

# Tissue vigilance in The Netherlands

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*Tulipa TRIP*

- Legislation
- Dutch situation, TRIP
- Tissue vigilance system
- Findings 2006-2010
- Where next

# Legislation

European Directive 2004/23/EC

“Daughter” Directives 2006/17/EC, 2006/86/EC

## Objective

This Directive lays down standards of **quality and safety for human tissues and cells** intended for human applications, in order to ensure a high level of protection of human health.

Implemented in national legislation (2006)

Licensing of tissue establishments

Traceability; reporting of Serious Adverse Reactions and Events (SARE)



# Scope

- This Directive shall apply to the **donation, procurement, testing, processing, preservation, storage and distribution** of human tissues and cells intended for human applications and of manufactured products derived from human tissues and cells intended for human applications.

....including haematopoietic peripheral blood, umbilical-cord (blood) and bone-marrow stem cells, reproductive cells (eggs, sperm), foetal tissues and cells and adult and embryonic stem cells

\* Cells and tissues that are applied to the human body in **clinical trials** should comply

\* Tissues and cells intended to be used **for industrially manufactured products, including medical devices** ...

as far as donation, procurement and testing are concerned

\* The Directive does not include tissues and cells used as an autologous graft within one and the same procedure.



# Tissues and Cells

**Post-mortem donors**  
(Donor register)

**Living donors (incl. autologous)**

Bone, hematopoietic stem cells, cardiac valves, reproductive cells, cartilage, etc.

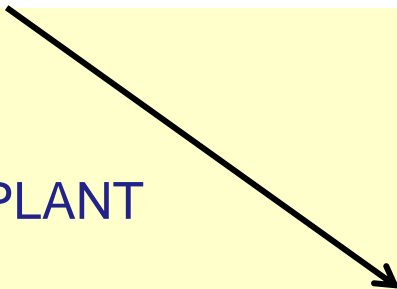
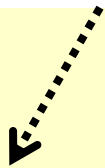
NETHERLANDS TRANSPLANTATION FOUNDATION

EUROTRANSPLANT  
(organs)

