Hemovigilance: Where are we in 2012?

14th IHS

Montréal, Québec: April 25-27, 2012

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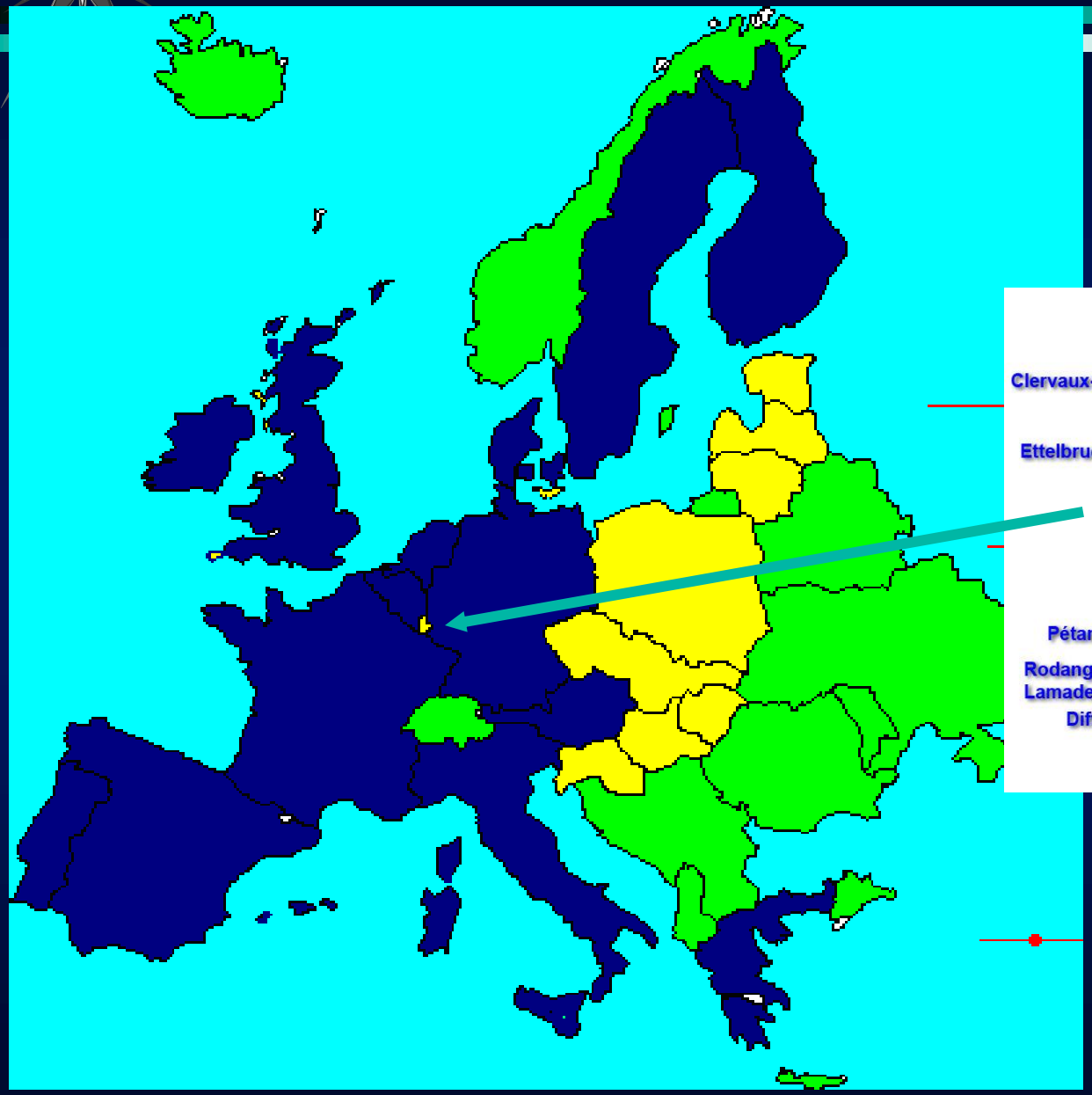
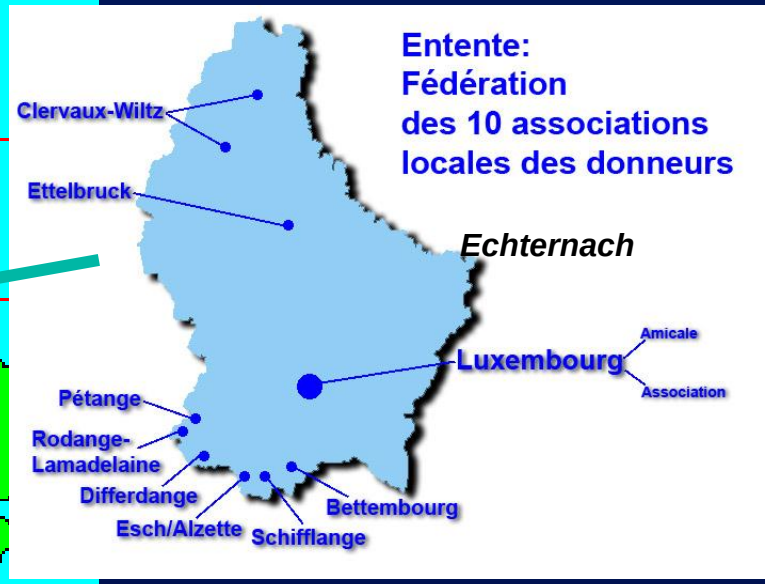
Luxembourg: 490 000 pop., 2 700 km2, 1 BTC -> Red Cross: 30 000 donations / year





