must be able to clearly justify carrying out a particular trial on a specific patient population. Patient selection should be on the basis of informed consent from motivated patients willing to accept the special conditions that will be required by the trial. Patients and close contacts should be effectively educated about their treatment to encourage compliance and to minimize risks for themselves and for society. Participation in xenotransplantation will usually require pre-and post-treatment, and the long-term storage of animal and patient samples, as well as records. It will require life-long follow up of recipients and possibly their close contacts. There must be rigorous analysis of trial outcomes. Xenotransplant product recipients must be registered in an appropriate database with traceability to the donor animal, while ensuring that patient privacy is protected.

Medical teams must have appropriate expertise and understand the risks to the patients, themselves and the community. Because of the risk of infectious disease for the community, there must be a system in place for vigilance and surveillance with contingency plans to identify and respond to any indication of xenotransplantation-related infection in a timely manner.

The first WHO Global Consultation on Regulatory Requirements for Xenotransplantation Clinical Trials was held in Changsha, China, in November 2008. The principles of the Changsha Communiqué state that:

- Successful xenotransplantation has the potential to treat a wide range of serious diseases such as diabetes, heart and kidney disease. Successful xenotransplantation could provide transplants for people who currently would not get a transplant.

- There needs to be a global system for exchanging information, preventing unregulated xenotransplantation, providing support for states, and coordinating xenotransplantation vigilance, surveillance and response to suspected infections.

- Because of the potential benefits of successful xenotransplantation, consideration should be given from the beginning to future equitable access to this therapy, and the public sector should be encouraged to support xenotransplantation research and development.

2.5.6 Tissue banking: the Korean experience

Professor Yong-Koo Kang, from the Republic of Korea, gave a presentation on tissue banking and discussed the growing need of allograft transplantation in the Republic of Korea for orthopaedics (reconstruction for bone and soft tissue tumours, sports injuries, spine fusion); plastic surgery (skin graft for burn patients, dermal tissue transplantation); cardiac surgery (heart valve replacement, heart transplantation); urologic, general surgery; dental surgery; ossicle transplantation and amnion graft.

The law for safety and quality control of human tissues in the Republic of Korea was established in 2003 and requires mandatory registration of all 104 tissue banks with the Korean Food and Drug Administration (KFDA), quality assessment by KFDA and annual reporting of tissue bank's activities. The law is applicable to musculoskeletal tissues (bone, cartilage, tendon, ligament, fascia) skin, amnion, heart valves and blood vessels. Until 2008, a total of 101 307 tissues were sourced from different tissue banks, of which 64% were imported from other countries and 36% were produced in the Republic of Korea.

Quality assessment is conducted by KFDA and the process has progressed from chemical disinfection to radiation sterilization. Some of the causes of failure in quality assessment include inadequate facilities, equipment, and manpower; poor quality control on laboratory tests; and, weak documentation. Training demands for tissue bank operators are provided on a regular basis. The lack of public awareness, professional education and non-profit regional banks, however, is a big deterrent.

2.5.7 The role of the regulatory authorities: a global perspective

Dr Dierdre Fehilly, Inspector, Tissues and Cells, Italian National Transplant Centre, spoke about the role of regulatory authorities. World Health Assembly (WHA) Resolution 57.18 on Cell Tissue and Organ Transplantation urged Member States to implement effective national oversight of procurement, processing and transplantation of human cells, tissues and organs, including ensuring accountability for human material for transplantation and its traceability.

Health products which include human cells, tissues and organs are of an exceptional nature because they are donated altruistically for the benefit of others. In these cases, an ethical framework is needed - the "starting material" cannot be completely standardized or guaranteed as risk-free so, there is need for a special approach to quality and safety.

Some key features of tissues and cells for transplantation include the fact that they are usually life-enhancing, not life-saving, and that there are both benefits and risks associated with storing and processing them (including added value and the potential for profit). Improper storage and processing can also result in contamination and cross-contamination, poor quality due to inadequate preservation, mislabelling and source mix-ups, and, ultimately, loss of traceability.

With cells and tissues from one donor going to many recipients, and the possibility of export/import of tissues and cells (global circulation), the risk of commercialization and potential for exploitation is strong. Some examples of global circulation include facts such as:

- 40% of bone marrow donations are transplanted outside their country of origin;
- 36 000 (out of 46 000) corneas distributed by the Sri Lanka Eye Bank go to over 61 countries; and,
- in Canada, 100% of dental bone and 70% of other tissues implanted are imported.

A WHO consultation held in Madrid in 2003 highlighted the following issues in cell and tissue banking:

- poor levels of education, training and research in tissue banking globally;
- limited or non-existent evidence for efficacy of transplantation of some tissues;
- inability to provide "origin to destiny" traceability of tissues;
- lack of harmonization of regulatory standards leading to high costs for tissue banks;
- inconsistent approaches to donor consent;
- unregulated commercialization;
- existence of the trafficking of tissues on a global basis; and,
- balancing self-sustainability of "not-for-profit banks" with prevention of excessive income at "for-profit banks" that use altruistically-donated human material.

The WHO Global Consultation in Ottawa (2004) on "Quality and Safety of Cells and Tissues for Transplantation" was attended by participants from 29 countries and included clinicians, regulators and members of professional organizations. Conclusions of the Global Consultation included:

- the recognition of Human Cells and Tissues for Transplantation (HCTT) as a specific class of health products because of the risks inherent to human origin;

- the naming of health authorities as the protector of donor and patient safety and clinical efficacy; and,

- the recognition of a comprehensive regulatory framework (including surveillance system and accreditation) as mandatory.

2.5.8 Hemopoietic cell transplantation: the Japanese experience

Dr Yoshihisa Kodera, Chairman, Japan Society for Hemopoietic Cell Transplantation, spoke about the Japanese experience which included data from Japan's marrow donor programme, Japan's cord blood bank network, the Asia-Pacific blood and marrow transplant group and a worldwide network for blood and marrow transplantation. A computer-based registry was developed in 2006 called the Transplant Registry Unified Management Program (TRUMP). It enables smooth functioning of the registry.

