

# Global Status of Transfusion and Transplantation Safety

Advisory Committee on Blood Safety and Availability

31<sup>st</sup> Meeting, 10-11 May 2007

Washington D.C.

Clinical Procedures - Transplantation





# Current State of Safety in Transfusion and Transplantation



World Health  
Organization

Health Technology  
and Pharmaceuticals

Essential  
Health Technologies

# What is Safe Blood?

## **Blood for transfusion is considered safe when it is:**

- donated by a healthy, voluntary, unpaid donor after assessing suitability for blood donation
- tested to assess freedom from any infections that could be harmful to the patient
- correctly stored and transported
- transfused only upon need and used for the benefit of the patients' health and well-being



# Safe Transfusion or Transplantation

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- Safety, Quality, Efficacy Of Health Products of Human Origin (HPOHO)
- Best Clinical Practices
- Standards and Safeguards against unexpected adverse events and reactions

# 57<sup>th</sup> World Health Assembly Resolution WHA 57.18

## Human Organ and Tissue Transplantation

The Fifty-seventh World Health Assembly,

1. URGES Member States:

- (1) 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**;

# WHO Tools for Assessing the Global Situation in Transfusion and Transplantation

- **Global Data Base on Blood Safety (GDDBS)**
- **Global Knowledge Base on Transplantation (GKT)**
  - Cells, tissues and organs
  - GKT 1 : activity and practices
  - GKT 2 : legal and organizational framework
  - GKT 3 : threats and responses, safety and ethical
- **Revealing but with limitations**
  - Incomplete national consolidation (health authorities)
  - Cross-boundary exchanges, trafficking
  - Poor hospital records
- **Improving**
  - GDDBS 2004-05
  - GKT1&2 Global Observatory on Donation and Transplantation (Spain ONT)

# Global Knowledge Base on Transplantation

<http://www.who.int/transplantation/knowledgebase/en/>

Dirección  <http://www.who.int/transplantation/knowledgebase/en/>

 **World Health Organization**

عربي | 中文 | English | Français | Русский | Español

All WHO  This site only

<b>Home</b>	<b>Transplantation</b>
<b>About WHO</b>	<a href="#">WHO</a> > <a href="#">WHO sites</a> > <a href="#">Transplantation</a>
<b>Countries</b>	<b>Global Knowledge Base on Transplantation (GKT)</b>
<b>Health topics</b>	
<b>Publications</b>	<ul style="list-style-type: none"><li>:: <a href="#">GKT1 Activity and Practices</a></li><li>:: <a href="#">GKT2 Legal framework and organizational structure</a></li><li>:: <a href="#">GKT3 Vigilance, Threats and Responses</a></li><li>:: <a href="#">GKT4 Xenotransplantation</a></li></ul>
<b>Research tools</b>	
<b>WHO sites</b>	<p>Through the GKT, the World Health Organization aims to bring together in one database information on organ, tissue and cell donation and transplantation from around the world. The GKT will be a source of information for all involved from the lay public, whose willingness to donate relies on an understanding of the value of transplantation and who might some day benefit as a recipient, to health professionals and health authorities responsible for the success, safety and quality of cell, tissue and organ transplantation, while maintaining the dignity of donors and recipients.</p>
<b>Transplantation</b>	<b>Global Transparency in Cell, Tissue and Organ Transplantation</b>
<b>Donation and transplantation</b>	<p>Access to information is key to understanding the value of transplantation and to increasing the motivation to donate. The provision of transplantation information is the proof of transparency and is essential</p>
<b>Cell and tissue transplantation</b>	
<b>Organ transplantation</b>	
<b>Xenotransplantation</b>	
<b>Activities</b>	
<b>Global knowledge base on transplantation (GKT)</b>	
<b>Partnerships and collaborations</b>	

**Contact information**

World Health Organization  
Department of Essential Health Technologies  
(HTP/EHT/CPR)  
20 Avenue Appia  
1211, Geneva 27  
Switzerland  
Tel: +41 22 791 3681  
Fax: +41 22 791 4836  
Email: [neoll@who.int](mailto:neoll@who.int)

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**PUBLICATIONS**  
[Documentation centre](#)

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**LINKS**  
[Information resources](#)

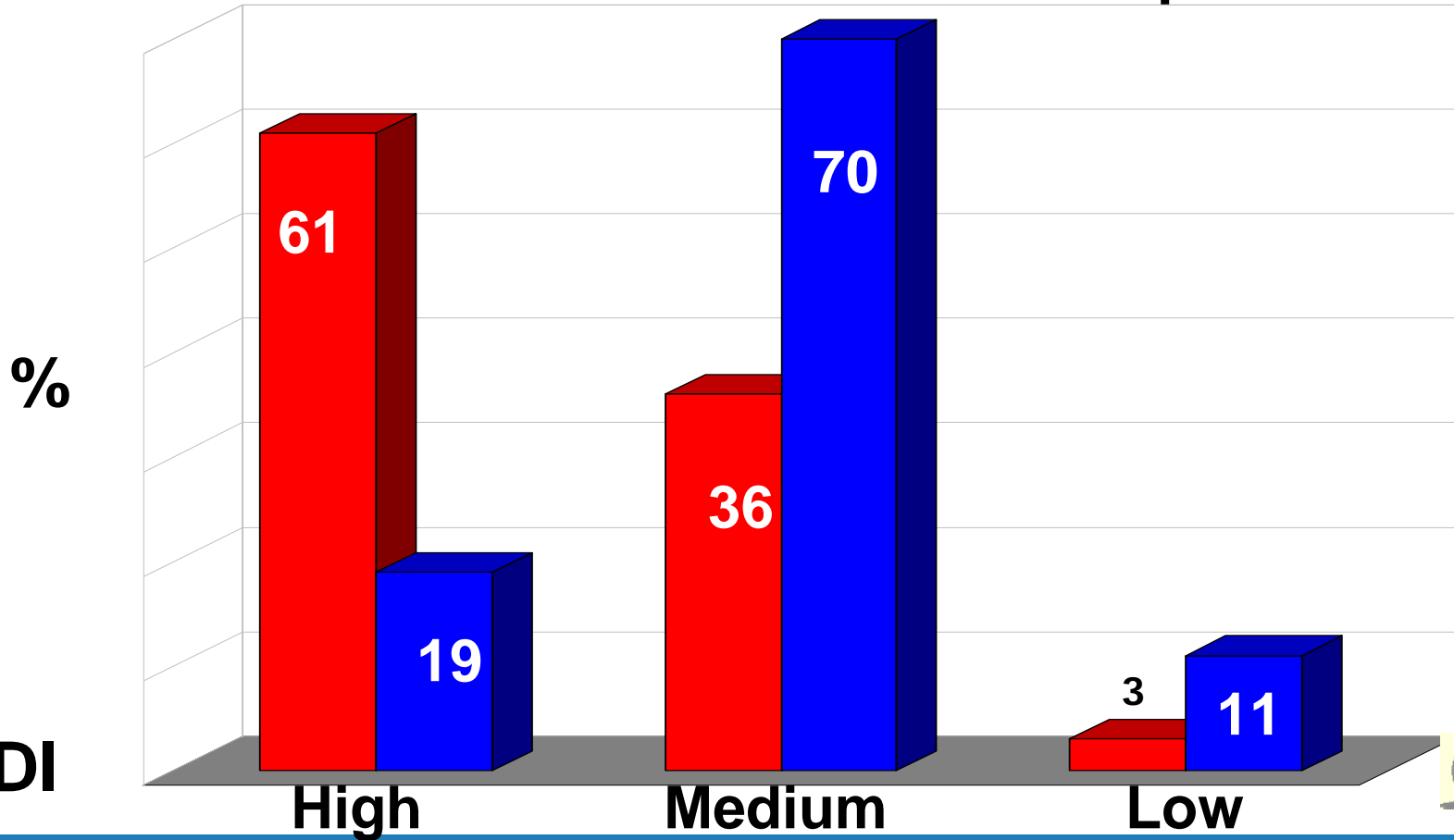
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**UPCOMING**  
[Events](#)