Hopping Procession in Echternach in honour of St Willibrord

classified UNESCO Cultural Heritage

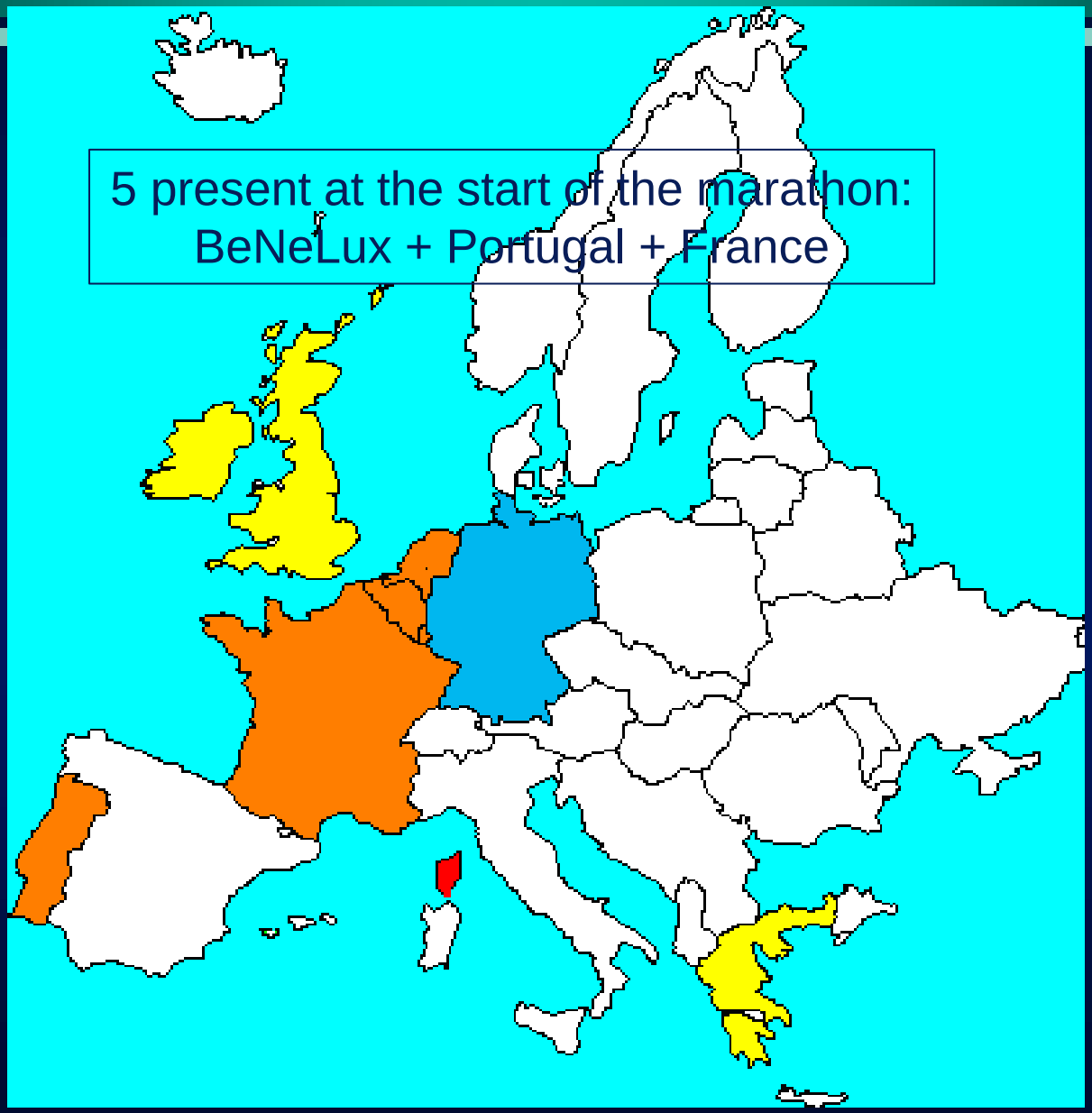
Dance through the streets in Echternach: 3 forwards, 2 backwards

The way to Montreal 2012: 14th IHS, April 2012

1. Bordeaux, FR, Nov. 1997
2. Lyon, FR, Nov. 1999
3. Montpellier, FR, Sep. 2000
4. Athens, GR, Dec. 2001
5. Amsterdam, NL, Feb. 2003
6. Zurich, CH, Feb. 2004
7. London, UK, Feb. 2005
8. Porto, PT, Feb. 2006
9. Dublin, IR, Feb. 2007
10. Frankfurt, DE, Feb. 2008
11. Rome, IT, Feb. 2009
12. Dubrovnik, HZ, Feb. 2010
13. Amsterdam, NL, Feb. 2011

15th IHS
March ?, 2013 in ?

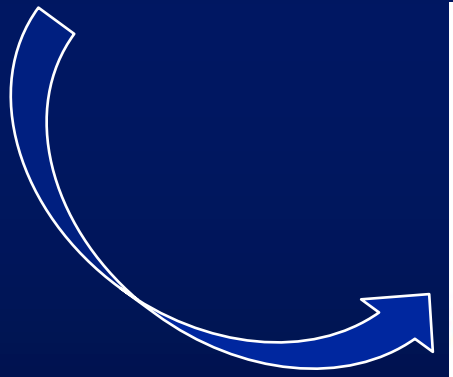
From Regional to European …



… to International

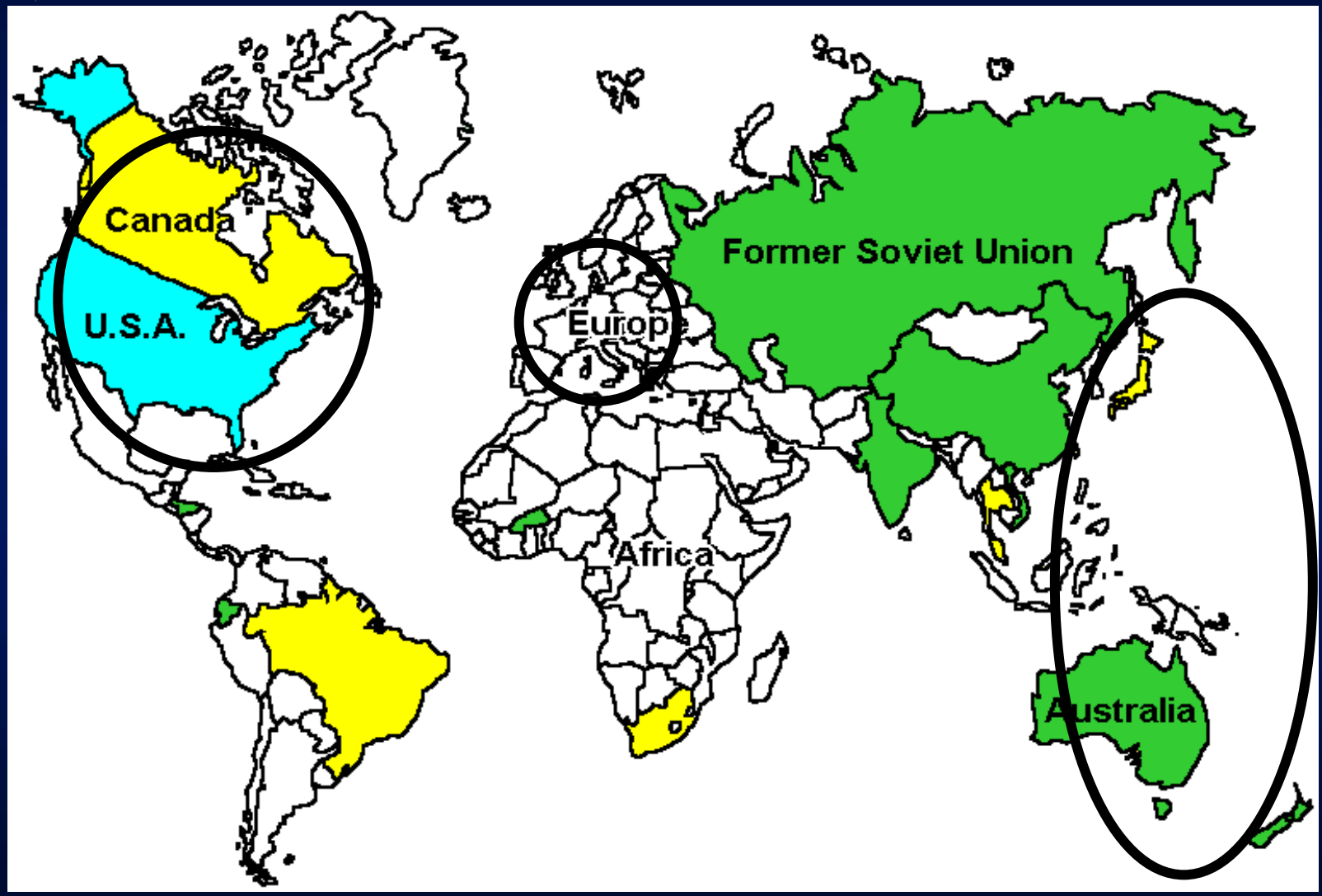
European Haemovigilance Network
WWW.EHN-ORG.NET