Japan has successful international collaboration for bone marrow exchange with several countries.

There are 11 national core blood banks in Japan where procedures related to peripheral blood stem cell transplantation (PBSCT) are being carried out. There is an established standard that is followed to determine the eligibility of PBSC family donors. There is a family donor follow-up

system in place, which includes both short and long-term follow-up (up to five years) and monitoring of adverse events.

Throughout Japan, there is a good distribution of transplant teams (a total of 404 in number.) The clinical conditions for which hematopoietic cell transplantation occurs include leukemia/myelodysplastic syndrome, multiple myeloma, myeloid leukemia, aplasia, solid tumours, etc. The different modalities include allogeneic and autologous bone marrow transplants, autologous and allogeneic peripheral blood stem cell transplants; and cord blood stem cell transplants. Medical expenses related to hospitalization for hematopoietic stem cell transplantation are covered by public health insurance, the national government, medical insurance and contributions.

There are plans for continuing the development and expansion of the hematopoietic cell transplantation project in Japan. There is international collaboration with the Asia Pacific Blood and Marrow Transplant Group (APBMT). This organization started in 2006 and comprises membership from 14 countries. It allows physicians across Asia involved in clinical bone marrow transplantation to share their experiences and develop cooperative studies. The APBMT also aims to promote all aspects associated with hematopoietic stem cell transplantation, including basic and clinical research. This exercise resulted in the Asian BMT Registry, which assists in providing the updated status of HSCT in Asian countries, and the establishment of a database from Asia. The APBMT data centre is situated in Nagoya (Japan) and each country has equal ability to access and use the data through the contact person for the country. APBMT has become a member of the Worldwide Network for Blood and Marrow Transplantation (WBMT) in order to improve and make efficient regional and global communication between partners a reality.

2.5.9 The role of scientific and professional societies in donation and transplantation activities at the national, regional and global levels

Professor Jeremy Chapman, Director, Acute Intervention Medicine, Westmead Hospital, Australia and President of The Transplantation Society, spoke about the role of scientific and professional societies in donation and transplantation activities at national, regional and global level. According to Professor Chapman, the roles of professional societies include:

- facilitating professional communication;
- assisting professional collaboration in technological research and education;
- ensuring the provision of relevant metrics for activity and outcome analysis;
- setting national and international professional ethical standards;
- providing expert technical and peer review advice;
- keeping national governments and health authorities honest; and,
- doing what national health authorities cannot do.

Professor Chapman discussed three professional societies, including The Transplantation Society, the World Marrow Donor Association, and the Alliance for Harmonization for Cell Therapy Accreditation.

(1) The Transplantation Society (TTS) provides the focus for global leadership in transplantation through:

- the development of the science and clinical practice;
- scientific communication;
- continuing education; and,
- guidance on ethical practices.

Membership in The Transplantation Society is a prerequisite for effective professional, clinical and scientific practice in the field of transplantation worldwide. The functions of this Society include:

- creating a global forum for scientific discussion and professional development;
- organizing and facilitating international congresses;
- contributing to publications;
- facilitating in-depth discussion of the ethics of transplantation;
- developing consensus documents; and,
- linking with WHO's related global networks, regional and national meetings, science and research, and communications.

An initiative of The Transplantation Society is the "Global Alliance for Transplantation." Its goals are to:

- advance the safe, effective and ethical practice of transplantation for all patients in need;
- develop guidelines (i.e. care of the transplant recipient, deceased donation, and recompense of living donors); and,
- standardize the Global Data Dictionary.

(2) The World Marrow Donor Association (WMDA) is a network of 62 registries worldwide from 41 different countries active in the international field of unrelated stem cell transplantation. The goal of the WMDA is to secure and make available high-quality haematopoietic stem cell products for all patients worldwide, while maintaining the health and welfare of the stem cell donors. The Regulatory Committee of WMDA provides WMDA membership with accurate, up-to-date and usable guidance regarding the relevant worldwide regulatory landscape and encourages proactive, international collaboration towards effective, harmonized regulatory standards.

(3) The Alliance for Harmonization for Cellular Therapy Accreditation (AHCTA) is an alliance of global professional societies, some of which are the American Association of Blood Banks (AABB), the American Society for Blood and Marrow Transplantation (ASBMT), the European Federation for Immunogenetics (EFI), and the International Society for Cellular Therapy. Their functions include maintaining global quality standards, reporting adverse events, and maintaining a Serious and Adverse Effects Registry (SEAR).

2.5.10 Health care resources and transplantation: utility versus equity

Dr Harjit Singh of Malaysia introduced the topic and said that although global health is a fundamental right, which should be accessible to all, universal access to health care remains a dream. The causes include limited health care resources (transplant co-coordinators, surgeons); lack of adequate infrastructural facilities (e.g. tissue typing laboratories); and poor allocation of financial resources (e.g. for consumables/drugs).

Transplantation has both wanted and unwanted effects for the individual (it can prolong both suffering and benefit for the patient) as well as for society (e.g. redistribution of limited health care resources). Therefore, with the limited available health care resources, it remains a challenge to achieve the greatest possible medical benefit and utility maximization.

Health care providers in Malaysia include the public, private and academic facilities. While the public hospital system is nearly 100% subsidized by the government, the private system is self-funded or derives monies from health care insurance. Primary health care is well developed with basic health care facilities available within every five kilometres and throughout the country. The

private health care sector comprises 45% of doctors who cater to 25% of hospital beds, but access is limited by inability to pay for those services.

The challenges that face the health care services in Malaysia include:

(1) urban-rural mismatch;

(2) lack of public and private integration;

(3) health care expenditure (2003) as a percentage of GDP is 3.7%, compared to 9.5% in Australia and 7.6% in Spain; and,

(4) per capita spending in Malaysia is RM 282 (US$ 80), compared to Australia (US$1354) and Spain (US$850.)