# Global Population and Blood Supply

Global Data Base on Blood Safety 2001-2002

■ % Donations 81 million      ■ % Population



HDI

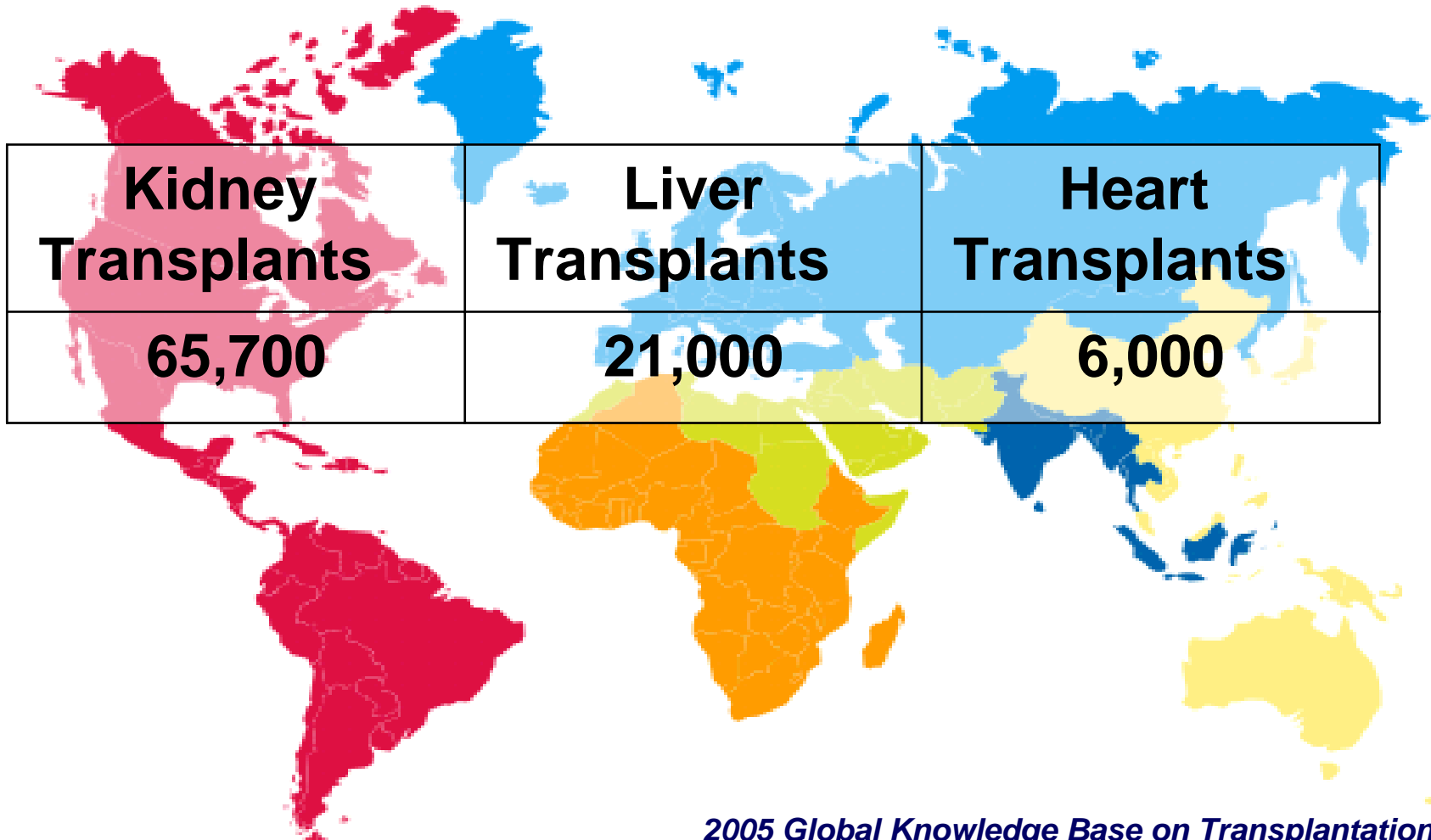
High

Medium

Low



# Annual Global Estimates: Organs



*2005 Global Knowledge Base on Transplantation  
Global Observatory of Donation and Transplantation*