	European	Non-European
IHN members	21	7
IHS Participants	>23	>11



INTERNATIONAL HAEMOVIGILANCE NETWORK
WWW.IHN-ORG.NET

Haemovigilance: … a global affair?



HV in the early days

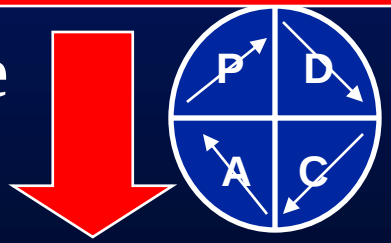
HO-Recipients

sAR

Patients

collection and analysis of data

incomplete Quality cycle



stepwise improvement of quality

State-of-the-art HΘ : **triple** approach in a **single** concept

HΘ-Recipients ***HΘ-P/P*** ***HΘ-Donors***

AR AE AR/Compl.

Clinical use

errors

near-misses

Patients Processes / Products Donors

collection and analysis of data

Deming Quality cycle

continuous improvement of quality

Haemovigilance has **two** major goals:

1. Optimal safety of blood transfusion

2. **Optimal use** of blood products

Because that is:

. fair to the donor

. beneficial for the patient

. cost-effective

Did we succeed?

HV: cost, result/outcome, efficacy, efficiency,…

Direct costs (staff, infrastructure, material,…)

Indirect costs (volunteers,…)

Intrinsic costs (setting up and running HV)

Subsequent costs (action upon recommendations/ requirements trough HV)

Outcome → ? €

Efficacy

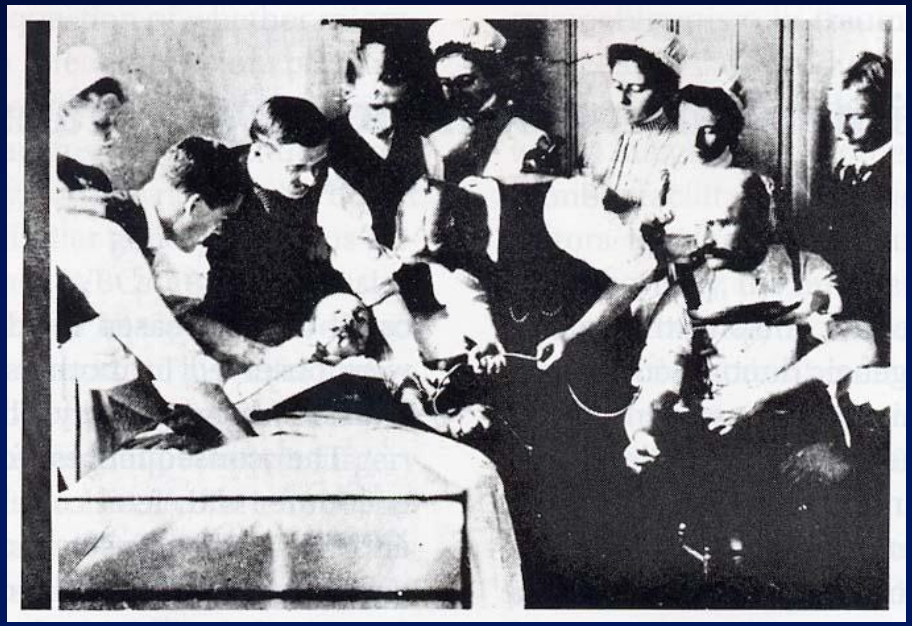
Efficiency

N.B. UK-SHOT 1997: 1 staff and 20k£ ; 2010: 8 staff and 400k£

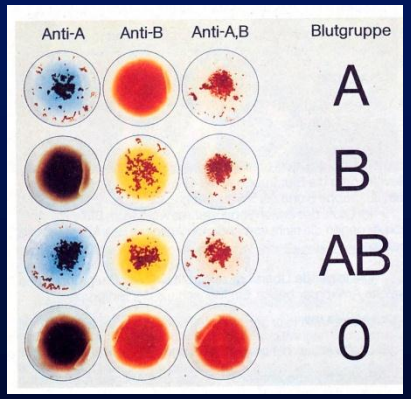
(Lorna Williamson, IHS Amsterdam 11.02.2011)