**Europdonor**  
(unrelated donor registry  
for hematopoietic stem  
cells)

**Tissue Establishments**  
(independent / within hospitals)

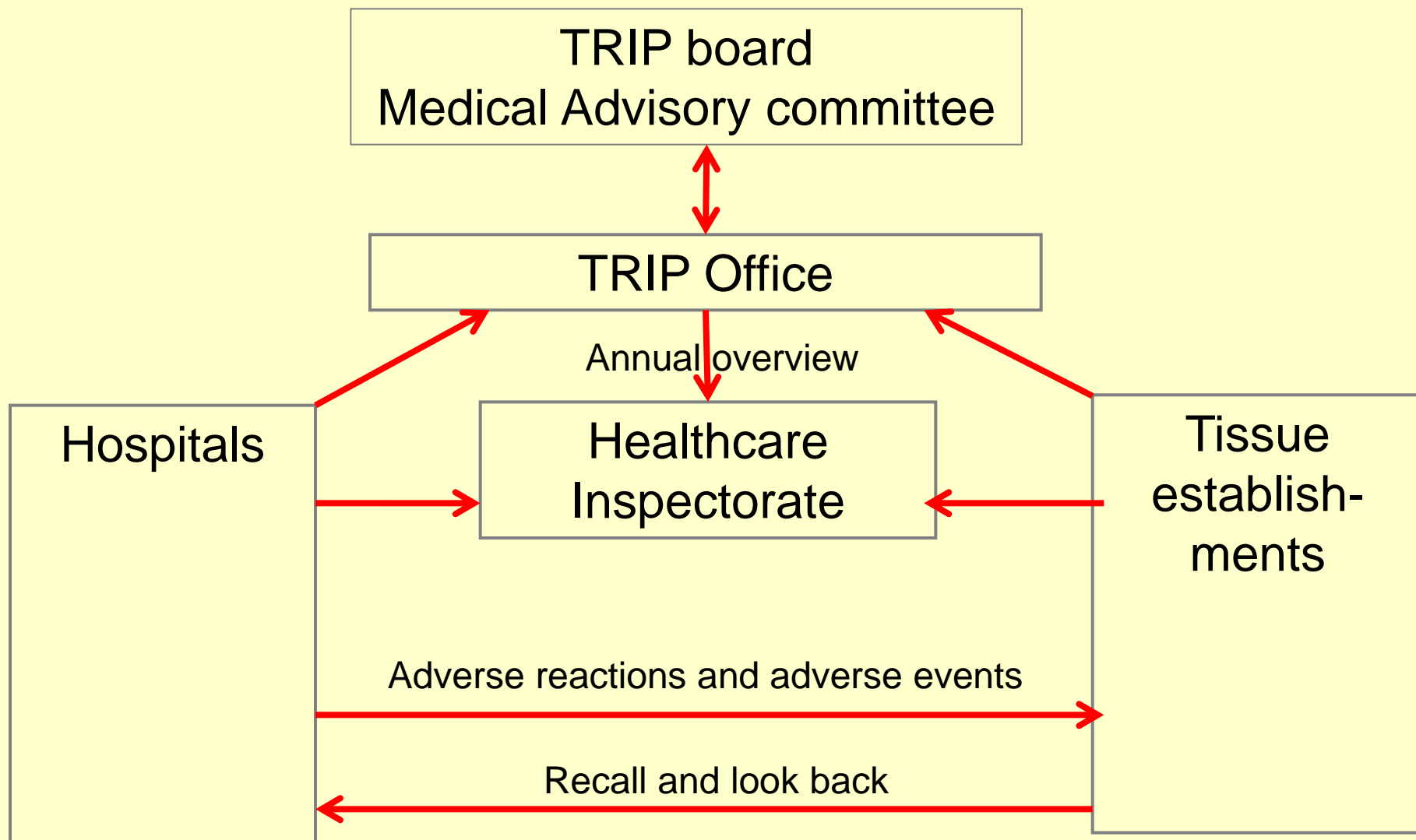
Hospitals and clinics



## **Dutch National Hemovigilance Office**

- Registry for reports on adverse reactions and incidents associated with transfusion of labile blood products.
- Analysis, public report, recommendations
- Annual overview of serious adverse reactions and incidents (SARE) for the Competent Authority
- **Since 2006: reporting system for (serious) adverse reactions and events **which may be related to quality or safety** of human tissues or cells**

# Tissue vigilance reporting





# Annual meeting





# Voluntary or mandatory?

Senior inspector at tissue vigilance symposium (2009):

“Report everything to TRIP, report the very serious events to the Inspectorate”

## Minister of Health

- Legislation
- Financing arrangements

## Healthcare Inspectorate (=acting for Competent Authority)


- Inspections of TE
- Oversight of product safety
- Oversight of care quality (separate department)

## TRIP

- Comprehensive system shaped with professionals
- Prepares annual overview for CA
- European reporting
- Public report

## Melding van een bijwerking (nieuw)

[Terug naar het overzichtsscher](#)

\*) verplicht veld, klik op  voor toelichting over de in te vullen gegevens. [Print het volledige helpscher](#)

### 1. Instellingsgegevens

Instellingscode

Instellingsdatum melding \*

Instellingsnummer

### 2. Betrokken persoon

Patiënt / donor \*

Geslacht \*

Geboortedatum

### 3. Behandeling- / transplantatiegegevens

Datum

Tijdstip

Transplantatie indicatie/ procedure

Datum constatering bijwerking \*

Tijdstip constatering bijwerking

### 4. Productgegevens

Productnummer

Bron materiaal

Soort cellen / weefsel

Beschrijving type materiaal

Toegepaste bewerking / bewaarcondities

Imputabiliteit

Toelichting / genomen  
acties / eventuele  
aanbevelingen

## 7. TRIP registratie

Datum voorlopige  
melding

Melding is tevens

melding ernstige bijwerking of voorval aan IGZ 

Bijwerking is  
gemeld aan  
producent

melding ernstige bijwerking of voorval aan IGZ  
calamiteitmelding aan IGZ

Onderstaande grijze velden worden door bureau TRIP ingevuld

TRIP-nummer

TRIP-datum

Registratiejaar (yyyy)