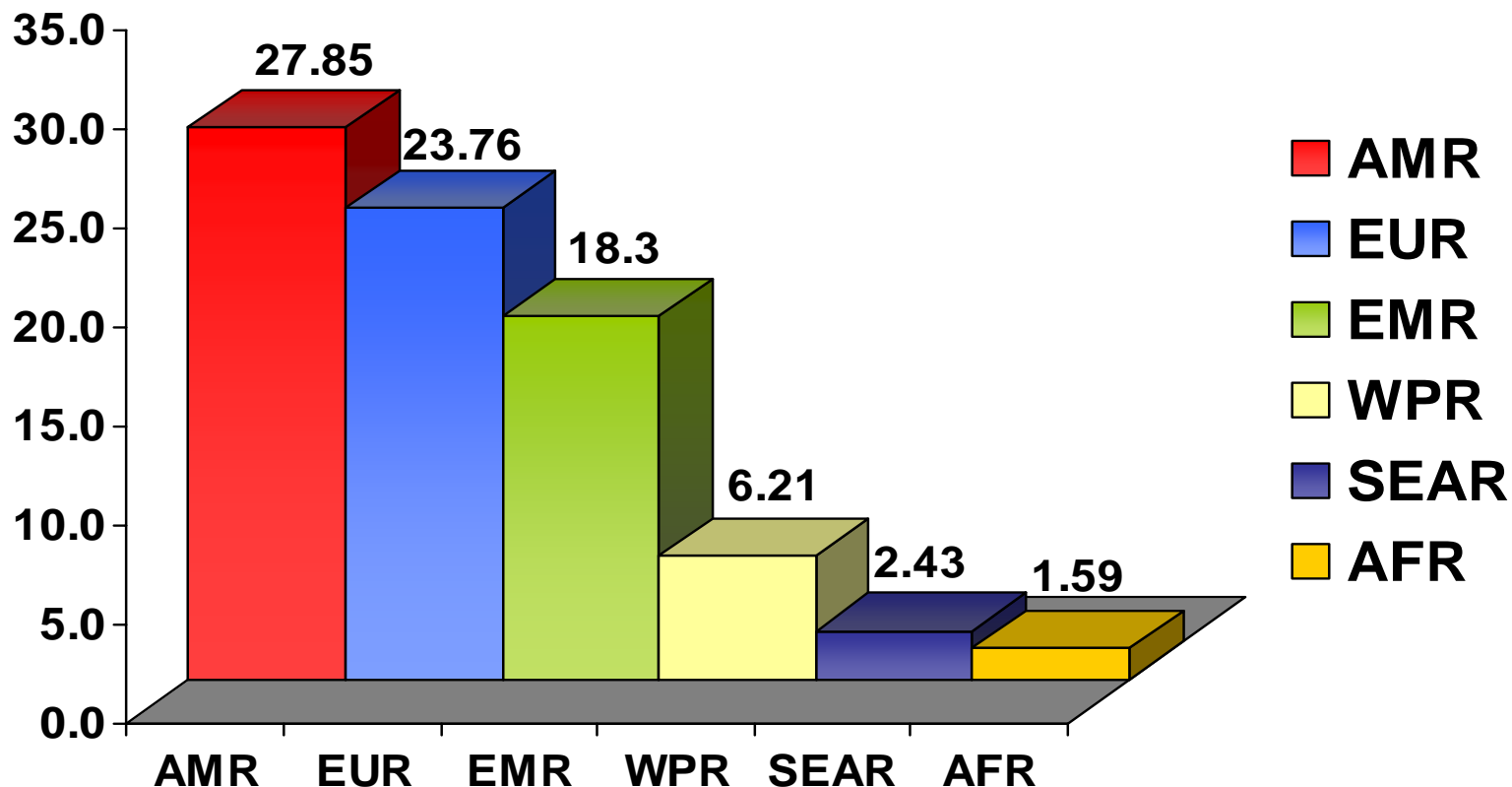


World Health  
Organization

Health Technology  
and Pharmaceuticals

Essential  
Health Technologies

# Kidney Transplantations in WHO Regions per million population



*2005 Global Knowledge Base on Transplantation  
Global Observatory of Donation and Transplantation*



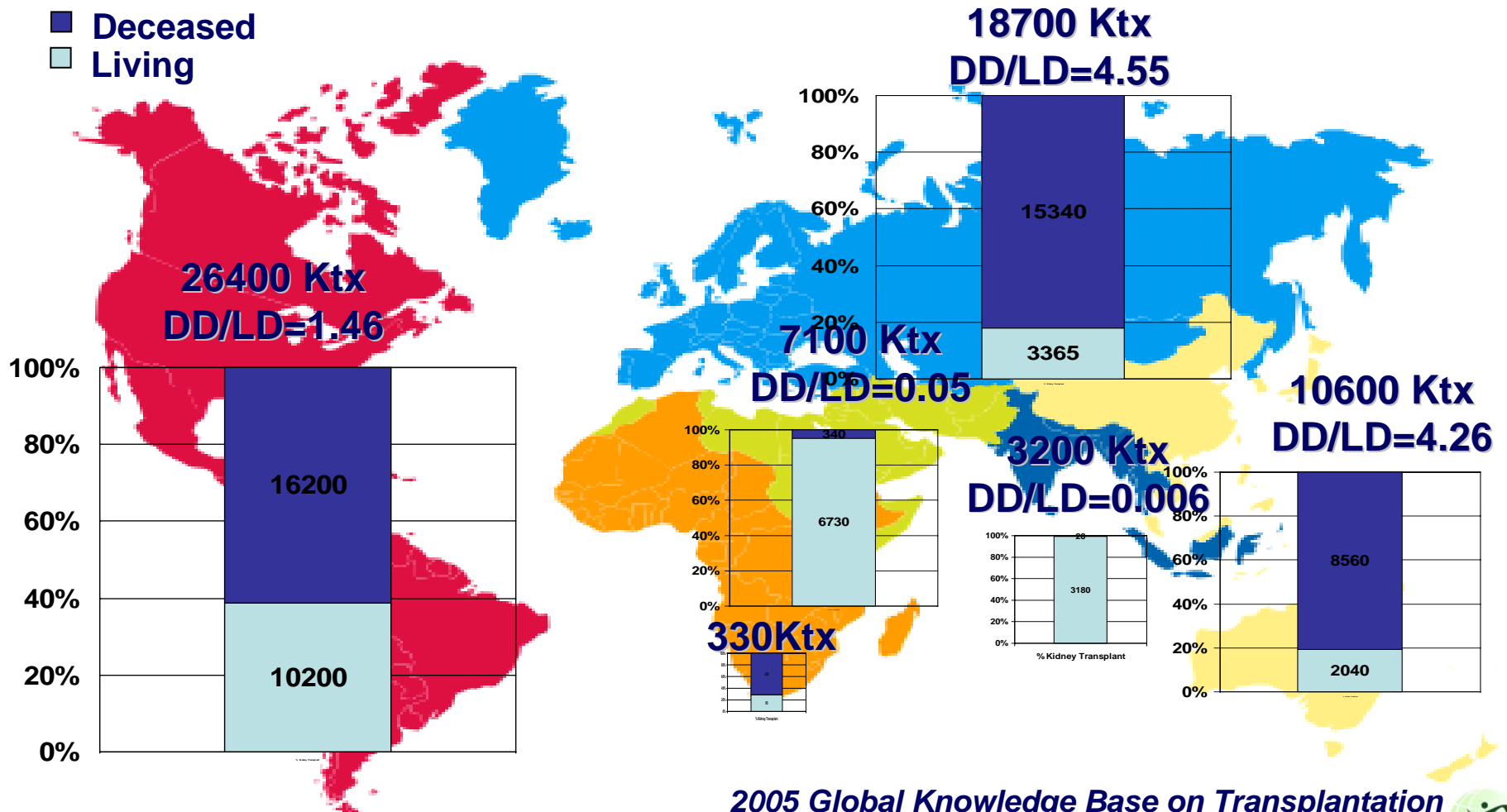
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Health Technologies