«History» of Haemovigilance: …mainly incompatibilities

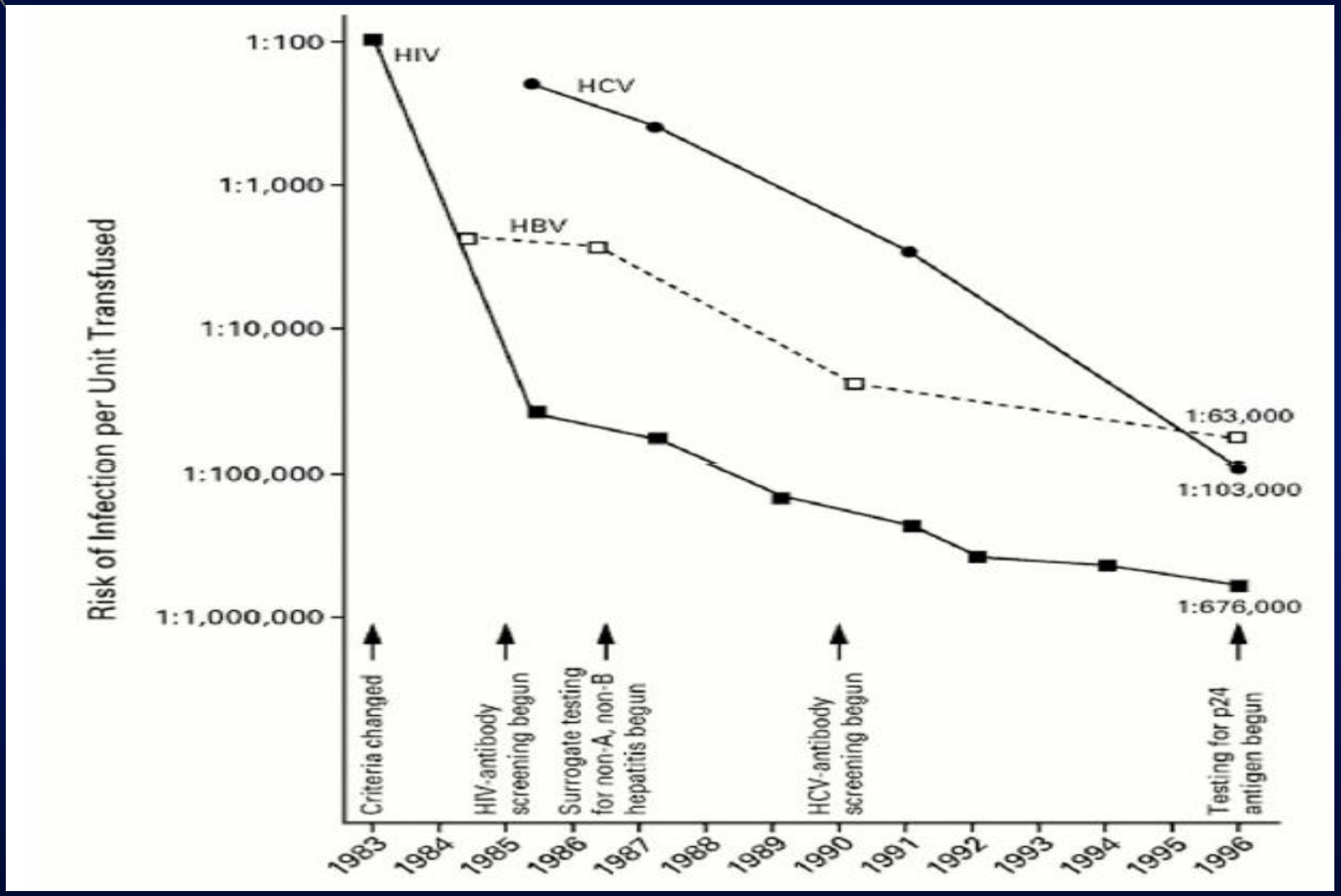
- Spontaneous, episodical descriptions of accidents during/ after blood transfusion (Denis, Blundell,…)



- Landsteiner's observations and work (and others)



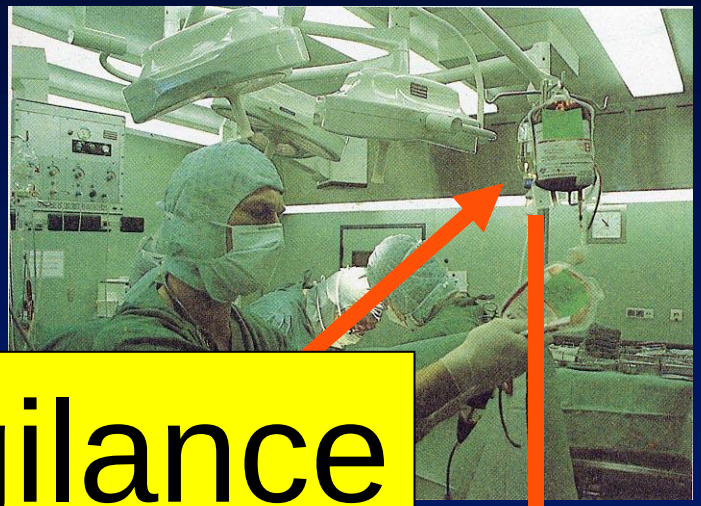
… more recent past (Goodnough 1999): dominated by TTI



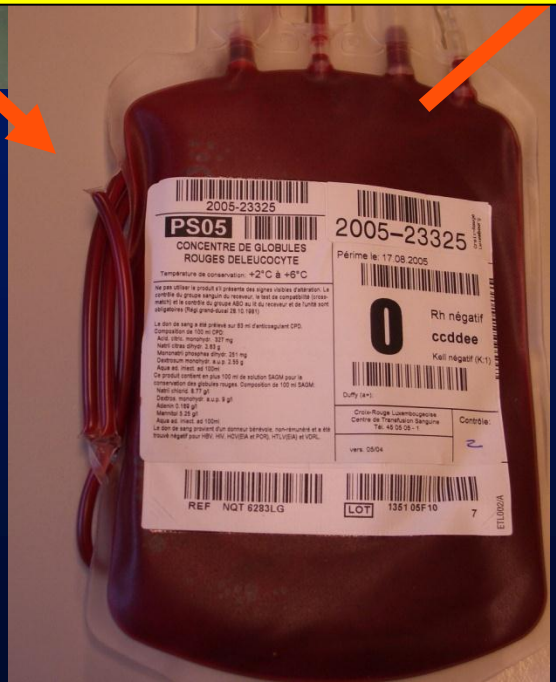
… and now more of technical, organizational, behavioral nature

- errors and near misses are quite common
- clinical use of blood is not always appropriate (sometimes with irrational habits)
- medical prescription is not seldom inadequate, communication in the hospital is not always direct and strong
- non-compliance is recognized regularly as a major problem
- non-conformities, complaints, errors is a major issue in many blood establishments (despite the fact that most of the BE have established QMS, also due to reporting as an active part of it)
- IT problems are unexpectedly frequent (most due to inadequate validation, frequently in the context of installation of software updates)
- **wrong patient ID (and incorrect bedside test) remain a major weakness in the hospital system**

The entire blood chain is prone to risks, threats and dangers



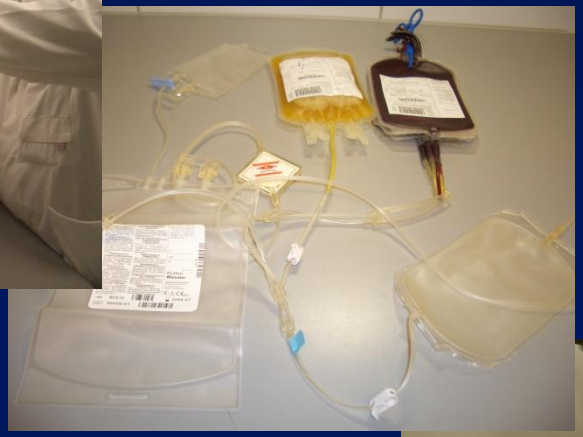
Haemovigilance



The producers in the Blood Chain

pooling of 4 buffy-coats

Processing of whole blood and preparation of pooled BC-PLT - under stringent cGMP