Vragen van TRIP  
over deze melding  
bij retourneren

Uw toelichting op  
deze melding /  
reactie op vragen  
van TRIP

Ernstige bijwerking

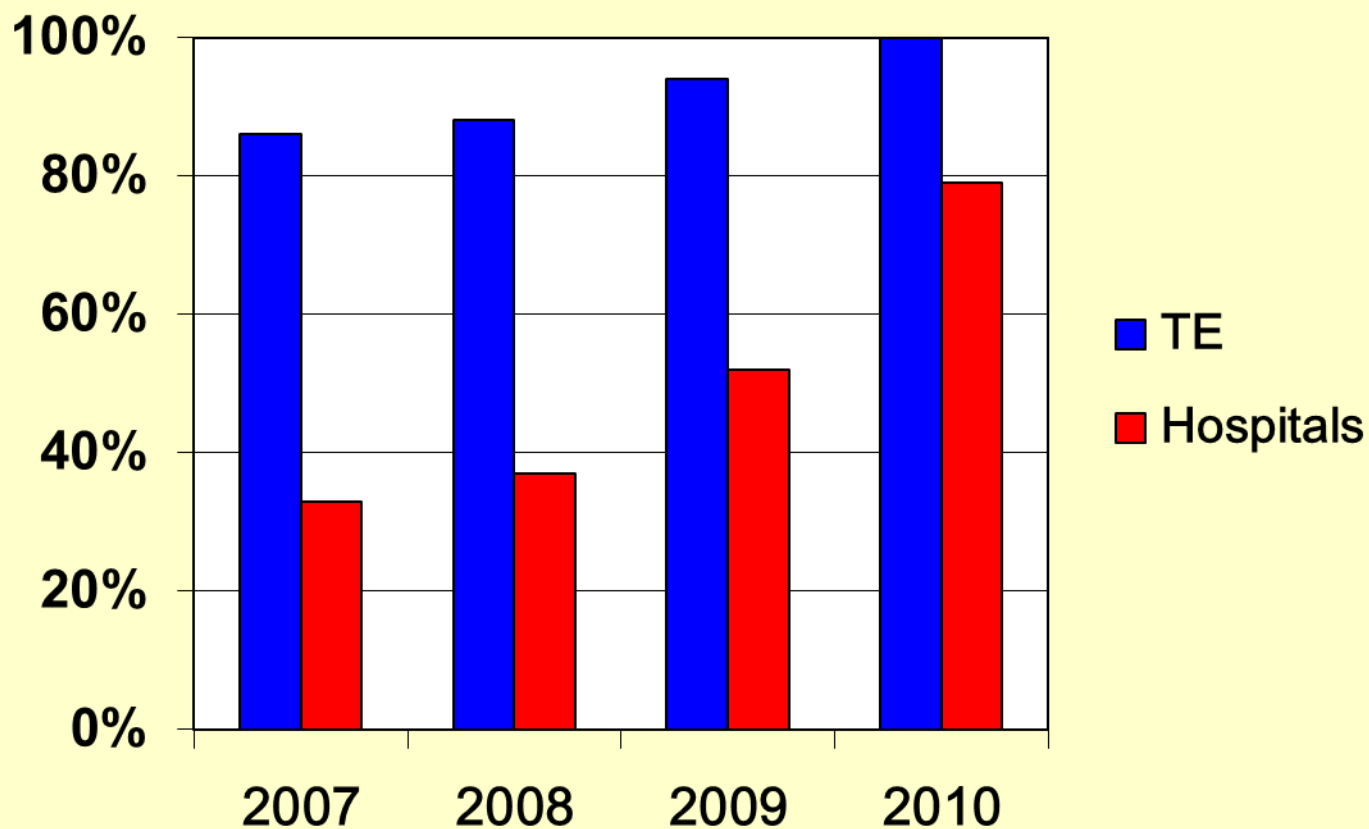
Paraaf TRIP  
medewerker

## 8. Afhandeling melding

Paraaf weefselvigilantie-  
medewerker

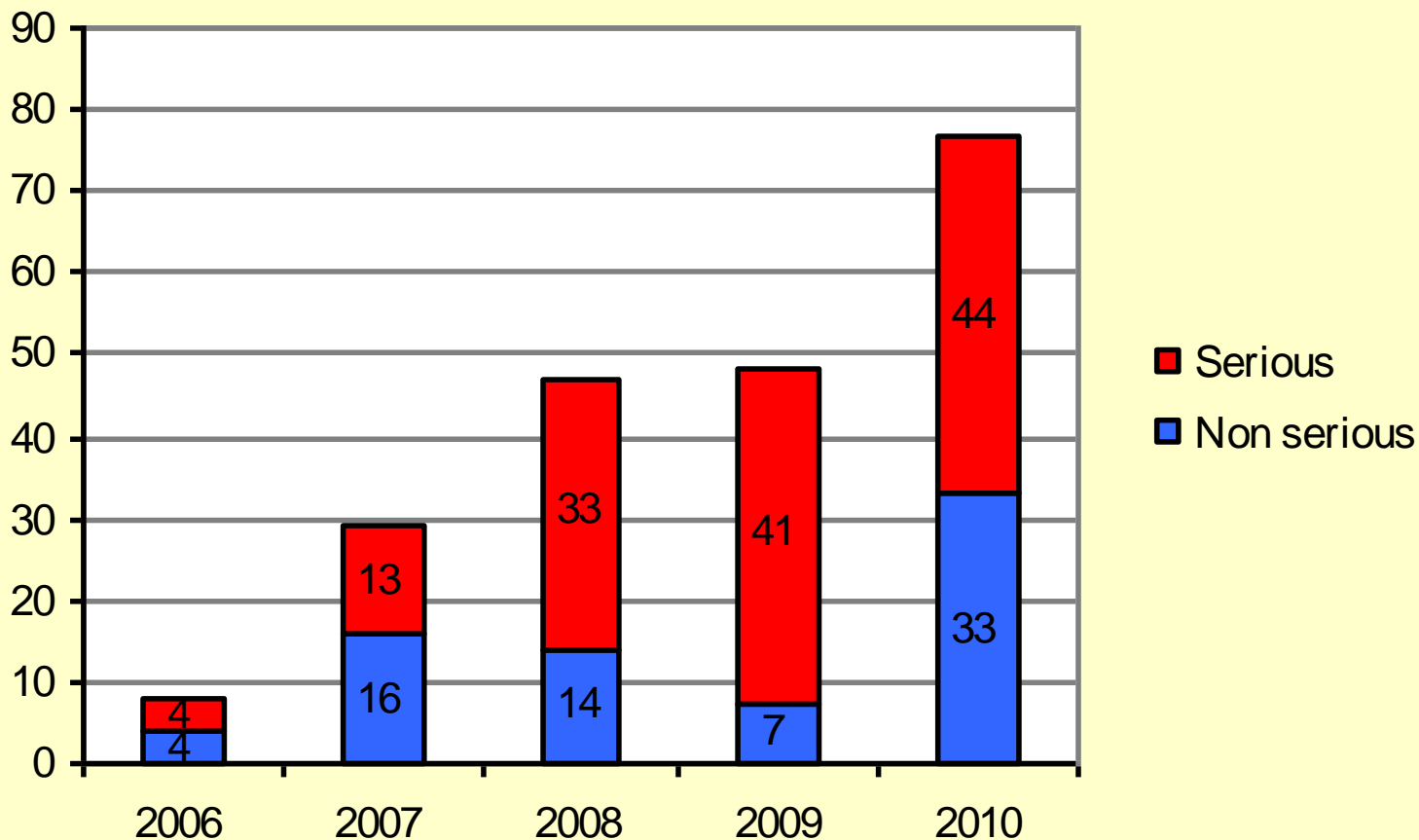
(optioneel)