# Kidney Transplantation WHO Regions

■ Deceased  
■ Living



2005 Global Knowledge Base on Transplantation  
Global Observatory of Donation and Transplantation



# One Year Kidney Graft Survival

## Live Donor / Deceased Donor

Global Knowledge base on Transplantation



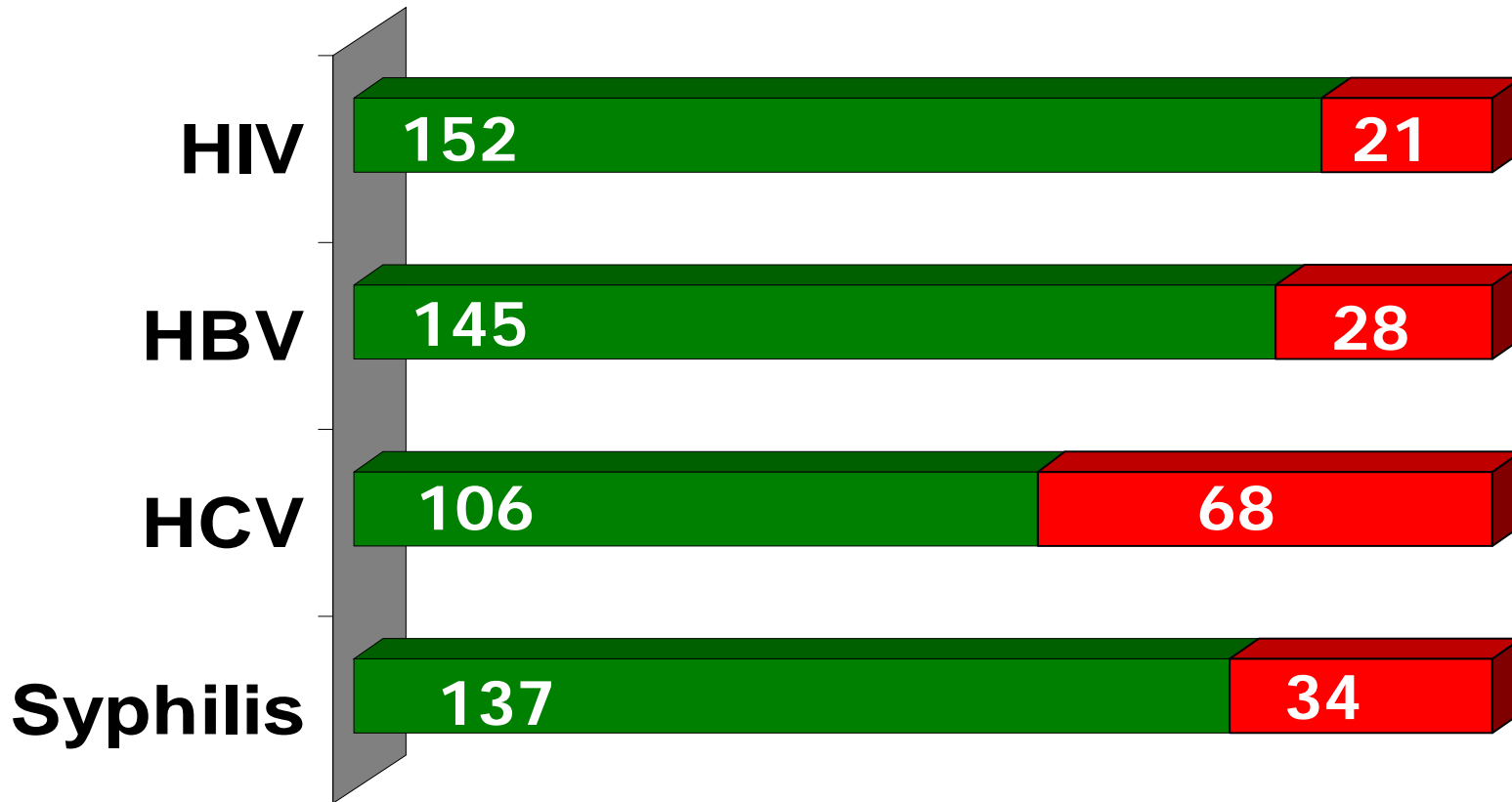
[http://www.who.int/transplantation/gkt/statistics/kidney\\_outcomes/en/index.html](http://www.who.int/transplantation/gkt/statistics/kidney_outcomes/en/index.html)



# Countries **WITHOUT** 100% Blood Screening

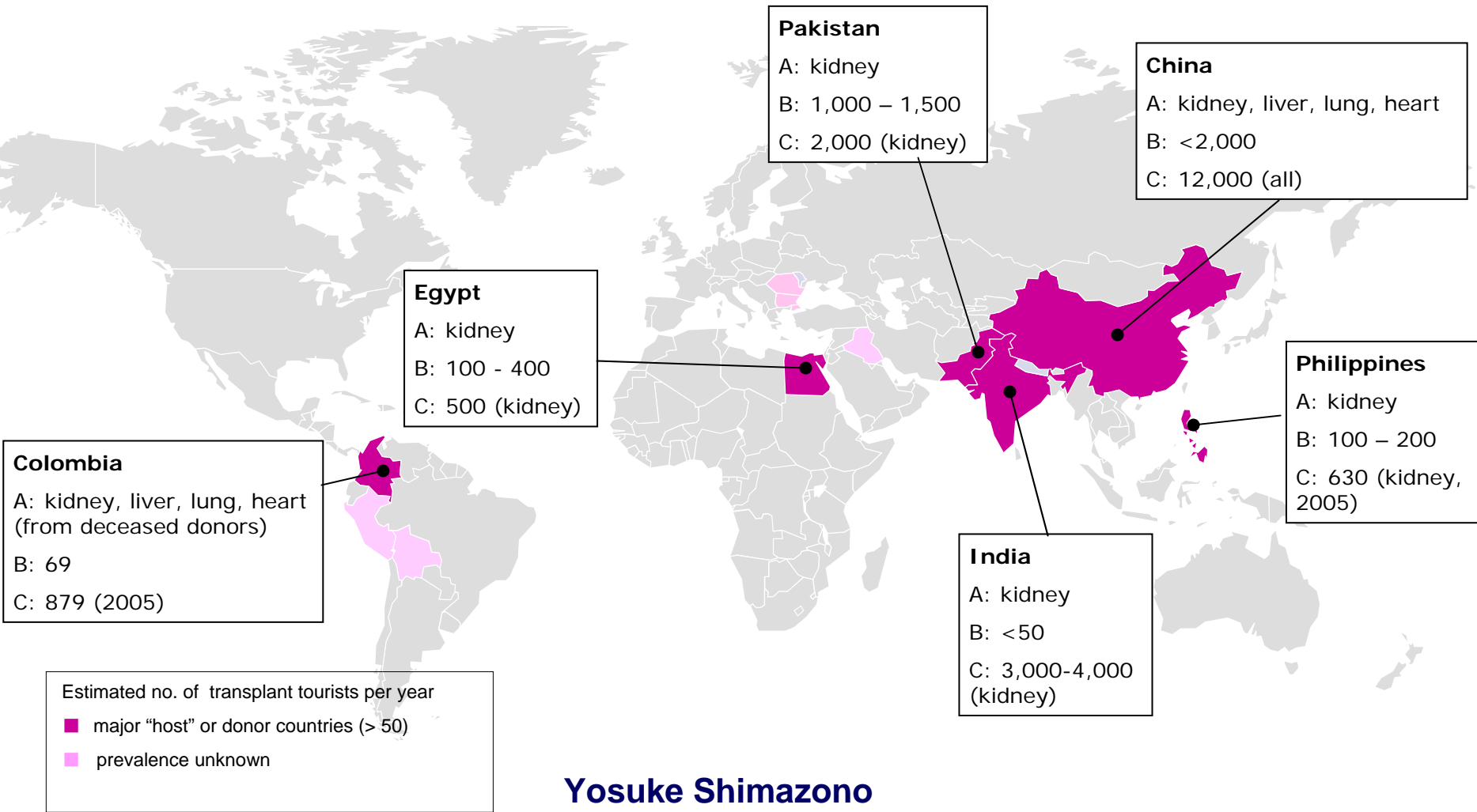
Global Data Base on Blood Safety 2001-2002

■ 100% testing    ■ Less than 100% testing



# "Transplant Tourism", Major Destinations: "host" countries (2005/6)

**Countries**  
 A: type of organ  
 B: estimated no. of transplant tourists  
 C: estimated no. of transplantations



**Yosuke Shimazono**  
 2nd WHO Global Consultation on Human Transplantation,  
 Geneva, 28-30 March 2007

# Commercial Renal Transplantation, Harm to Recipients

## Outcomes of Commercial Renal Transplantation: A Canadian Experience

G.V. Ramesh Prasad,<sup>1,2</sup> Ashutosh Shukla,<sup>1</sup> Michael Huang,<sup>2</sup> R. John D'A Honey,<sup>2,3</sup>  
and Jeffrey S. Zaltzman<sup>1,2,4</sup>

**Background.** Financial compensation in exchange for live kidney donation is prohibited in Canada. However, patients in Canada with end-stage renal disease and without a suitable biologically or emotionally related live donor face substantial waiting times on lists for deceased donor kidneys, and so may therefore choose to acquire organs from a live donor in a procedure performed outside Canada as part of a commercial transaction.