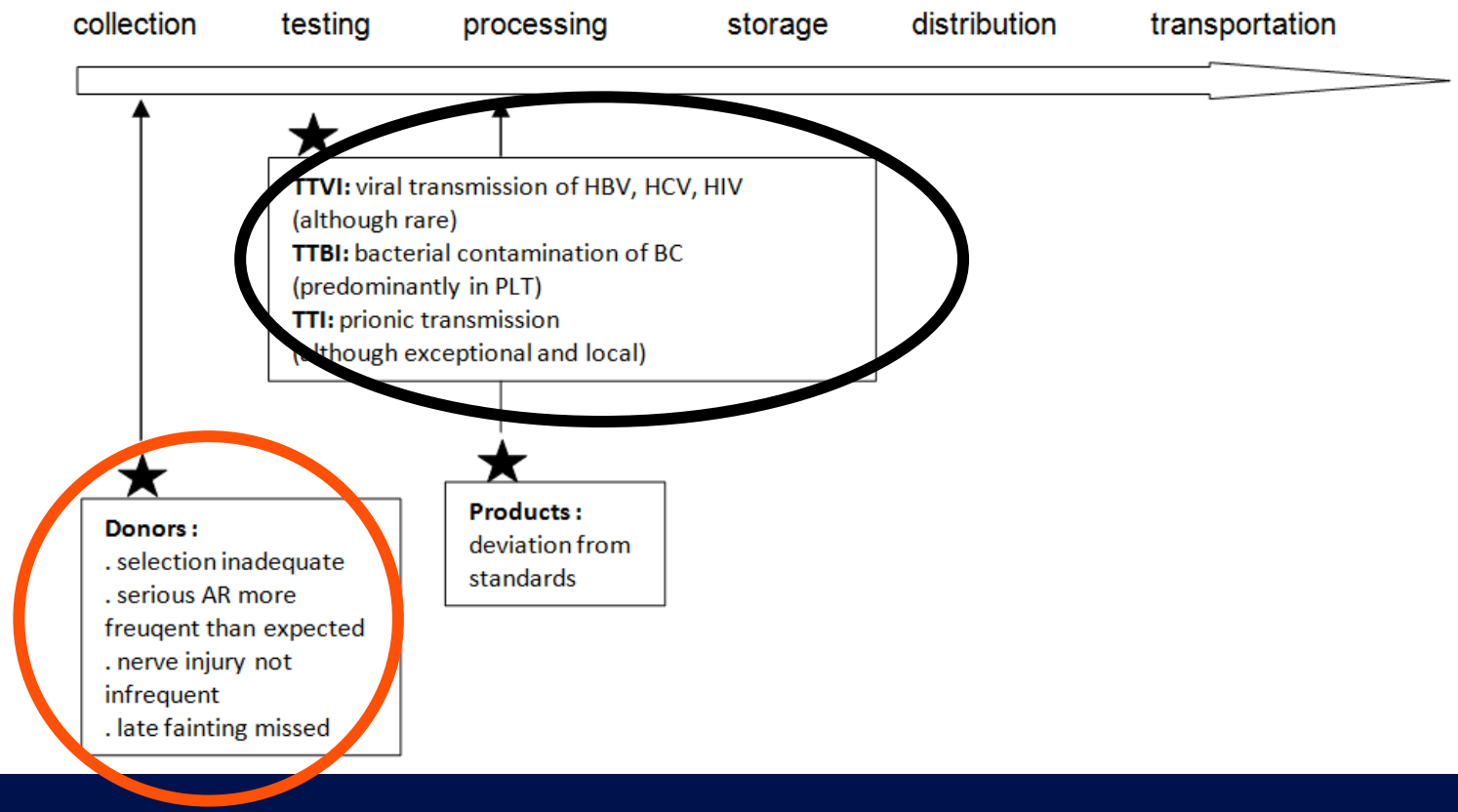


addition of 1 unit of plasma

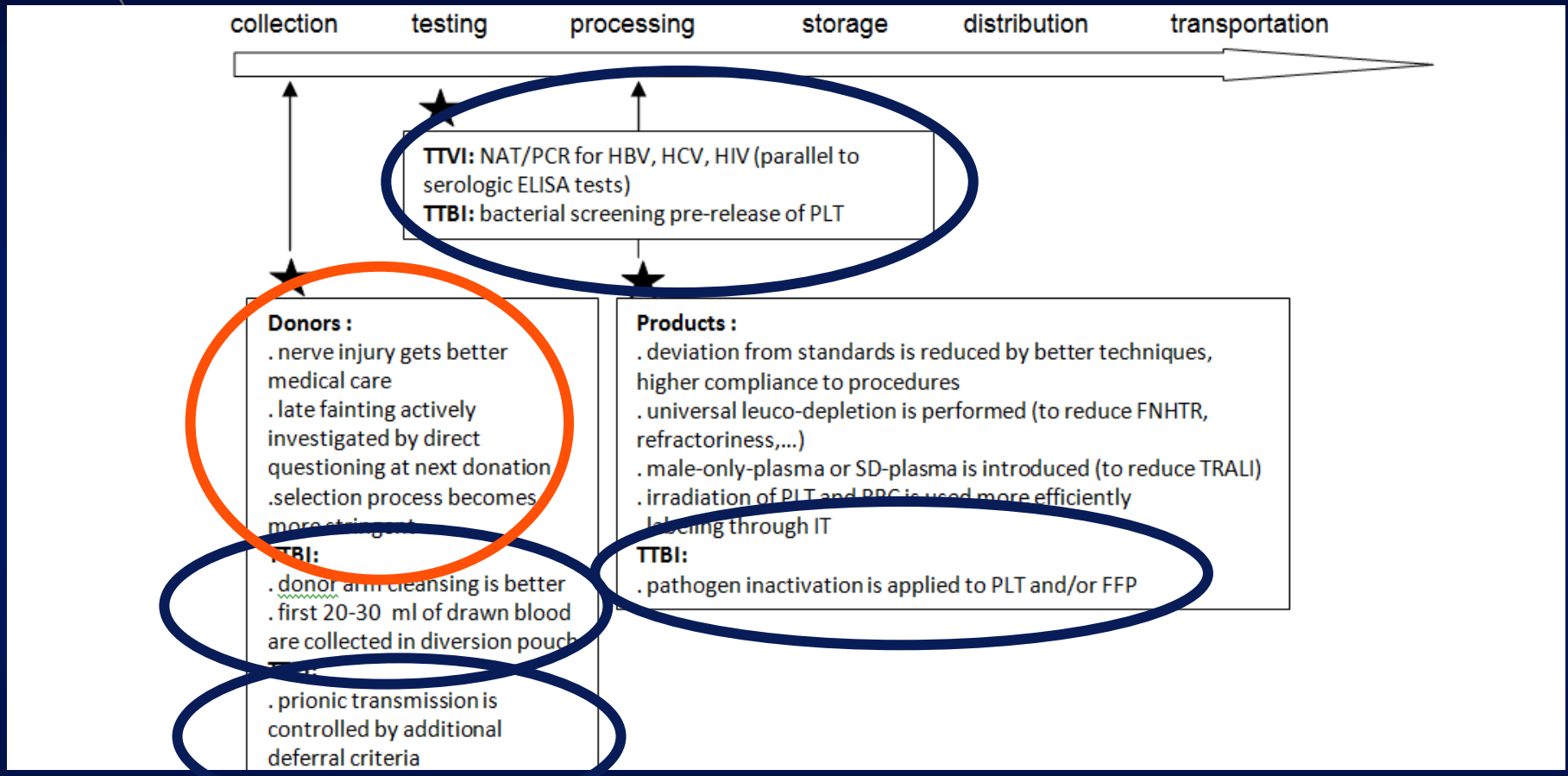
2nd centrifugation

separation and u-LD

Production segment (BE): risks "recognized" through HV



Production segment (BE): measures taken CAPA



. sterile connections
. protection of bags (integrity of plastic)
...