Transplantation activities in Malaysia started in 1975 with kidney transplants and include heart, lung and liver transplantation. It is regulated by the Human Tissue Act (1974) for consent for donation after death and the National Organ & Tissue Transplant Policy (2007). The organizational structure includes the National Transplant Coordinating Committee (NTCC); the Transplant Program Committee (TPC); the Local Hospital Coordinating Units, and the Transplant Division within the Ministry of Health.

Issues affecting transplantation include:

(1) allocation of funds: competing with priority for basic health care services;

(2) human resource: migration health care professionals from public to private facilities;

(3) lack of donors: awareness of public and health care professionals; (e.g., religious and cultural barriers)

(4) infrastructure: shortage of ICU beds (60% of patients denied admission to ICU because of shortage of beds); laboratory facilities; and,

(5) unregulated and commercial stem cell therapy in the private sector.

2.6 Group discussions

The updated Guiding Principles pertain to organ donors, physicians, health facilities and regulatory authorities. These issues were taken up extensively in group discussions by all the participants. The primary objective was to have an understanding of the Guiding Principles and their related respective commentary so that their implementation in the country context can be facilitated.

3. CONCLUSIONS AND RECOMMENDATIONS

3.1 Conclusions

The participants unanimously endorsed the updated WHO Guiding Principles on Cell, Tissue and Organ Transplantation and described these as critical fundamental components of a template on which the national policies and programmes can be built.

3.2 Recommendations

The following recommendations were made:

3.2.1 For Member States:

(1) to develop comprehensive national legislation and a national programme on transplantation using the WHO Guiding Principles as a template;

(2) to develop legislation for cell, tissue and organ transplantation to apply to both public and private institutions;

(3) to institute an effective oversight mechanism to assure compliance with national regulations on organ transplantation;

(4) to strengthen health system requirements, including those of physical infrastructure and skilled human resources to meet the multidisciplinary requirements of transplantation with quality and safety as the fundamental principles;

(5) to develop a deceased donor organ programme to enhance availability of organs;

(6) to have in place a surveillance system for adverse events in organ donors and recipients;

(7) to promote community awareness to overcome religious, social and cultural myths associated with organ donation and stimulate the community and altruistic feelings; and

(8) to seek intercountry cooperation to harmonize cross-border activities and regulations.

3.2.2 For WHO:

(1) to undertake advocacy with national authorities to develop and implement national legislation and programmes on organ transplantation to meet the national needs;

(2) to support capacity-building in various aspects of management, technical skills and regulatory mechanism of organ transplantation;

(3) in collaboration with professional societies, to develop and disseminate technical guidelines, standards, models and distance learning materials to enhance knowledge, promote standardization and assure quality;

(4) to facilitate intercountry cooperation, especially in areas of capacity-building;

(5) to collect and share global data on all aspects of transplantation; and

(6) to organize regional meetings on a regular basis for exchange of experiences within the Region.

4. CLOSING

Dr Gayatri Ghadiok, Technical Officer, Essential Health Technologies Adviser, thanked all participants for their active participation.

ANNEX 1

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ANNEX 2

Regional Meeting on WHO Guiding Principles on Human Organ Transplantation

Kuala Lumpur , Malaysia, 08-10 June, 2009

PROVISIONAL PROGRAMME

Day 1 **8 Jun 09**	**Topic**	**Speaker**
08:30 – 09:00	Registration	
09:00 – 09:45	Inaugural program ▪ Welcome address ▪ Welcome remarks by WR Malaysia on behalf of Regional Director WPRO ▪ Address by Director General of Health, Malaysia ,Tan Sri Dato' Seri Dr. Hj. Mohd Ismail Bin Merican ▪ Objectives of the meeting ▪ Introduction of participants ▪ Adoption of provisional agenda & programme ▪ Election of Chair and Rapporteur ▪ Group photograph	
09:45-10:00	**Tea/Coffee break**	
10:00 -10:15	WHO and transplantation: World Health Assembly dedicated Resolutions	Luc Noel
10:15-10:30	Global overview of human cell, tissue and organ donation and transplantation	Mar Carmona
10:30-13:00	Transplantation activities in WPR countries (12 country reports x 10 min each)	Country Reports
13:00 – 14:00	**Lunch**	
14:00 -14:20	Overview of Transplantation activities in WPR countries	Gayatri Ghadiok
14:20 -14:45	The WHO global observatory for transplantation	Mar Carmona
14:45 -15:30	Genesis of revised WHO Guiding Principles and implications for the countries	Luc Noel
15:30 – 15:45	**Tea/Coffee break**	
15:45 -16:30	Key components of the legal framework for the oversight of human cell, tissue and organ donation and transplantation	Peter Doyle
16:30 -17:15	The Istanbul Declaration and the role of professionals in maintaining ethical value	Frank Delmonico
17:15 -18:00	Organ donation from deceased donors: lessons to be learnt from global experience	Rafael Matesanz
19:30	**Reception & Dinner**	

Day 2 9 Jun 09	Topic	Speaker
09:00-09:30	Xenotransplantation	Peter Doyle
09:30-10:00	Tissue banking : Korean experience	Yoo-Koo Kang
10:00 – 10:15	**Tea/Coffee break**	
10:15-12:00	WHO revised Guiding Principles as applied to organ donors • *Identification of gaps and needs* • *Country resolutions*	**Group Work 1**
12:00-13:00	Presentation from group work 1	
13:00 – 14:00	**Lunch**	
14:00-15:00	WHO revised Guiding Principles as applied to physicians and health facilities	**Group Work 2**
15:00-16:00	Presentation from group work 2	
16:00 – 16:15	**Tea/Coffee break**	
16:15-17:00	The role of regulatory authorities : a Global perspective	Deirdre Fehily
17:00-17:30	Hematopoietic cell transplantation : Japanese experience	Yoshihisa Kodera