**Methods.** We describe the clinical outcomes in such patients transplanted between 1998 and 2005, managed after their surgery at a single Canadian transplant center.

**Results.** Patient and graft survival at three years were significantly worse in this group compared to recipients of live biologically related ( $P < 0.0001$ ) and emotionally related transplants ( $P < 0.01$ ) performed in Canada during this period. A number of different surgical and infectious complications were seen, requiring frequent and often lengthy hospitalization.

**Conclusion.** Patients considering this method of acquiring live-donated kidneys should be counseled of the inherent risks and possible adverse outcomes including diminished dialysis-free survival.

**Keywords:** Commercial renal transplantation, Live donor, Graft survival, Patient survival.

(*Transplantation* 2006;82: 1130–1135)



# Consequences of Selling a Kidney: Similar for Poor People in all Regions

Loss of health and income,  
stigmatization,

- Brazil
  - Egypt
  - India
  - Moldova
  - Pakistan
  - Philippines
  - South Africa
- ...etc.

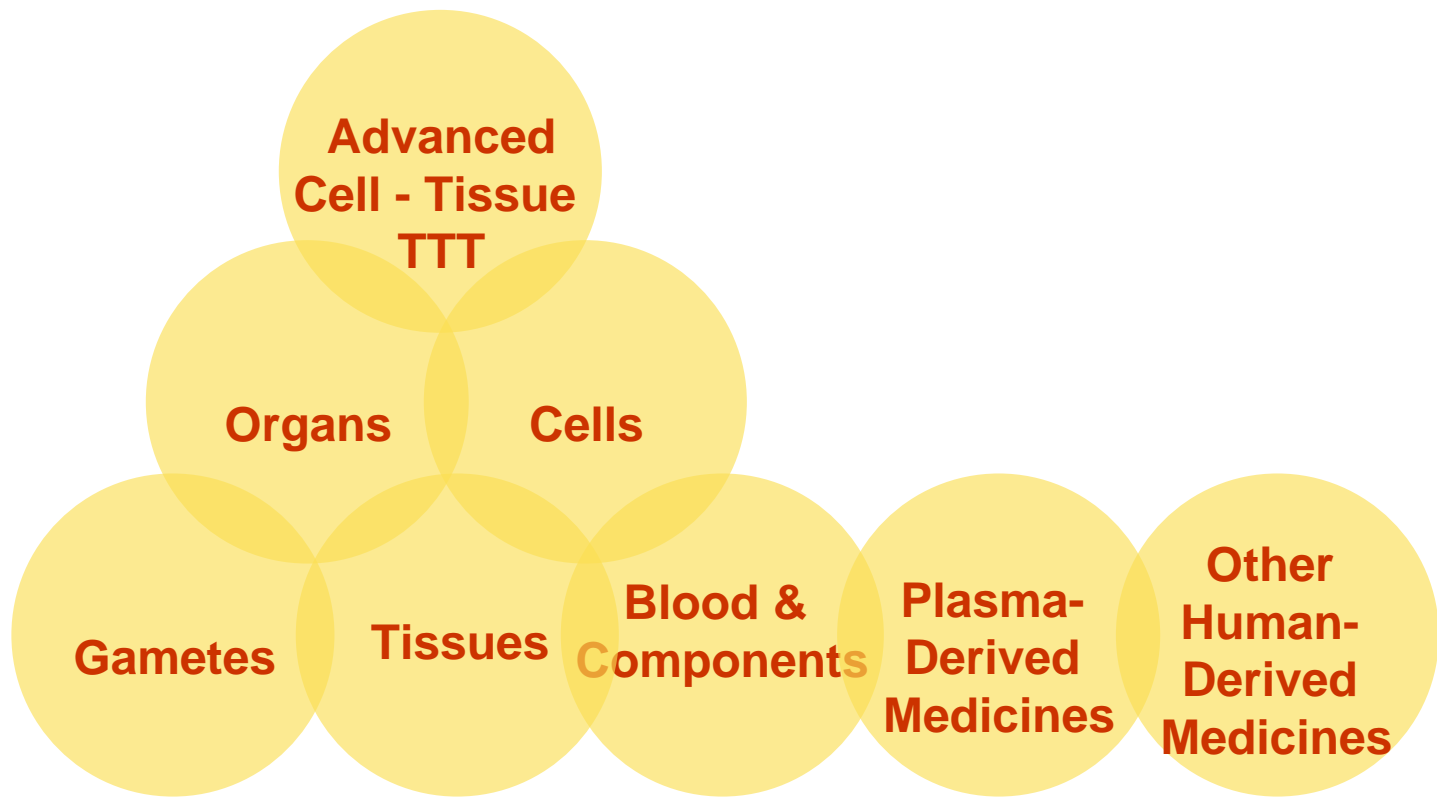






# Areas of Commonality with Blood Products, Cord, Progenitor, Bone Marrow, Tissue and Organ

# Health Products Of Human Origin (HPOHO)

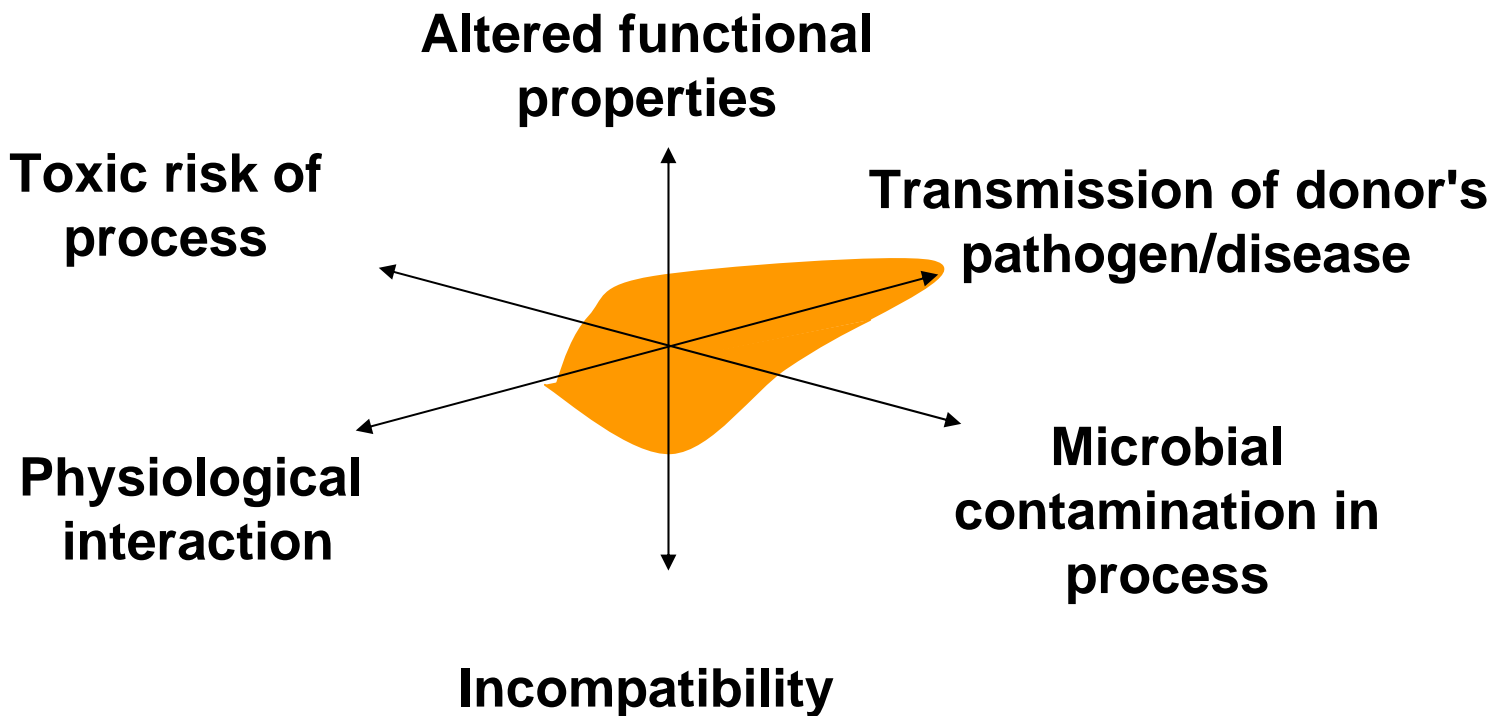


# Human Origin: Ethical Issues

- Need for consistency between HPOHO and around the world