## Participation

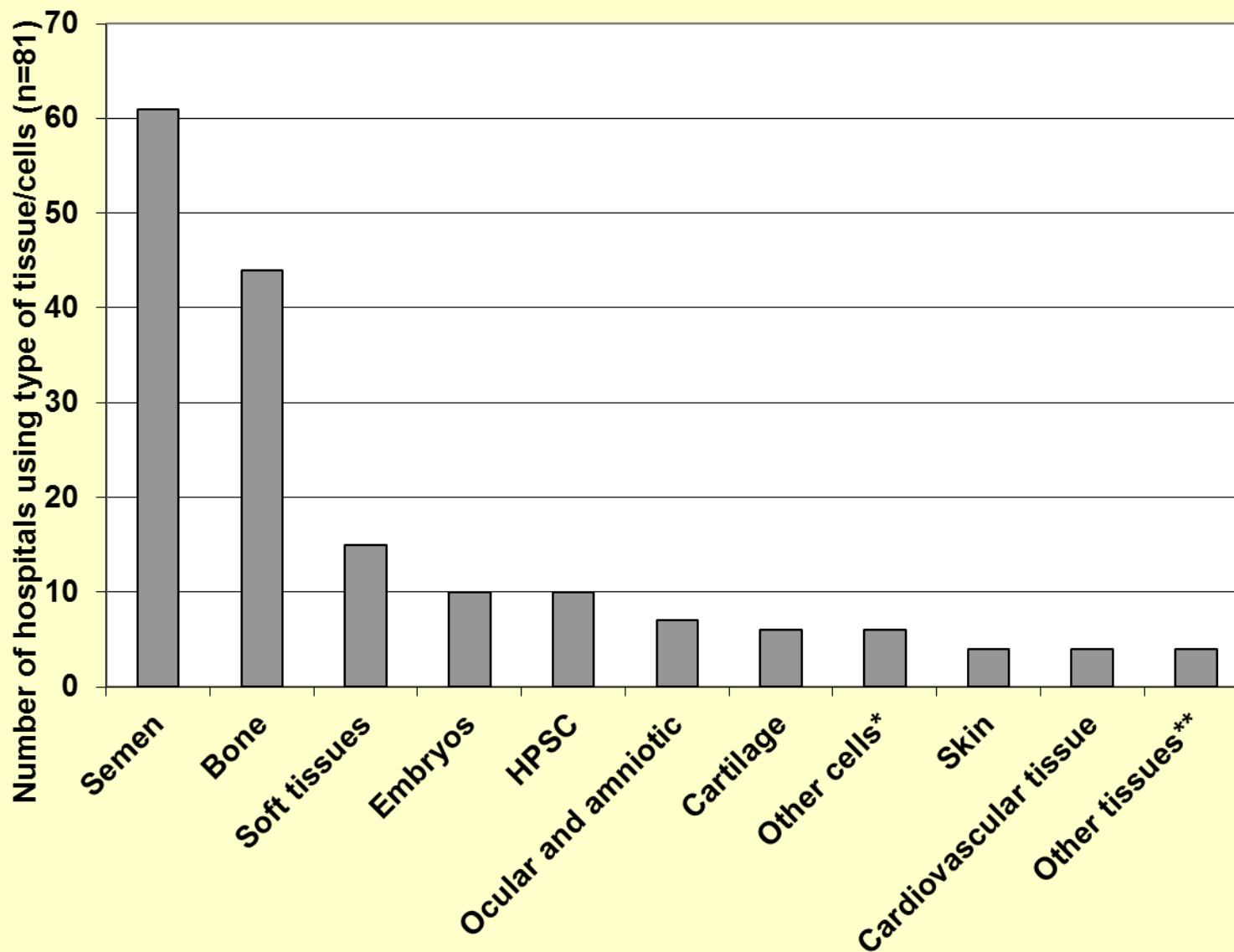


Participation = reported or nil to report statement +  
data on units processed/distributed/applied