Day 3 10 Jun 09	Topic	Speaker
09:00-09:30	The role of scientific and professional societies in donation and transplantation activities at national, regional and global level	Jeremy Chapman
09:30-10:00	Healthcare Resources & Transplantation: Utility versus Equity	Harjit Singh
10:00 – 10:15	**Tea/Coffee break**	
10:15-12:00	WHO revised Guiding Principles as applied to health systems & national regulatory agency	**Group Work 3**
12:00-13:00	Presentation from group work 3	
13:00 – 14:00	**Lunch**	
14:00-15:00	Increasing safety and availability of transplantation services in coordination with improved quality of care	Plenary: Luc Noel
15:00 – 15:15	**Tea/Coffee break**	
15:15-16:15	Recommendations and next steps	
16:15-17:00	Closing session	

ANNEX 3

Speech Of Dr Shin Young-Soo, WHO Regional Director for the Western Pacific, to be delivered by Dr Han Tieru, WHO Representative for Malaysia, Brunei Darussalam and Singapore, at the opening ceremony of the Regional Meeting on the WHO Guiding Principles on Organ Transplantation, Kuala Lumpur, Malaysia, 8 June 2009

Honourable Tan Sri Dato' Seri Dr. Hj. Mohd Ismail Bin Merican,
Director General Of Health, Malaysia,

Distinguished Guests, Ladies And Gentlemen.

On behalf of WHO and our Regional Director for the Western Pacific, Dr Shin Young-soo, I am pleased to welcome you to the regional meeting on the WHO Guiding Principles on Organ Transplantation.

I would like to thank the Government of Malaysia for hosting this important regional meeting. Malaysia has supported WHO's efforts to introduce and implement the Guiding Principles on organ transplantation, and we are delighted to be joined today by 13 Member States from the Western Pacific Region.

Surgical transplantation of human organs from deceased, as well as living donors, began in the 1940s. Over the past 50 years, transplantation of human organs, tissues and cells has become a worldwide practice that has extended and greatly enhanced the quality of hundreds of thousands of lives. Continuous improvements in medical technology, particularly in relation to organ and tissue rejection, have enhanced the cost-effectiveness and utility of transplantation as an

important intervention in fighting chronic disabling or life-threatening diseases. This, however, has also led to an increase in the demand for organs which has always exceeded supply.

Recognizing the importance of these issues and responding to World Health Assembly Resolutions, WHO in 1991 developed the Guiding Principles on Human Organ Transplantation. Over the past 17 years, the Guiding Principles have greatly influenced professional codes and practices, as well as legislation, around the world.

In light of changes in practices and attitudes regarding transplantation, and in response to additional World Health Assembly Resolutions, WHO updated these Guiding Principles on Human Organ Transplantation in 2008 after an extensive process of global consultation.

The revised Guiding Principles are intended to provide an orderly, ethical and acceptable framework for the acquisition and transplantation of human cells, tissues and organs for therapeutic purposes. These address the issues of access, quality, safety and ethics. In addition, WHO launched a global knowledge base on transplantation in 2006 to collect global data on transplantation-related activities and practices, legal frameworks, organizational structures and xeno-transplantation.

WHO estimates that globally, about 66000 kidney transplants take place every year. In addition, 21000 liver and 6000 heart transplants are undertaken. Data from 2007 shows that the estimated number of kidney transplants was around 11000, performed in about 400 centres in the Western Pacific Region. Almost 45% of kidney donors in the Region are live, unrelated donors, and the number of heart and liver transplants in the Western Pacific Region is not small.

Non-availability of adequate numbers of donors is a major challenge, and in some countries this huge gap between supply and demand has the potential to lead to unethical practices. Several Member States report the availability of legal frameworks on transplantation of

human organs, however, commercialization and trafficking in human organs is ongoing and also frequently highlighted in the media. Thus, ethical practices in organ donation and transplantation, as well as access to adequate numbers of organs, are both major issues in the Region.

The revised WHO Guiding Principles on Organ Transplantation address these issues. Member States are encouraged to incorporate these into their national regulations and practices.

This meeting has been organized to disseminate the revised WHO Guiding Principles, with the hope they can help to improve legislation, ethical practices and technologies on organ transplantation. It will address the challenges of establishing and promoting a deceased donor program; prevention of trade in organs and exploitation of humans; improvement of the quality, efficacy and safety of donations and transplantation; and transparency in practices. It will also discuss recent advances in xeno-transplantation and tissue banking.

This meeting also provides an opportunity to share experiences and develop future plans for strengthening the organ, tissue and cell transplantation programme and ensuring effective service delivery. The meeting is being facilitated by an eminent group of international experts who have contributed immensely in updating the WHO Guiding Principles.

I wish to reiterate that, as a follow-up of this meeting and to support national efforts, WHO shall continue to provide the required technical support in strengthening health systems to provide improved services for organ transplantation. I wish the meeting every success and thank the Government of Malaysia for hosting us. I wish all of you a successful and productive programme over the next few days.

World Health Organization

WHO GUIDING PRINCIPLES ON HUMAN CELL, TISSUE AND ORGAN TRANSPLANTATION[1]

PREAMBLE

1. As the Director-General's report to the Executive Board at its Seventy-ninth session pointed out,[2] human organ transplantation began with a series of experimental studies at the beginning of the twentieth century. The report drew attention to some of the major clinical and scientific advances in the field since Alexis Carrel was awarded the Nobel Prize in 1912 for his pioneering work. Surgical transplantation of human organs from deceased, as well as living, donors to sick and dying patients began after the Second World War. Over the past 50 years, the transplantation of human organs, tissues and cells has become a worldwide practice which has extended, and greatly enhanced the quality of, hundreds of thousands of lives. Continuous improvements in medical technology, particularly in relation to organ and tissue rejection, have led to an increase in the demand for organs and tissues, which has always exceeded supply despite substantial expansion in deceased organ donation as well as greater reliance on donation from living persons in recent years.