Production segment (BE): types of actions

Measures taken rely on:

- ***new analytic*** technologies:

  NAT / PCR – large scale (pool, single; in-house, proprietary,…)

- ***existing analytic*** technologies:

  bacterial culture – for release

- ***new processing*** technologies:

  pathogen inactivation (PLT, FFP; Intercept®, Mirasol®, SD..)

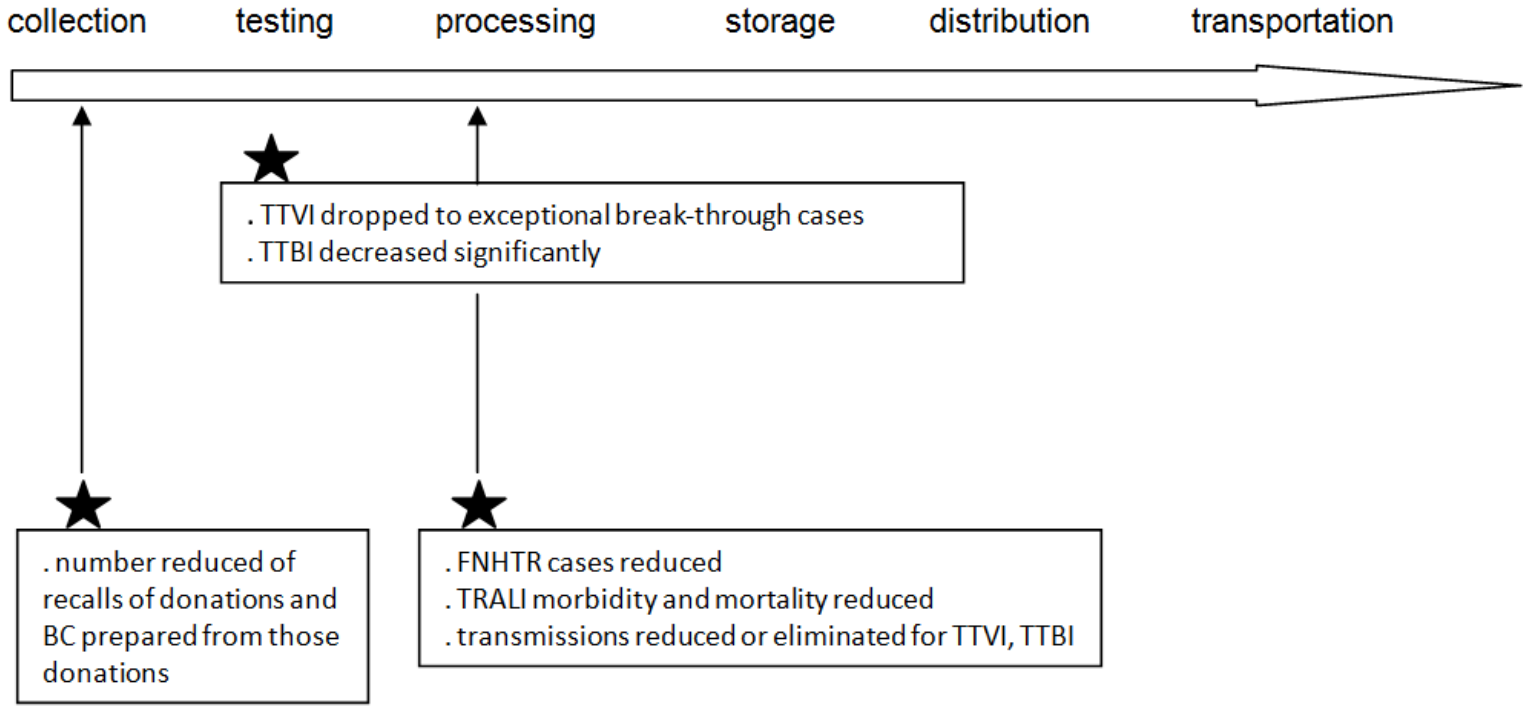
- ***existing processing*** technologies:

  filtration – universal leucodepletion; irradiation

- ***organizational*** changes:

  centralization, QM (translated to BE-QMS:ISO 9001,17025,15189)

Production segment (BE): improvement triggered through HV



HV and Achievements

number of **recalls** of donations and of blood components (BC, prepared from index donations) **decreased:**

- *medical questionnaire* to assess donor eligibility *reviewed* and *updated* (rendering questions clearer and adding more precise/direct questions on risk behavior) → *Mindy Goldman, CAN*
- process of *medical selection* of donors *strengthened* (increasing compliance to the acceptance criteria after training and re-training of staff in charge).

HV and Achievements

number of **transfusion transmitted viral infections** (TTVI) **decreased** (dropping to *exceptional break-through cases*, transgressing all safety barriers including testing - negative results in ELISA as well as in PCR for donors coming to donate blood, very shortly after viral contamination)

- introduction of systematic *NAT testing*, parallel to the classical serological screening

Emerging pathogens → Roger Dodd, US

N.B. This is especially true for countries with a higher prevalence of relevant viruses in the general population

HV and Achievements

number of **transfusion transmitted bacterial infections** (TTBI) **dropped:**

- *platelet concentrates* (most at risk) subject to *bacterial pre-release testing* (culturing in the laboratory of the BE of samples from the finished product until the product is distributed upon negative test result).

HV and Achievements

residual transmissions of infectious agents through transfusion **eliminated:**

- *pathogen inactivation* of PLTs and/or FFP

→ *Larry Corash, US; Morven Rüesch, CH*

N.B

. Technology not available for the moment for RBCs or WB

. Effect less visible for viral transmissions (already exceptional after introduction of NAT)

. Effect evident for bacterial contaminations through transfusion of certain BC

. Less visible for parasites

. No effect on prions, nor spores

HV and Achievements

FNHTR greatly **reduced:**

- *universal pre-storage leuco-depletion* of RBCs and PLTs (filtration of the intermediate products during processing lowers the number of residual leucocytes to a level that no longer allows sufficient production of cytokines - of different kinds - during the following storage, thus decreasing the incidence of the typical symptoms of FNHTR).