# Number of reports of adverse events and reactions



# Extent of use





# Extent of use (2010): difficult to obtain hospital data

Type	Hospital and clinics*		Independent tissue establishment**		Transplanted***	Recipients****
	Processed / distributed		Processed/ distributed			
<b>Hematopoietic stem cells ( autologous)</b>						
Bone marrow	88	51			75	57
Peripheral blood stem cells	1829	1522	812	642	1536	438
Cord blood			24494	7		
<b>Other cells</b>						
Mesenchymal stem cells	39	43			88	40
Lymphocytes	150	92		3	100	67
Dendritic cells	26	26			54	28
<b>Reproductive cells</b>						
Semen (donor)	11360	6663			6456	1698
Semen (partner)	37771	25643			22029	8851
Oocytes	106059	34				
Embryos	30447	23540			21295	11576
<b>Other tissues</b>						
Testicular tissue	401				104	78
Ovarian tissue	149	198			-	-
Langerhans' islets	41	-			6	4
Umbilical cord tissue		6	11115			
Adipose tissue			24			

\* Data submitted by 63 hospitals and clinics (62%), internal distribution by hospitals/clinics with licence for tissue establishment

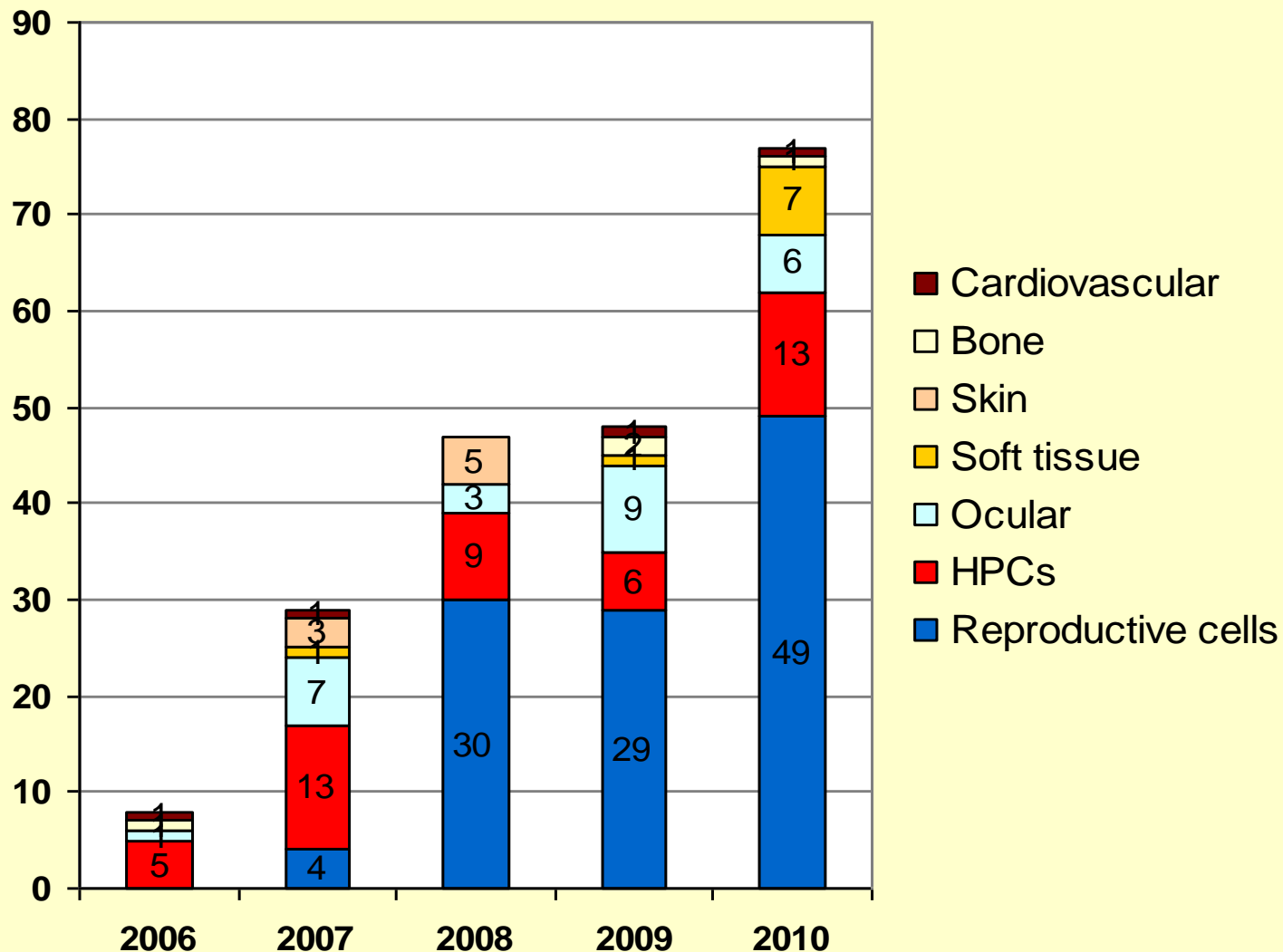
\*\* Data submitted by 19 independent tissue establishments/tissue banks(100%)