2. The shortage of available organs has not only prompted many countries to develop procedures and systems to increase supply but has also stimulated commercial traffic in human organs, particularly from living donors who are unrelated to recipients. The evidence of such commerce, along with the related traffic in human beings, has become clearer in recent decades. Moreover, the growing ease of international communication and travel has led many patients to travel abroad to medical centres that advertise their ability to perform transplants and to supply donor organs for a single, inclusive charge.

3. Resolutions WHA40.13 and WHA42.5 first expressed the Health Assembly's concern over commercial trade in organs and the need for global standards for transplantation. Based on a process of consultation undertaken by the Secretariat, the Health Assembly then endorsed the WHO Guiding Principles on Human Organ Transplantation in resolution WHA44.25. Over the past 17 years the Guiding Principles have greatly influenced professional codes and practices as well as legislation around the world. In the light of changes in practices and attitudes regarding organ and tissue transplantation, the Fifty-seventh World Health Assembly in resolution WHA.57.18 requested the Director-General, inter alia, "to continue examining and collecting global data on the practices, safety, quality, efficacy and epidemiology of allogeneic transplantation and on ethical issues, including living donation, in order to update the Guiding Principles on Human Organ Transplantation".

4. The following Guiding Principles are intended to provide an orderly, ethical and acceptable framework for the acquisition and transplantation of human cells, tissues and organs for therapeutic purposes. Each jurisdiction will determine the means of implementing the Guiding Principles. They preserve the essential points of the 1991 version while incorporating new provisions in response to current trends in transplantation, particularly organ transplants from living donors and the increasing use of human cells and tissues. The Guiding Principles do not apply to transplantation of gametes, ovarian or testicular tissue, or embryos for reproductive purposes, or to blood or blood constituents collected for transfusion purposes.

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[1] The revised official WHO Guiding Principles on Human Cell, Tissue and Organ Transplantation were contained in EB123/5 noted by the Executive Board at its 123d session on 26 May 2008, with a requested modification.

[2] Document EB79/8.

Annex 4

Cells, tissues and organs may be removed from deceased and living persons for the purpose of transplantation, only in accordance with the following Guiding Principles.

Guiding Principle 1

Cells, tissues and organs may be removed from the bodies of deceased persons for the purpose of transplantation if:
(a) any consent required by law is obtained, and
(b) there is no reason to believe that the deceased person objected to such removal.

Commentary on Guiding Principle 1

Consent is the ethical cornerstone of all medical interventions. National authorities are responsible for defining the process of obtaining and recording consent for cell, tissue and organ donation in the light of international ethical standards, the manner in which organ procurement is organized in their country, and the practical role of consent as a safeguard against abuses and safety breaches.

Whether consent to procure organs and tissues from deceased persons is "explicit" or "presumed" depends upon each country's social, medical and cultural traditions, including the manner in which families are involved in decision-making about health care generally. Under both systems any valid indication of deceased persons' opposition to posthumous removal of their cells, tissues or organs will prevent such removal.

Under a regime of explicit consent – sometimes referred to as "opting in" – cells, tissues or organs may be removed from a deceased person if the person had expressly consented to such removal during his or her lifetime; depending upon domestic law, such consent may be made orally or recorded on a donor card, driver's license or identity card or in the medical record or a donor registry. When the deceased has neither consented nor clearly expressed opposition to organ removal, permission should be obtained from a legally specified surrogate, usually a family member.

The alternative, presumed consent system – termed "opting (or contracting) out" – permits material to be removed from the body of a deceased person for transplantation and, in some countries, for anatomical study or research, unless the person had expressed his or her opposition before death by filing an objection with an identified office, or an informed party reports that the deceased definitely voiced an objection to donation. Given the ethical importance of consent, such a system should ensure that people are fully informed about the policy and are provided with an easy means to opt out.

Although expressed consent is not required in an opting-out system before removal of the cells, tissues or organs of a deceased person who had not objected while still alive, procurement programmes may be reluctant to proceed if the relatives personally oppose the donation; likewise, in opting-in systems, programmes typically seek permission from the family even when the deceased gave pre-mortem consent. Programmes are more able to rely on the deceased's explicit or presumed consent, without seeking further permission from family members, when the public's understanding and acceptance of the process of donating cells, tissues and organs is deep-seated and unambiguous. Even when permission is not sought from relatives, donor programmes need to review the deceased's medical and behavioural history with family members who knew him or her well, since accurate information about donors helps to increase the safety of transplantation.

For tissue donation, which entails slightly less challenging time constraints, it is recommended always to seek the approval of the next of kin. An important point to be addressed is the manner in which the appearance of the deceased's body will be restored after the tissues are removed.

Guiding Principle 2

Physicians determining that a potential donor has died should not be directly involved in cell, tissue or organ removal from the donor or subsequent transplantation procedures; nor should they be responsible for the care of any intended recipient of such cells, tissues and organs.

Commentary on Guiding Principle 2

This Principle is designed to avoid the conflict of interest that would arise were the physician or physicians determining the death of a potential donor to be responsible in addition for the care of other patients whose welfare depended on cells, tissues or organs transplanted from that donor.

National authorities will set out the legal standards for determining that death has occurred and specify how the criteria and process for determining death will be formulated and applied.

Guiding Principle 3

Donation from deceased persons should be developed to its maximum therapeutic potential, but adult living persons may donate organs as permitted by domestic regulations. In general living donors should be genetically, legally or emotionally related to their recipients.

Live donations are acceptable when the donor's informed and voluntary consent is obtained, when professional care of donors is ensured and follow-up is well organized, and when selection criteria for donors are scrupulously applied and monitored. Live donors should be informed of the probable risks, benefits and consequences of donation in a complete and understandable fashion; they should be legally competent and capable of weighing the information; and they should be acting willingly, free of any undue influence or coercion.

Commentary on Guiding Principle 3

The Principle emphasizes the importance both of taking the legal and logistical steps needed to develop deceased donor programmes where these do not exist and of making existing programmes as effective and efficient as possible.