HV and Achievements

TRALI morbidity and mortality significantly **reduced:**

introduction of *new plasma components* for transfusion:

- *male-only plasma* (prepared from donations of non-transfused male donors) eliminating passive transfer of leucocyte-antibodies from donor to recipient - a prerequisite for development of TRALI

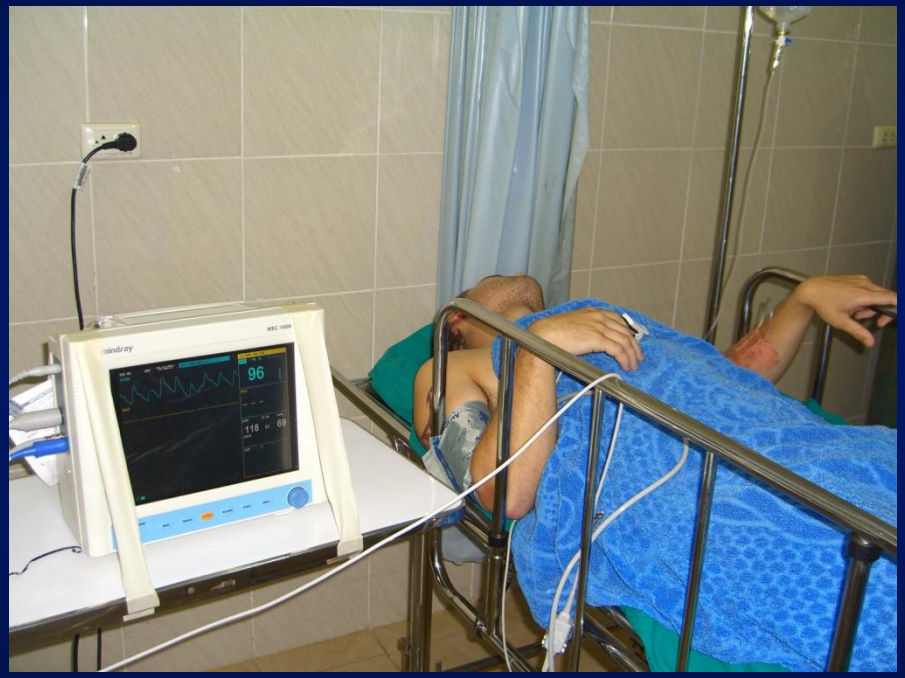
  → *Anne Eder, US*

- *SD-plasma* (prepared from a pool of multiple plasmas and subject to treatment by solvent-detergent) – diluting leucocyte-antibodies (if present) during pooling to a point where they can no longer trigger the pathomechanism for TRALI.

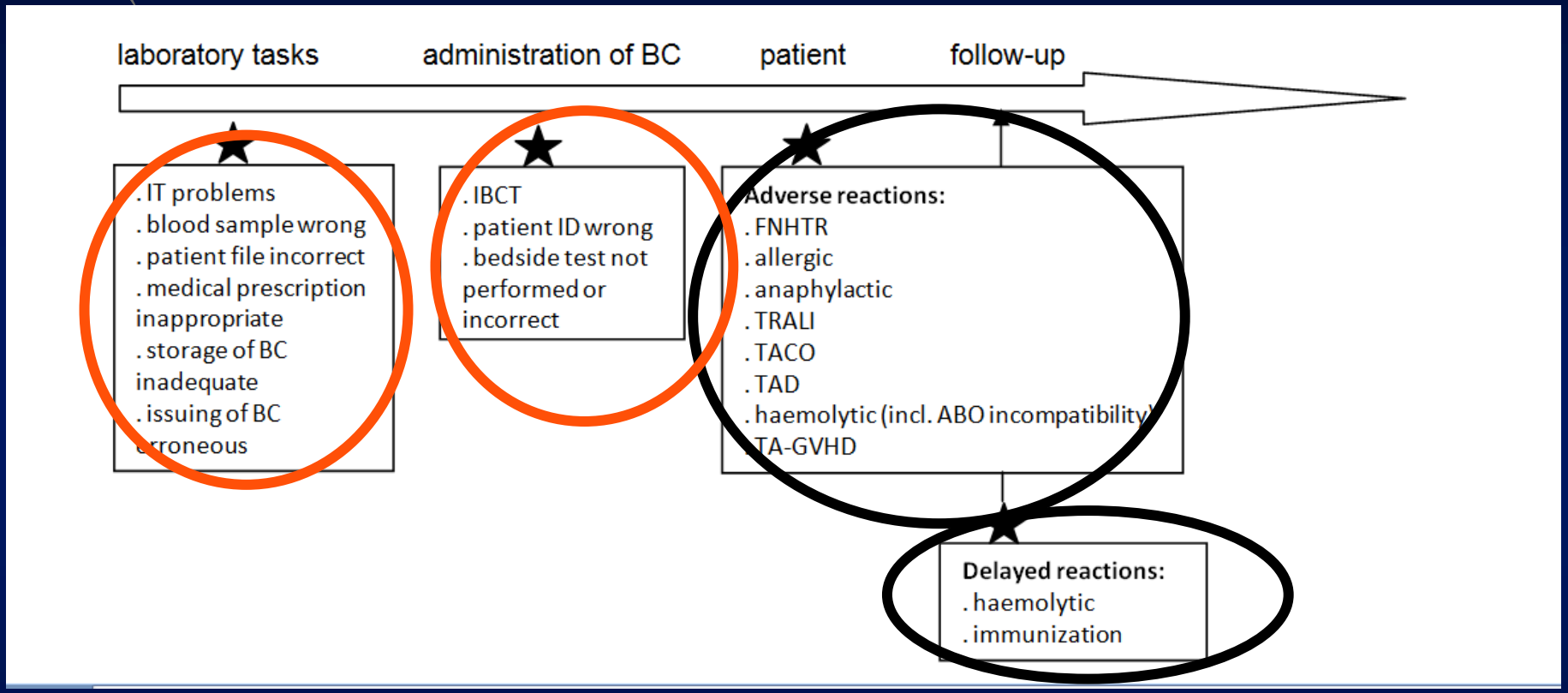
N.B. Residual TRALI - transfusion of RBCs and PLTs (containing some plasma): trend to use of additive solutions