\*\*\* Data submitted by 81 out of 102 hospitals/clinics (79%)

\*\*\*\* Data submitted by 72 out of 102 hospitals/clinics (71%)

# Reports 2006-2010

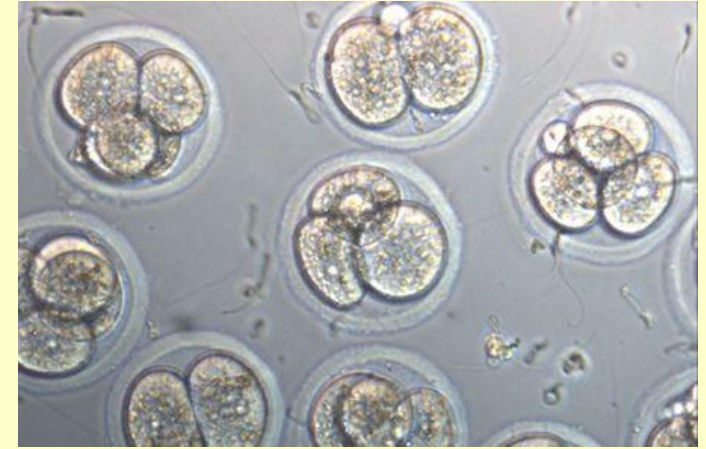
# Reports per type of tissues and cells



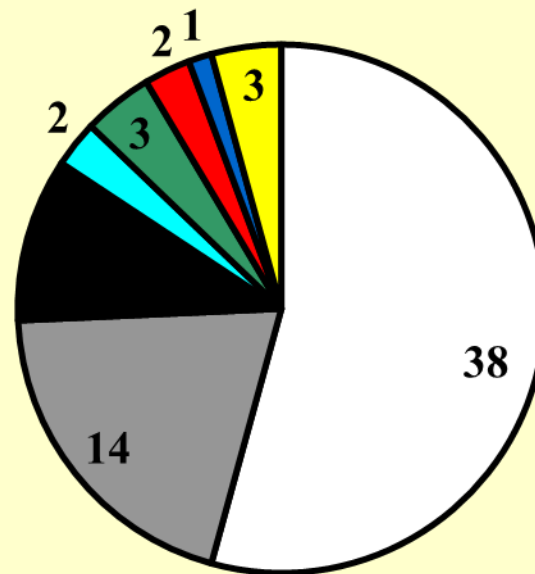
# Reproductive cells

## Sperm, ova and embryos

- 110 adverse events
- 2 reactions (EUG, allergic reaction)



- 6 'near miss' events
- 1 viral contamination
- 3 bacterial contamination
- 4 genetic abnormality
- 70 loss of cells or tissue(s)
- 23 other incidents
- 3 mix-ups



- Processing
- Technical
- Identification
- Communication
- Administrative
- Storage
- Product
- Other

Nature of "loss of cells or tissue"

## Femoral head, cranial bone

- 4 adverse events
- 1 bacterial transmission (M. tuberculosis)
- 1 traceability failure
- 1 loss of tissue, due to lack of identification
- 1 bacterial contamination



Picture: Sanquin Bone Bank

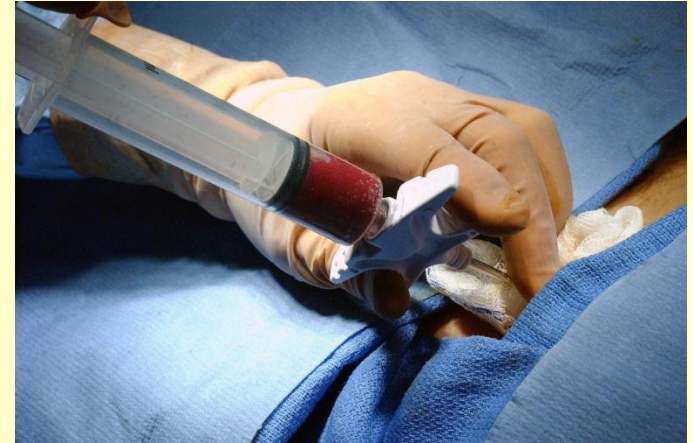


Picture W. Koolwijk, HagaZiekenhuis  
The Hague

# Hematopoietic stem cells

## Bone marrow, cord blood, peripheral blood stem cells

- 20 adverse events
- 26 reactions
- product incidents (unfit product)
- delayed/non engraftment
- broken bags (loss of product)
- bacterial contamination
- donor complication
- hemolytic reaction
- allergic reaction (incl. anaphylactic)
- TACO and TRALI
- neurologic reaction (5x)
- hypotensive, febrile reactions