While favouring the maximal development of transplant programmes that avoid the inherent risks to live donors, the Principle also sets forth basic conditions for live donation. A genetic relationship between donor and recipient may be therapeutically advantageous and can provide reassurance that the donor is motivated by genuine concern for the recipient, as can a legal relationship (such as that between spouses). Many altruistic donations also originate from emotionally related donors, though the strength of a claimed connection may be difficult to evaluate. Donations by unrelated donors have been a source of concern, though some such cases are unexceptionable, such as in hematopoietic stem cell transplantation (where a wide donor pool is therapeutically advisable) or when an exchange of kidneys is made because the donors are not immunologically well matched with the recipients to whom they are related.

With live donation, particularly by unrelated donors, psychosocial evaluation is needed to guard against coercion of the donor or the commercialism banned by Principle 5. The national health authority should ensure that the evaluation is carried out by an appropriately qualified, independent party. By assessing the donor's motivation and the donor's and recipient's expectations regarding

outcomes, such evaluations may help identify – and avert – donations that are forced or are actually paid transactions.

The Principle underscores the necessity of genuine and well-informed choice, which requires full, objective, and locally relevant information and excludes vulnerable persons who are incapable of fulfilling the requirements for voluntary and knowledgeable consent. Voluntary consent also implies that adequate provisions exist for withdrawal of consent up until medical interventions on the recipient have reached the point where the recipient would be in acute danger if the transplant did not proceed. This should be communicated at the time of consent.

Finally, this Principle stresses the importance of protecting the health of living donors during the process of selection, donation, and necessary aftercare to ensure that the potential untoward consequences of the donation are unlikely to disadvantage the remainder of the donor's life. Care for the donor should match care for the recipient, and health authorities have the same responsibility for the welfare of both.

Guiding Principle 4

No cells, tissues or organs should be removed from the body of a living minor for the purpose of transplantation other than narrow exceptions allowed under national law. Specific measures should be in place to protect the minor and, wherever possible the minor's assent should be obtained before donation. What is applicable to minors also applies to any legally incompetent person.

Commentary on Guiding Principle 4

This Principle states a general prohibition on the removal of cells, tissues or organs from legal minors for transplantation. The major exceptions that may be authorized are familial donation of regenerative cells (when a therapeutically comparable adult donor is not available) and kidney transplants between identical twins (where avoiding immunosuppression represents a benefit to the recipient adequate to justify the exception, in the absence of a genetic disorder that could adversely affect the donor in the future).

While the permission of the parent(s) or the legal guardian for organ removal is usually sufficient, they may have a conflict of interest if they are responsible for the welfare of the intended recipient. In such cases, review and approval by an independent body, such as a court or other competent authority, should be required. In any event, a minor's objection to making a donation should prevail over the permission provided by any other party. The professional counselling provided to potential living donors in order to assess, and when needed, address any pressure in the decision to donate, is especially important for minor donors.

Guiding Principle 5

Cells, tissues and organs should only be donated freely, without any monetary payment or other reward of monetary value. Purchasing, or offering to purchase, cells, tissues or organs for transplantation, or their sale by living persons or by the next of kin for deceased persons, should be banned.

The prohibition on sale or purchase of cells, tissues and organs does not preclude reimbursing reasonable and verifiable expenses incurred by the donor, including loss of income, or paying the costs of recovering, processing, preserving and supplying human cells, tissues or organs for transplantation.

Commentary on Guiding Principle 5

Payment for cells, tissues and organs is likely to take unfair advantage of the poorest and most vulnerable groups, undermines altruistic donation, and leads to profiteering and human trafficking. Such payment conveys the idea that some persons lack dignity, that they are mere objects to be used by others.

Besides preventing trafficking in human materials, this Principle aims to affirm the special merit of donating human materials to save and enhance life. However, it allows for circumstances where it is customary to provide donors with tokens of gratitude that cannot be assigned a value in monetary terms. National law should ensure that any gifts or rewards are not, in fact, disguised forms of payment for donated cells, tissues or organs. Incentives in the form of "rewards" with monetary value that can be transferred to third parties are not different from monetary payments.

While the worst abuses involve living organ donors, dangers also arise when payments for cells, tissues and organs are made to next of kin of deceased persons, to vendors or brokers, or to institutions (such as mortuaries) having charge of dead bodies. Financial returns to such parties should be forbidden.

This Principle permits compensation for the costs of making donations (including medical expenses and lost earnings for live donors), lest they operate as a disincentive to donation. The need to cover legitimate costs of procurement and of ensuring the safety, quality and efficacy of human cell and tissue products and organs for transplantation is also accepted.

Incentives that encompass essential items which donors would otherwise be unable to afford, such as medical care or health insurance coverage, raise concerns. Access to the highest attainable standard of health is a fundamental right, not something to be purchased in exchange for body parts. However, free periodic medical assessments related to the donation and insurance for death or complications that arise from the donation may legitimately be provided to living donors.

Health authorities should promote donation motivated by the need of the recipient and the benefit for the community. Any measures to encourage donation should respect the dignity of the donor and foster societal recognition of the altruistic nature of cell, tissue and organ donation. In any event, all practices to encourage the procurement of cells, tissues and organs for transplantation should be defined explicitly by health authorities in a transparent fashion.

National legal frameworks should address each country's particular circumstances because the risks to donors and recipients vary. Each jurisdiction will determine the details and method of the prohibitions it will use, including sanctions which may encompass joint action with other countries in the region. The ban on paying for cells, tissues and organs should apply to all individuals, including transplant recipients who attempt to circumvent domestic regulations by travelling to locales where prohibitions on commercialization are not enforced.

Guiding Principle 6

Promotion of altruistic donation of human cells, tissues or organs by means of advertisement or public appeal may be undertaken in accordance with domestic regulation.

Advertising the need for or availability of cells, tissues or organs, with a view to offering or seeking payment to individuals for their cells, tissues or organs, or, to the next of kin, where the individual is deceased, should be prohibited. Brokering that involves payment to such individuals or to third parties should also be prohibited.