- Sale and purchase, availability of the human body, the person as a means rather than an end
  - Safety of the Live Donor
- Consent and protection of the vulnerable
- Equitable allocation
- Public trust and preparedness to give as much as to receive

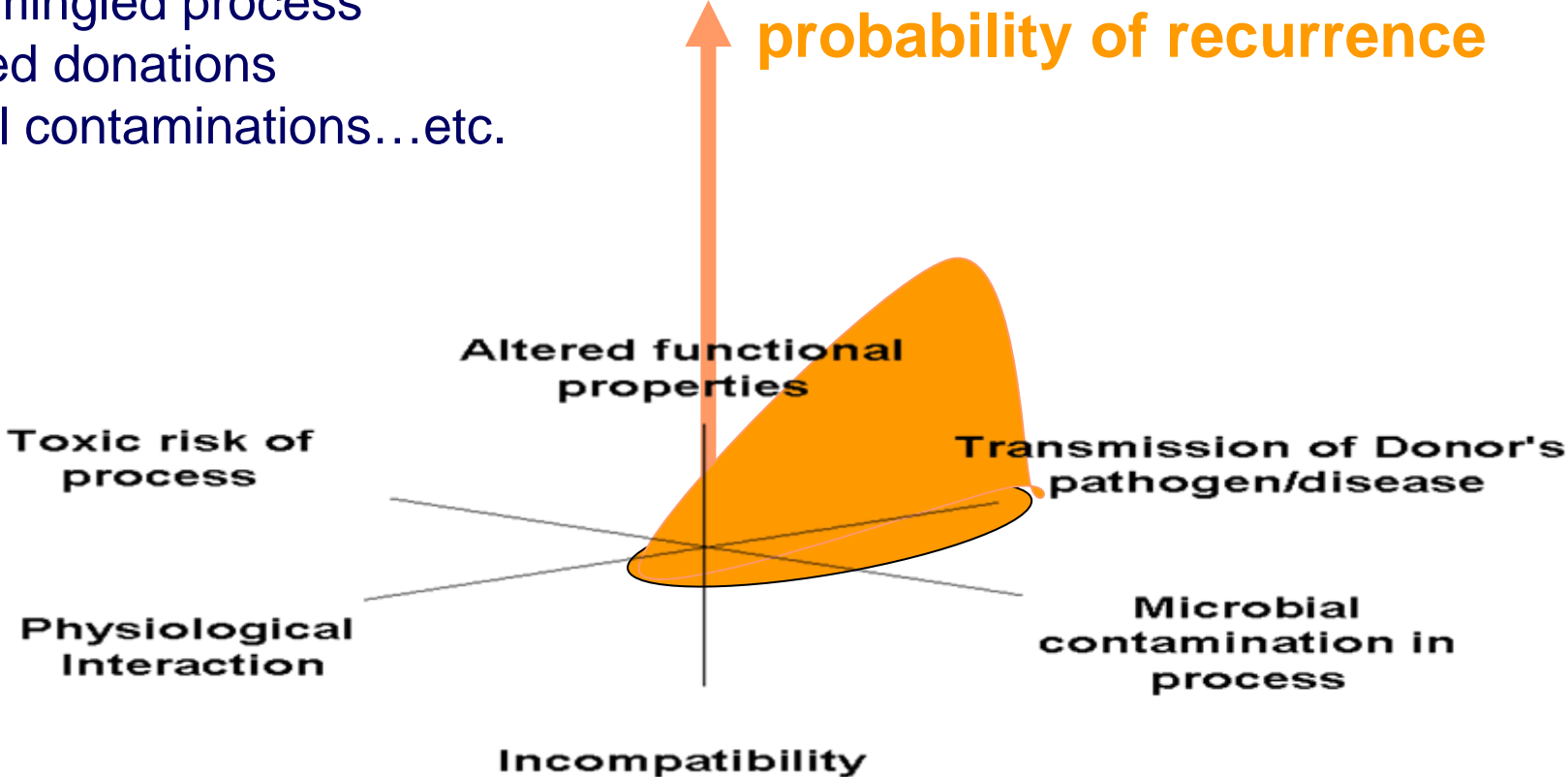


# Variety of Shared Safety Risks of HPOHOs



# Recurrence of Safety Risk of HPOHOs

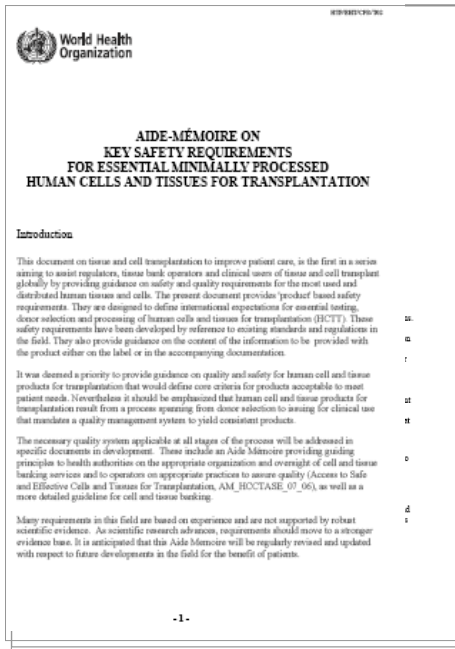
- Multiple HPOHOs from same donor
- Commingled process
- Pooled donations
- Serial contaminations...etc.



# Key Safety Requirements for Essential Minimally Processed Human Cells and Tissues for Transplantation

The shortlist of products for which specifications have been drafted is as follows:

- Frozen Bone and Tendon
- Freeze-dried Bone
- Human Skin
- Human Amniotic Membrane
- Cryopreserved Cardiac Valve
- Human Cornea
- Fresh Haematopoietic Stem Cells (unrelated, bone marrow and peripheral blood stem cells)
- Cryopreserved Cord Blood Stem Cells (unrelated)



[http://www.who.int/transplantation/cell\\_tissue/en/](http://www.who.int/transplantation/cell_tissue/en/)

# Access to Safe and Effective Cells and Tissues for Transplantation

Cell and tissue transplantation carries the risk of disease transmission. Viruses (including HIV, hepatitis B and C), bacteria, fungi, parasites and prion agents have been transmitted to tissue and cell recipients causing disease.