# Ocular tissue

## Cornea and sclera

- 24 adverse events
- 2 reactions

2 post Tx bacterial infection

- 7 bacterial contamination
- 10 contra-indication for donation found at autopsy
- 1 contra-indication for donation, malaria risk
- 2 fungal contamination
- 1 possible viral contamination
- 1 incorrect product transplanted (processing error)
- 2 loss of tissue
- 2011: several hospitals noted central haze of cornea following transplantation



Picture: Cornea Bank Amsterdam

# Cardiovascular tissue

## Heart valves

- 4 adverse events
- 2 serious
- 2 patients deceased after Tx (low imputability)
- 2 possible bacterial contamination



Pictures: Heart valve bank Rotterdam

## **Donor skin, autologous skin cells on donor skin, isolated autologous skin cells**

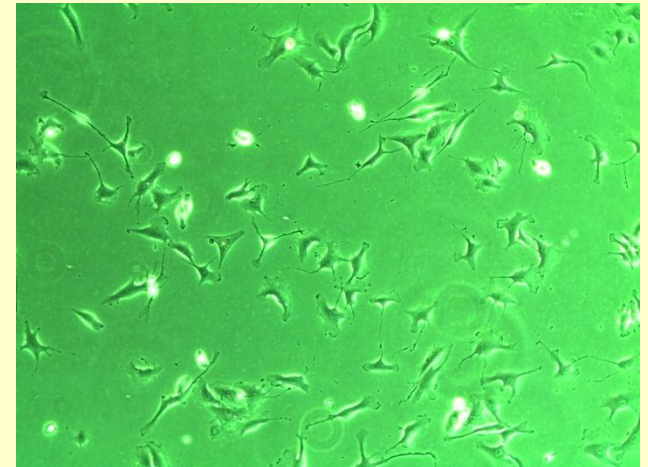
- 1 adverse event
- 7 reactions
- 1 incorrect product transplanted
- 2 allergic reactions
- 3 blood clot problems / thrombosis
- 1 post Tx bacterial infection
- 1 patient deceased, imputability excluded



A-skin

## Autologous cartilage cells

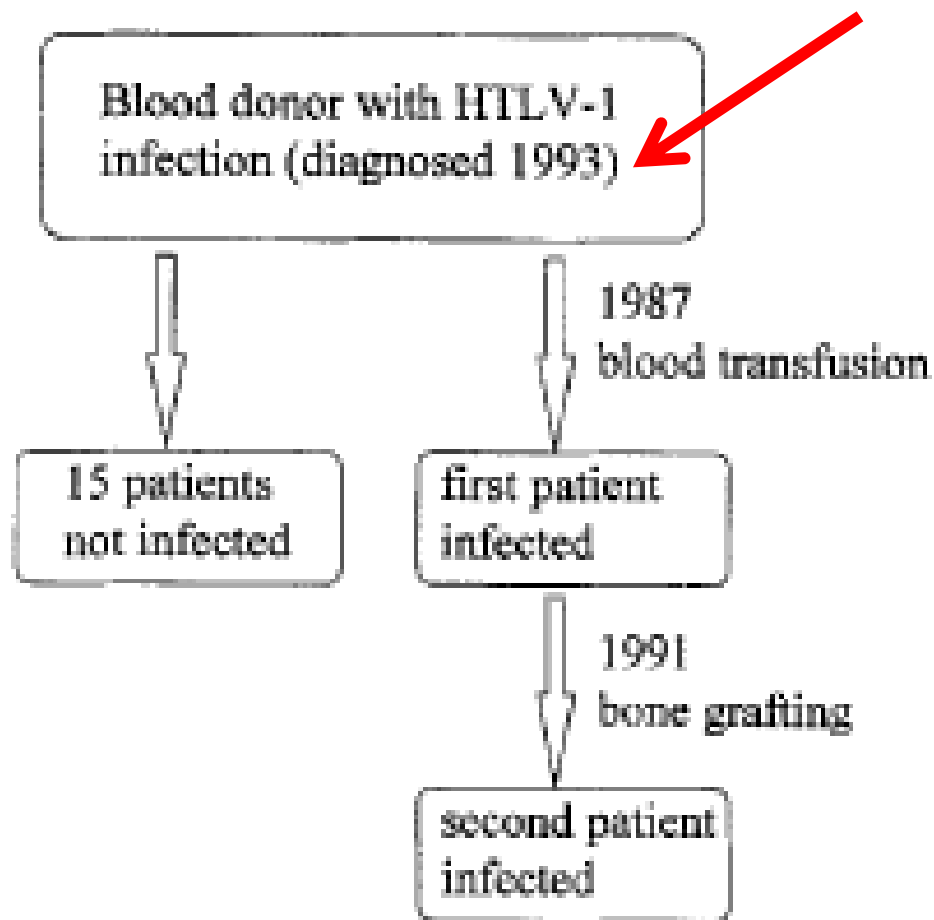
- 9 adverse events
- 2 poor growth of cells
- 1 bacterial contamination
- 3 loss of cells
- 1 mix-up
- 1 technical failure
- 1 non sterile medium



# Tissue vigilance and hemovigilance

- Similarity in (some) types of reports
  - Reactions (relatively few) esp. infection
  - Adverse events
- Tissues
  - shortage/unique product
    - “loss of tissues / cells”
  - Manual techniques
  - Smaller, diffuse terrain; commercial interests
- Crosslinks

# HTLV transmission



Flow chart illustrating the transmission of HTLV-1 virus from a blood donor to a bone graft recipient.