Commentary on Guiding Principle 6

This Principle does not affect general advertisements or public appeals to encourage altruistic donation of human cells, tissues or organs, provided that they do not subvert legally established systems of organ allocation. Instead, it aims to prohibit commercial solicitations, which include offering to pay individuals, the next of kin of deceased persons, or other parties in possession (such as undertakers), for cells, tissues or organs; it targets brokers and other intermediaries as well as direct purchasers.

Guiding Principle 7

Physicians and other health professionals should not engage in transplantation procedures, and health insurers and other payers should not cover such procedures, if the cells, tissues or organs concerned have been obtained through exploitation or coercion of, or payment to, the donor or the next of kin of a deceased donor.

Commentary on Guiding Principle 7

Health care professionals should only proceed with the removal, intermediate management or implantation of cells, tissues or organs when donations are unpaid and truly voluntary. (In the case of live donors, a psychosocial evaluation of the donor is usually indicated, as described in Guiding Principle 3). Failing to ensure that the person consenting to the donation has not been paid, coerced or exploited breaches professional obligations and should be sanctioned by the relevant professional organizations and government licensing or regulatory authorities.

Physicians and health care facilities should also not refer patients to transplant facilities in their own or other countries that make use of cells, tissues or organs obtained through payments to donors, their families or other vendors or brokers; nor may they seek or accept payment for doing so. Post-transplant care may be provided to patients who have undergone transplantation at such facilities, but physicians who decline to provide such care should not face professional sanctions for such refusals, provided that they refer such patients elsewhere.

Health insurers and other payers should reinforce adherence to high ethical standards by refusing to pay for transplants that violate the Guiding Principles.

Guiding Principle 8

All health care facilities and professionals involved in cell, tissue or organ procurement and transplantation procedures should be prohibited from receiving any payment that exceeds the justifiable fee for the services rendered.

Commentary on Guiding Principle 8

This provision reinforces Guiding Principles 5 and 7 by forbidding profiteering in cell, tissue and organ recovery and implantation. Health authorities should monitor the fees charged for transplantation services to ensure that they are not disguised charges for the cells, tissues or organs themselves. All persons and facilities involved should be accountable for all payments for transplantation services. A medical or other health care practitioner uncertain whether a fee is justifiable should seek the opinion of an appropriate licensing or disciplinary authority before proposing or levying the fee. Fees charged for similar services may be used as a reference.

Guiding Principle 9

The allocation of organs, cells and tissues should be guided by clinical criteria and ethical norms, not financial or other considerations. Allocation rules, defined by appropriately constituted committees, should be equitable, externally justified, and transparent.

Commentary on Guiding Principle 9

Where donation rates do not meet clinical demand, allocation criteria should be defined at national or subregional level by a committee that includes experts in the relevant medical specialties, bioethics and public health. Such multidisciplinarity is important to ensure that allocation takes into account not only medical factors but also community values and general ethical rules. The criteria for distributing cells, tissues and organs should accord with human rights and, in particular, should not be based on a recipient's gender, race, religion, or economic condition.

This principle implies that the cost of transplantation and follow-up, including immunosuppressive treatment where applicable, should be affordable to all patients concerned — that is, no recipient should be excluded solely for financial reasons.

The concept of transparency is not exclusive to the allocation process but is central to all aspects of transplantation (as is discussed in the commentary on Guiding Principle 11, below).

Guiding Principle 10

High-quality, safe and efficacious procedures are essential for donors and recipients alike. The long-term outcomes of cell, tissue and organ donation and transplantation should be assessed for the living donor as well as the recipient in order to document benefit and harm.

The level of safety, efficacy and quality of human cells, tissues and organs for transplantation, as health products of an exceptional nature, must be maintained and optimized on an ongoing basis. This requires implementation of quality systems including traceability and vigilance, with adverse events and reactions reported, both nationally and for exported human products.

Commentary on Guiding Principle 10

Optimizing the outcome of cell, tissue and organ transplantation entails a rules-based process that encompasses clinical interventions and *ex vivo* procedures from donor selection through long-term follow-up. Under the oversight of national health authorities, transplant programmes should monitor both donors and recipients to ensure that they receive appropriate care, including information regarding the transplantation team responsible for their care.

Evaluation of information regarding the long-term risks and benefits is essential to the consent process and for adequately balancing the interests of donors as well as recipients. The benefits to both must outweigh the risks associated with the donation and transplantation. Donors should not be permitted to donate in clinically hopeless situations.

Donation and transplant programmes are encouraged to participate in national and/or international transplant registries. All deviations from accepted processes that could elevate the risk to recipients or donors, as well as any untoward consequences of donation or transplantation, should be reported to and analysed by responsible health authorities.

Transplantation of human material which does not involve maintenance treatment may not require active, long-term follow-up, though traceability should be ensured for the anticipated lifetime of the donor and the recipient. Internationally agreed means of coding to identify tissues and cells used in transplantation are essential for full traceability.

Guiding Principle 11

The organization and execution of donation and transplantation activities, as well as their clinical results, must be transparent and open to scrutiny, while ensuring that the personal anonymity and privacy of donors and recipients are always protected.

Commentary on Guiding Principle 11

Transparency can be summarized as maintaining public access to regularly updated comprehensive data on processes, in particular allocation, transplant activities and outcomes for both recipients and living donors, as well as data on organization, budgets and funding. Such transparency is not inconsistent with shielding from public access information that could identify individual donors or recipients while still respecting the necessity of traceability recognized in Principle 10. The objective of the system should be not only to maximize the availability of data for scholarly study and governmental oversight but also to identify risks – and facilitate their correction – in order to minimize harm to donors or recipients.

World Health Organization

First WHO Global Consultation on Regulatory Requirements for Xenotransplantation Clinical Trials

Changsha, China, 19-21 November 2008

The Changsha Communiqué[1]

Principles

1. Successful xenotransplantation has the potential to treat a wide range of serious diseases such as diabetes, heart and kidney disease. Successful xenotransplantation could provide transplants for people who currently would not get a transplant.