**World Health Organization**

**AIDE-MEMOIRE**  
*for National Health Authorities\**

Tissue and cell transplantation represent essential and rapidly developing therapies in modern healthcare. It is the responsibility of national health authorities to ensure that the needs of patients are met with a supply of safe tissues and cells of appropriate and consistent quality. A nationally supported legislative framework which defines consent requirements and organ donation and a regulatory system which addresses tissue and cell banks are prerequisites to achieving this goal. Donation and transplantation activities should be organized in a transparent way with the provision of adequate information and data to enable the public to make informed choices.

Tissue and cell transplantation carry risks of disease transmission. Viruses (including HIV, hepatitis B and C), bacteria, fungi, parasites and prion agents have been transmitted in tissue and cell recipients causing disease. The safety of tissue and cells for transplantation is assured by the careful selection of donors on the basis of their medical and laboratory history, physical examination and by testing of donor blood samples for transmissible agents. Donations should be procured only from non-remunerated donors from low-risk populations. In addition, wherever possible, reduced pathogen-inactivation or removal processes should be applied. Transplantation of tissues and cells should only be carried out when there is no option for a safer, equally effective, alternative therapy.

Any organization engaged in the procurement (including donor identification, consent, donor selection testing and tissue or cell retrieval), processing, storage or distribution of tissues and cells for transplantation should implement a comprehensive quality system. The system should cover all aspects of its activities and ensure traceability from the identification of the donor to the transplantation of the product to a recipient. Management commitment and support are essential for the development, implementation and functioning of a quality system in order to ensure continuous improvement. All staff should be aware of the importance of quality and their role in achieving it consistently.

**Words of advice**

- Ensure that the legislative framework supports tissue and cell donation and transplantation.
- Identify national or international technical reference documents (standards).
- Create a network of all organisations that manufacture donors and/or retrieval, process, store or supply tissues and cells for transplantation.
- Clarify the implementation of safety systems in tissue and cell establishments.
- Designate an authority to control compliance with standards.
- Promote the education of health professionals and the public in relation to tissue and cell donation.
- Publish appropriate and clear information on tissue and cell donation and transplantation to ensure transparency.
- Provide correct use of tissues and cells.

Monitor adverse reactions in patients to allow corrective and preventive action

**Access to Safe and Effective Cells and Tissues for Transplantation**

Checklist

**National Oversight**

- Legislative/regulatory framework
- Appropriate institutional structure
- Inspection and authorization of screening, sorting, retrieval, processing, storage, distribution, repair and repair
- Surveillance and vigilance including transplantation transmitted disease monitoring and reporting of donations, processing, distribution, repair, repair and transplantation activities

**Transparency and Provision**

- Campaigns to promote unremunerated donation
- Education of health care professionals to ensure explanation of the national measures of tissue and cell donation

**Safety**

- Donor selection, consent, care and confidentiality
- Donor screening including for infectious disease markers
- Assurance of contamination and cross-contamination
- Monitoring of transplantation-transmitted infection

**Quality Systems**

- Clear defined organizational structure
- Adequate resources (staff and facilities)
- Quality management system (reference requirements)
- Comprehensive controlled documentation including Standard Operating Procedures (SOPs)
- Complete and accurate records to assure traceability
- Appropriate documented staff training and competency assessment

**Investment**

- Validation or full verification of each process and qualification of equipment
- Internal and external audits
- Error management, corrective and preventive action
- External quality assessment schemes

**Control Use**

- Traceability
- Appropriateness
- Check-out/sign-up of transplant recipients

[http://www.who.int/transplantation/cell\\_tissue/en/](http://www.who.int/transplantation/cell_tissue/en/)



# A New Arenavirus Responsible for the Death of Three Organ Recipients Australia, 22 April 2007

## news release



2007

### RARE VIRUS LINK IN ORGAN TRANSPLANT DEATHS

A newly-identified virus may be responsible for the deaths of three Victorians who received organs from the same donor in December.

Victoria's Acting Chief Health Officer Dr John Carnie said there was no evidence the virus represented a public health risk and its presence in these Victorian recipients is thought to be a world-first occurrence.

"Scientists working on both sides of the world have collaborated to find a likely cause of the deaths and had discovered a previously unknown virus," Dr Carnie said.

"This is a remarkable achievement in a short space of time."

"The discovery of this new virus is of national and international significance. Much more work is needed to fully understand the nature and behaviour of this virus," Dr Carnie said.

"This cutting-edge molecular techniques scientists at the Victorian Infectious Diseases Reference Laboratory (VIDRL) have used to identify the virus."

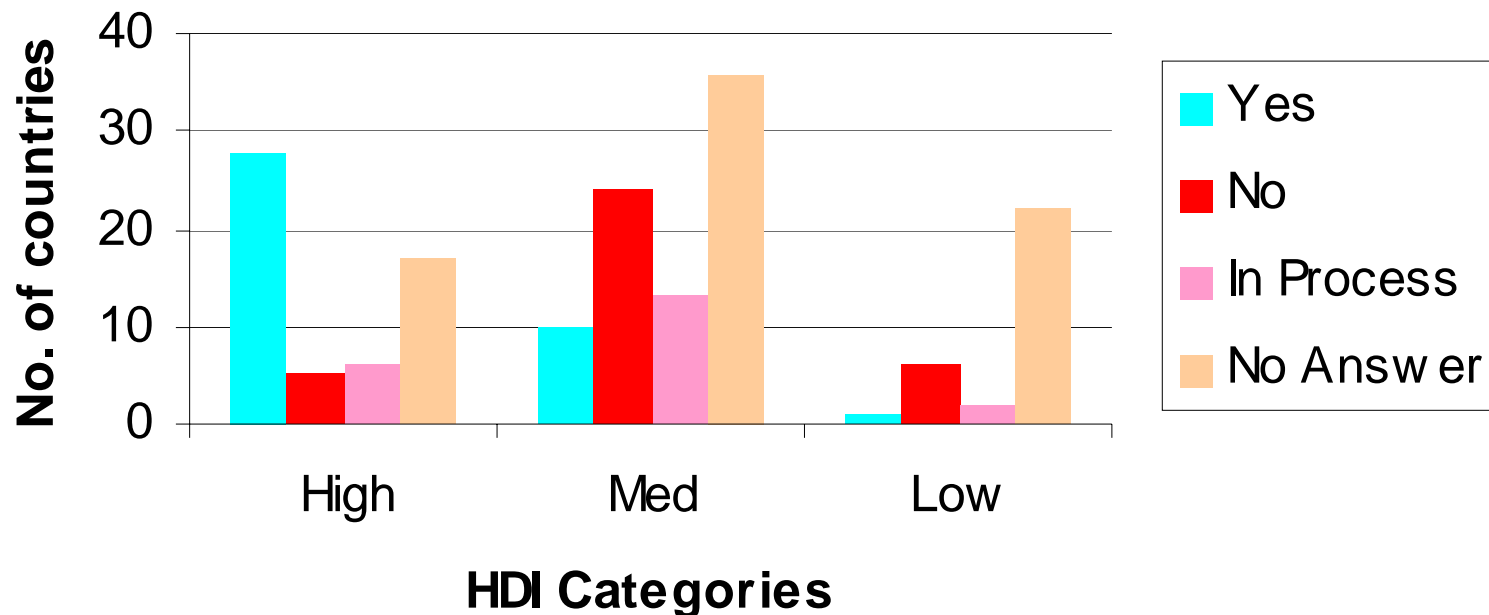




# National Haemovigilance System

Global Data Base on Blood Safety 2004-2005 Preliminary data

## Haemovigilance



# International Collaboration for V&S

- Improves
  - Sensitivity (denominator)
  - Relevancy (international circulation of donors and products)
  - Dissemination (alerts and information)
- A two-way exchange between all types of country
- Engages all stakeholders
  - Health authorities, regulators, public health agencies
  - Operators, health-care staff
  - Scientific and professional societies
- Associates all relevant vigilances
  - Devices, drugs and ancillary products
  - Infectious diseases surveillance