Patient admitted 1m after transfusion: temp, rash, temporary radial nerve palsy.  
*Retrospectively: seroconverted for HTLV*

Recipient: HTLV seropositive (asymptomatic)



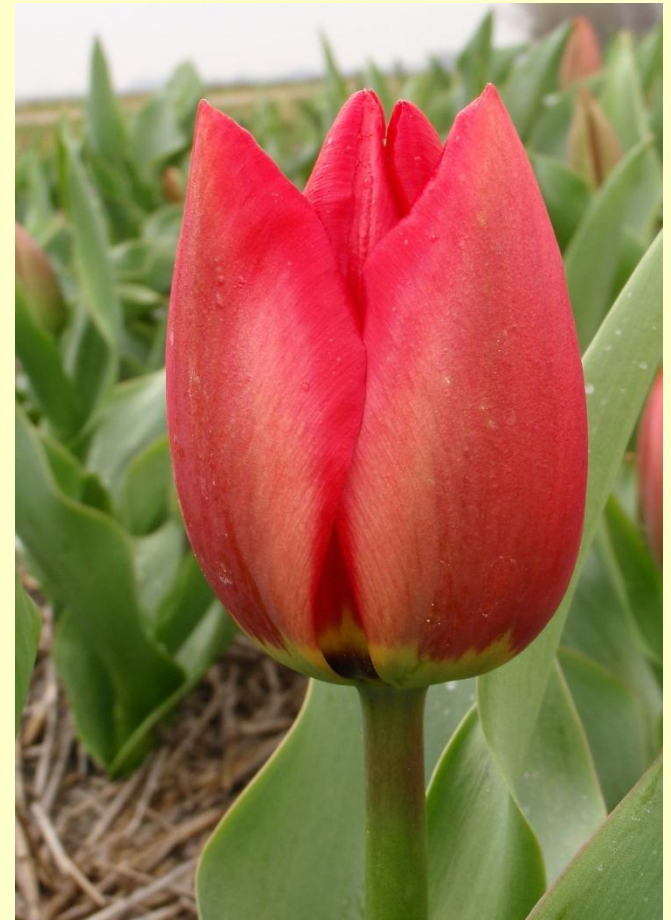
# Where next?

## Strengthening system

- Active promotion among professional groups
- Hospitals, denominators
- (Simple) quality system

Update our statutes

**TRIP** Biovigilance

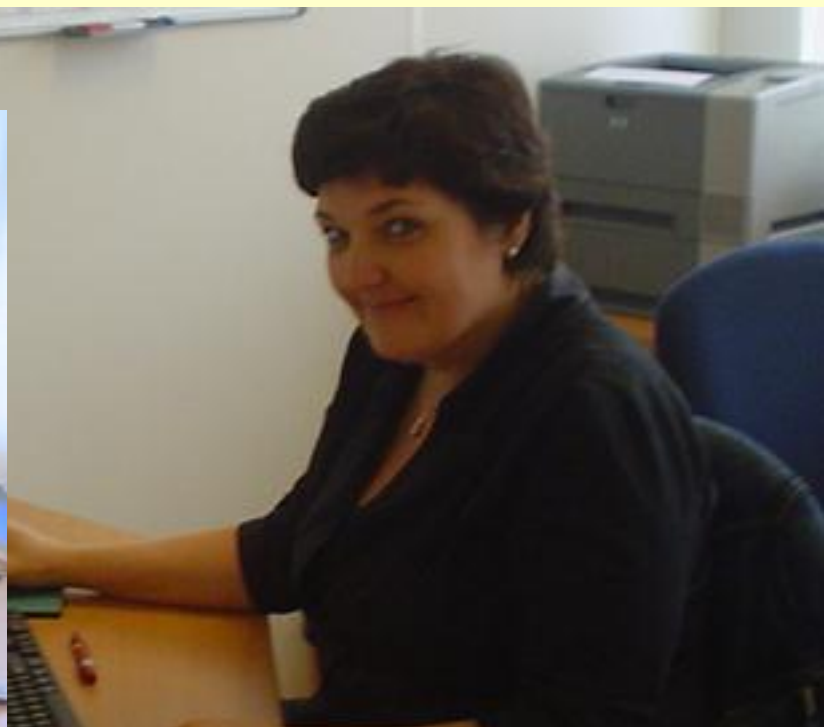


# Where next?

- Linking to **organ** vigilance
- Don't forget the **medical devices**
- International collaboration (ongoing)  
Improve reporting / definitions  
! Need for product identification system
- Yes/no linking to **hemovigilance?**

# Acknowledgements

- **TRIP** colleagues



- **TRIP** contact people