2. Potentially animals could provide a plentiful supply of readily available, high quality cells, tissues and organs for transplantation. Genetic modification of the animals may improve the effectiveness of such xenotransplant material. Animals used in xenotransplantation should be from a closed herd bred for the purpose and housed in a well-controlled, pathogen-free environment with high standards of animal welfare. Source animals should be extensively tested to ensure freedom from known pathogens with appropriate biosecurity and surveillance in place to ensure continued freedom from infectious disease.

3. Xenotransplantation is a complex process which carries risks, including graft rejection, inadequate graft function and transmission of recognized or unrecognized infectious diseases to the recipient. There is the risk of developing serious or novel infections which could infect not just the transplant recipient but also close contacts or the wider human or animal populations.

4. Because of these wider community risks, xenotransplantation clinical trials and procedures need to be effectively regulated. There should be no xenotransplantation in the absence of effective regulation by the government of the country. Regulation should have a legal basis with powers to ban unregulated procedures and enforce compliance with regulatory requirements. The regulatory system should be transparent, must include scientific and ethical assessment and should involve the public.

5. Because of the community risk, in proposed clinical trials of xenotransplantation there should be a high expectation of benefit to balance the risk. The level of this expectation should be in proportion to the level of the risk. The level of safety and efficacy should conform to recommendations from the international scientific community, when available, and requires rigorous pre-clinical studies using the most relevant animal models. Proposers of trials must provide all the information required by the regulatory authority to assess the risks and determine how the risks can be minimised.

[1] Disclaimer: These are the conclusions of the above meeting for which WHO was the Secretariat. These conclusions do not necessarily represent the decisions and policies of WHO.

6. Proposers of xenotransplantation clinical trials must be able to clearly justify carrying out a particular trial on a specific patient population. Patient selection should be on the basis of informed consent from motivated patients willing to accept the special conditions that will be required by the trial. Patients and close contacts should be effectively educated about their treatment to encourage compliance, and to minimize risks for themselves and for society.

7. Participation in xenotransplantation will usually require the long term storage of animal and patient samples, pre- and post-treatment, as well as records. It will require life-long follow up of recipients and possibly their close contacts. There must be rigorous analysis of trial outcomes. Xenotransplant product recipients must be registered in an appropriate database with traceability to the donor animal, while ensuring that patient privacy is protected. If anything happens to prevent the proposers from continuing the trial, there must be an adequate provision for all records, data and archived samples such as their transfer to the regulatory authority or other designated organization.

8. Medical teams must have appropriate expertise and understand the risks to the patients, themselves and the community. Because of the risk of infectious disease for the community, there must be a system in place for vigilance and surveillance with contingency plans to identify and respond to any indication of xenotransplantation-related infection in a timely manner.

9. There needs to be a global system for exchanging information, preventing unregulated xenotransplantation, providing support for states and coordinating xenotransplantation vigilance, surveillance and response to suspected infections.

10. Because of the potential benefits of successful xenotransplantation, consideration should be given from the beginning to future equitable access to this therapy and the public sector should be encouraged to support xenotransplantation research and development.

Key Recommendations

To WHO

1. WHO should have a dedicated resource to develop and support a plan for global action for xenotransplantation.

2. WHO should inform Member States of the need to assess xenotransplantation practices in their territories.

3. WHO should encourage and, if requested, support Member States to the extent possible in assessing their capacity to regulate xenotransplantation and in identifying xenotransplantation practices in their territories.

4. WHO should promote public awareness of the potential benefits of successful xenotransplantation and of the dangers of unregulated xenotransplantation, including xenotourism.

5. WHO should have in place a system for the identification of and response to any xenotransplantation infectious disease outbreak in a timely manner.

6. WHO should continue its support to the database of worldwide xenotransplantation practices.

7. WHO should maintain a register of xenotransplantation trials and a list of experts who can advise Member States on aspects of xenotransplantation and of specialized laboratories able to test for xenotransplantation-related pathogens.

8. WHO should promote future equitable access to successful xenotransplantation products.

To Member States

1. Member States should take immediate steps to identify any xenotransplantation practices in their territories and ban those that are unregulated. They should promote public awareness of these practices and their risks.

2. Member States should ensure that public health officials are aware of the infection risks of xenotransplantation, including those associated with patients travelling to receive xenotransplantation products outside their territories and have plans in place to timely identify and respond to any such infection.

3. Member States should review their laws to determine whether they have adequate authority to regulate xenotransplantation, ban unregulated xenotransplantation and provide appropriate sanction for failure to comply.

4. Member States should assess whether they have the resources and capacity to regulate xenotransplantation effectively. If they do not have such resources and capacity, they should ban xenotransplantation in their territories.

5. If a Member State has the capacity to regulate xenotransplantation and believes xenotransplantation should be carried out, it should ensure there is an effective national registry and regulatory process in place.

To investigators and proposers of clinical trials using xenotransplantation products

1. Investigators must ensure that source animals are bred for the purpose and as safe as possible, using a closed colony of consistently known specific pathogen-free animals housed in a well controlled pathogen-free environment with high levels of biosecurity.

2. Investigators must provide clear justification for the trial, including adequate pre-clinical data on safety and efficacy, usually from non-human primate testing.

3. Investigators should select trial participants for whom there is no adequately effective alternative therapy available and who understand the risks and consequences of the procedure, including the need for compliance with life-long follow up and who are motivated to modify their behaviour accordingly.

4. Investigators must provide appropriately trained and experienced personnel to provide the transplant material and conduct the clinical trial and surveillance.

5. Investigators must have a comprehensive plan for effective communication with public health authorities overseeing the trial.

6. Investigators must have a comprehensive plan for post-transplant long-term patient follow up and timely identification, reporting, and management of possible xenotransplant-related infection episodes.

7. Investigators must ensure storage of appropriate pre- and post-procedure specimens and maintain both the specimens and records in accordance with national regulatory guidelines (normally for 30 to 50 years).