# First Global Consultation on Regulatory Requirements for Human Cells and Tissues for Transplantation Ottawa, December 2004

## Vigilance and surveillance:

- Should be incorporated at an early stage
  - Human origin - Risk of transmissible agents - Susceptibility to microbial contamination - Limited experience in clinical trials of processing methods or clinical use
- Not only adverse event reporting, but should include active and comprehensive surveillance
- Opportunity for valuable collaboration of clinicians, operators, regulators and policy makers
- Requires international collaboration

# Second Global Consultation on Regulatory Requirements for Human Cells and Tissues for Transplantation

Geneva, June 2006

## Vigilance and surveillance:

- Many countries are in the process of developing systems for vigilance and surveillance
- There needs to be a global aspect to vigilance to ensure that risks and events are communicated and acted on appropriately
- Tools for inter-communicability between national/regional programmes are required. WHO's GKT will evolve to provide a global source of information on risk
- There was recognition of the pioneering value of the participation of WHO in the EUSTITE project and regulatory approaches and systems for vigilance and surveillance generally

# European Directive 2004/23/EC



**Directive 2004/23/EC of the European Parliament and of the Council** on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells

Preamble

*" As tissue and cell therapy is a field in which an intensive worldwide exchange is taking place, it is desirable to have worldwide standards."*

**Commission Directive 2006/86/EC**

adverse events and reaction reporting, traceability and coding system

# The EUSTITE Project



## European Union Standards and Training in the Inspection of Tissue Establishments



- 12 partners
- €2.5 M (co-funding)
- December 2006 - November 2009
- Inspection + adverse events and reactions reporting
- Website: [www.eustite.org](http://www.eustite.org)

# The EUSTITE Consortium

## Competent Authorities for Inspection

### Gametes and Embryos - Tissues and Cells



- **Centro Nazionale e Trapianti - Italy (co-ordination)**
- **Irish Medicines Board Inspectorate Department**
- **Federal Ministry of Health and Women/Unit III/A/4, Austria**
- **National Transplant Organisation (ONT), Spain**
- **Agence de la Biomédecine, France**
- **AFSSAPS, France**
- **University Hospital in Bratislava, Slovakia**
- **National Centre for Tissue and Cell Banking, Poland**
- **Human Fertilisation and Embryology Authority, UK**
- **Bulgarian Executive Agency for Transplantation** →
- **Danish Medicines Agency**
- **WHO Essential Health Technologies - Clinical Procedures**

# EUSTITE Vigilance and Surveillance EU and **Global** V&S Medical Advisory Committee

WHO is the main partner in the development of a model for the reporting and investigating of adverse events and reactions

- Madrid, March 2007

**EU MAC**

**US FDA, CDC  
Canada HC, PHAC**

- Rome, July 2007

**+ Non-EU participants**

**EU MAC**

**Global V&S MAC**

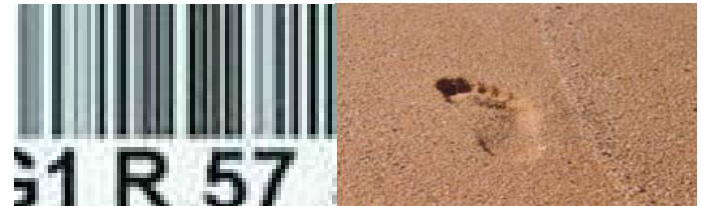


# Second Global Consultation on Regulatory Requirements for Human Cells and Tissues for Transplantation

Geneva, June 2006

## Coding Systems

- Indisputable need for globally standardized labelling (coding and description) for tissues
- Opportunity to work in a harmonized way before individual countries or regions develop disparate systems
- WHO could play a leading role in this
- Very positive milestone: the commitment to one global coding system for cellular therapy products by relevant scientific and professional societies at global level



# Second Global Consultation on Critical issues in Human Transplantation: Towards a Common Attitude to Transplantation

Geneva, 28-30 March, 2007

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## KEY POINTS

- Quality and safety are key issues of human CTO transplantation, since risks are real. Surveillance should be put in place, based on traceability (maintaining confidentiality) and codification, two critical prior steps
- Strong recommendation to WHO to lead global traceability by producing an “International Shared Coding System” for organs, tissues and cells

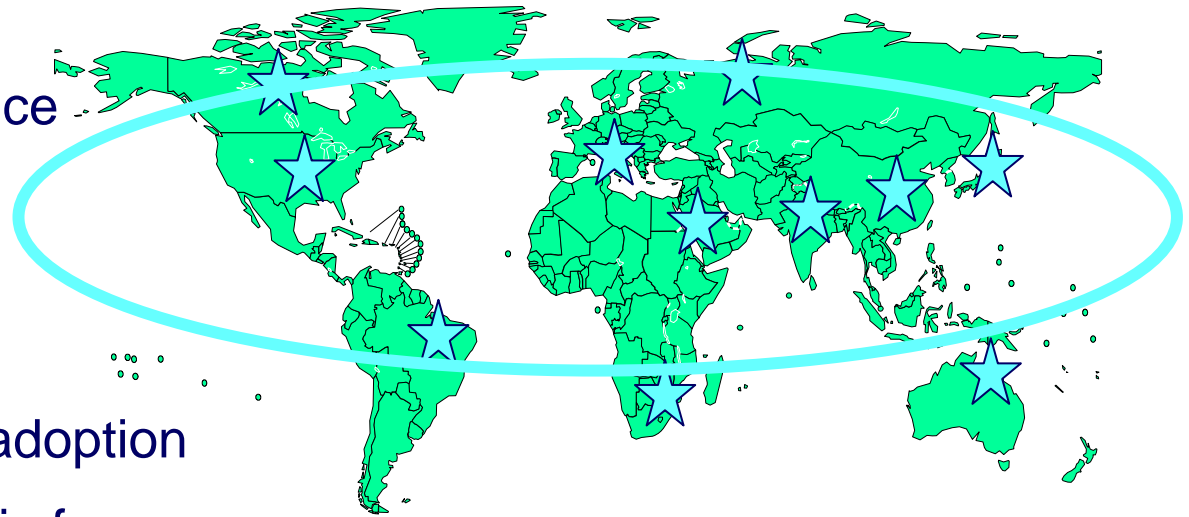
# *Draft* **Guiding Principle 10**

Quality of care, safety and efficacy of procedures are mandatory for donor and recipient alike. The long-term outcomes of cell, tissue and organ donation and transplantation should be assessed for both the donor and the recipient in order to document the benefit and harm for recipients and any harm to living donors.

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

# Proposed Resolution for WHO Executive Board January 2008

- To encourage the creation of a global network of collaborating centres on Vigilance and Surveillance for CTO transplantation



- WHO to facilitate the adoption of a common global basis for coding systems for CTO for transplantation

# Thank You

For more information

Contact:

Dr Luc Noël

Coordinator

Clinical Procedures (HTP/EHT/CPR)

World Health Organization

Tel: +41 22 791 3681

Fax:+41 22 791 4836

[noell@who.int](mailto:noell@who.int)

<http://www.who.int/transplantation>