TRALI outcome – one of the most visible and dramatic achievements through HV

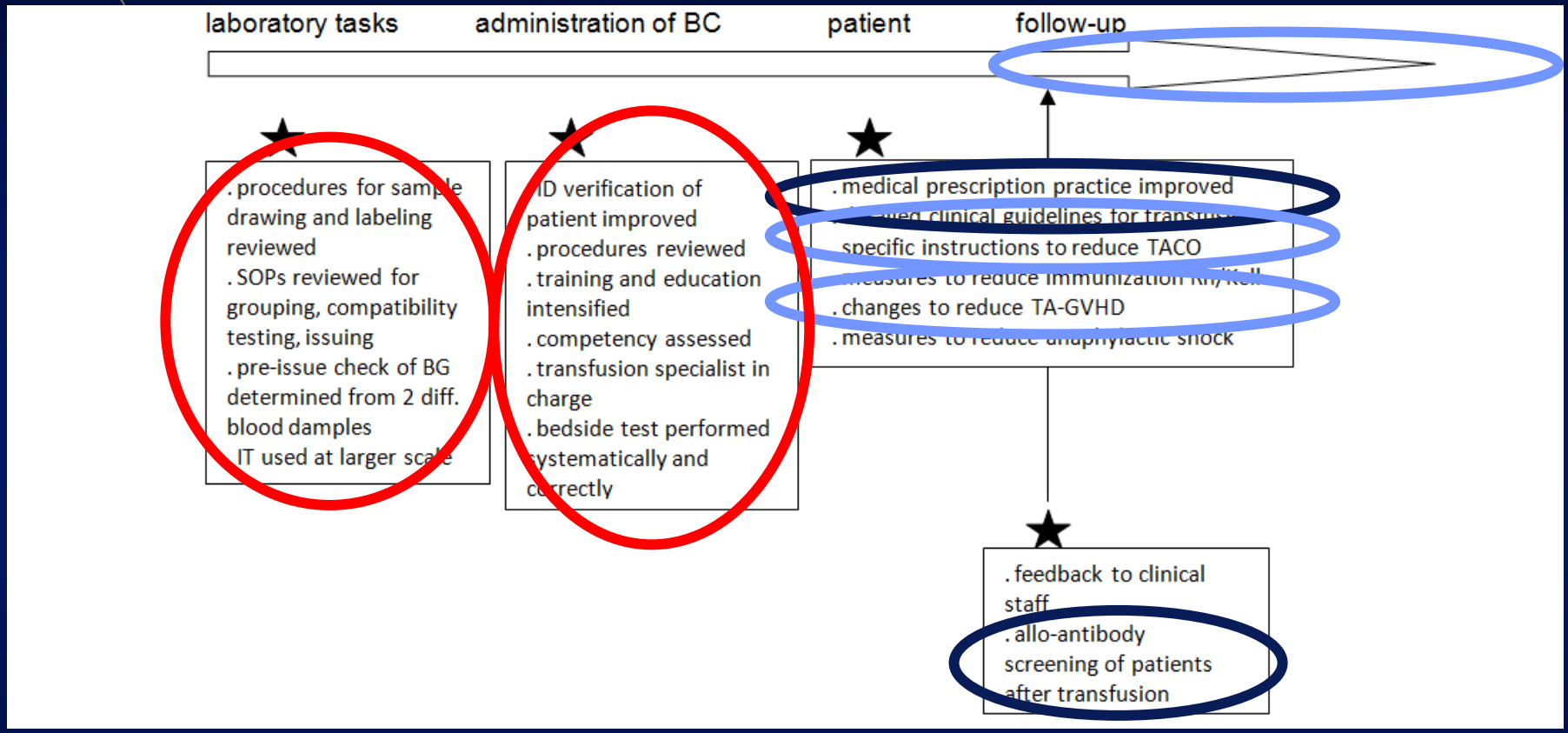
The users in the Blood Chain



Usage segment (Hospitals): risks "recognized" through HV



Usage segment (Hospitals): measures taken CAPA



Usage segment (Hospitals): types of action

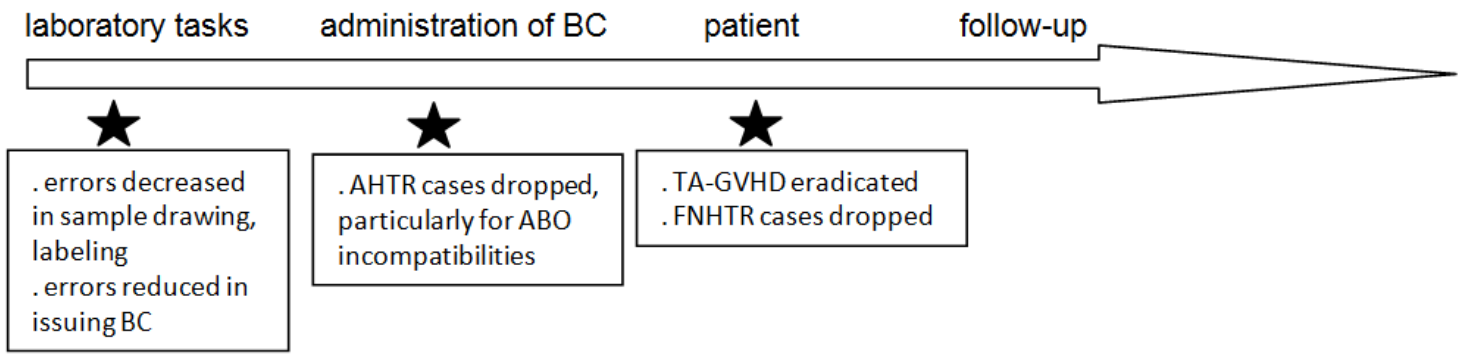
Most changes are related to **clinical practice**:

- improvement of *medical prescription* (unambiguous ID, clear instructions for transfusion, complying with guidelines,…)
- appropriate use of *blood components* (to avoid TA-GVHD: ordering exclusively irradiated BC; to reduce TACO: giving clear and detailed instructions on transfusion rate and volume in patients at risk; to decrease anaphylactic shock: identifying patients with haptoglobin or IgA deficiency)

but also:

- correct **ID of patient** (making sure that procedure is followed and that wrist bands are used) and **ID of product** to be transfused (performing clerical checks without exceptions)
- **bedside test** (ultimate safeguard – systematic and technically correct, with right interpretation of results).

Usage segment (Hospitals): improvement triggered through HV



HV and Achievements

TA-GVHD:

- **eradicated** where *routine irradiation of cellular BC* (elimination of the transfer through transfusion of viable T-lymphocytes from the donor to a patient) - *Japan*

- **reduced** drastically where *medical prescription practice improved* and medical orders followed in a disciplined way

HV and Achievements

HV has uncovered **sample drawing** and **tube labeling** as the most critical and vulnerable steps of the blood chain.

Despite **increase in notification/reporting** of errors and near-misses, most probably **reduction in incidents:**

- not a single corrective intervention but *several coordinated actions*:
  - better procedures
  - clearer SOPs
  - intensified training, re-training
  - increased compliance, …

N.B. This achievement through HV is an important and spectacular one.

HV and Achievements

HV also unveiled weakness in **issuing of BC** from the hospital blood bank to the requesting ward

Despite **increase in notification/reporting** of errors and near-misses, most probably **reduction in incidents:**

- not a single corrective intervention but *several coordinated actions*:
  - improved procedures in the laboratory in charge
  - better SOPs
  - more training
  - support by IT

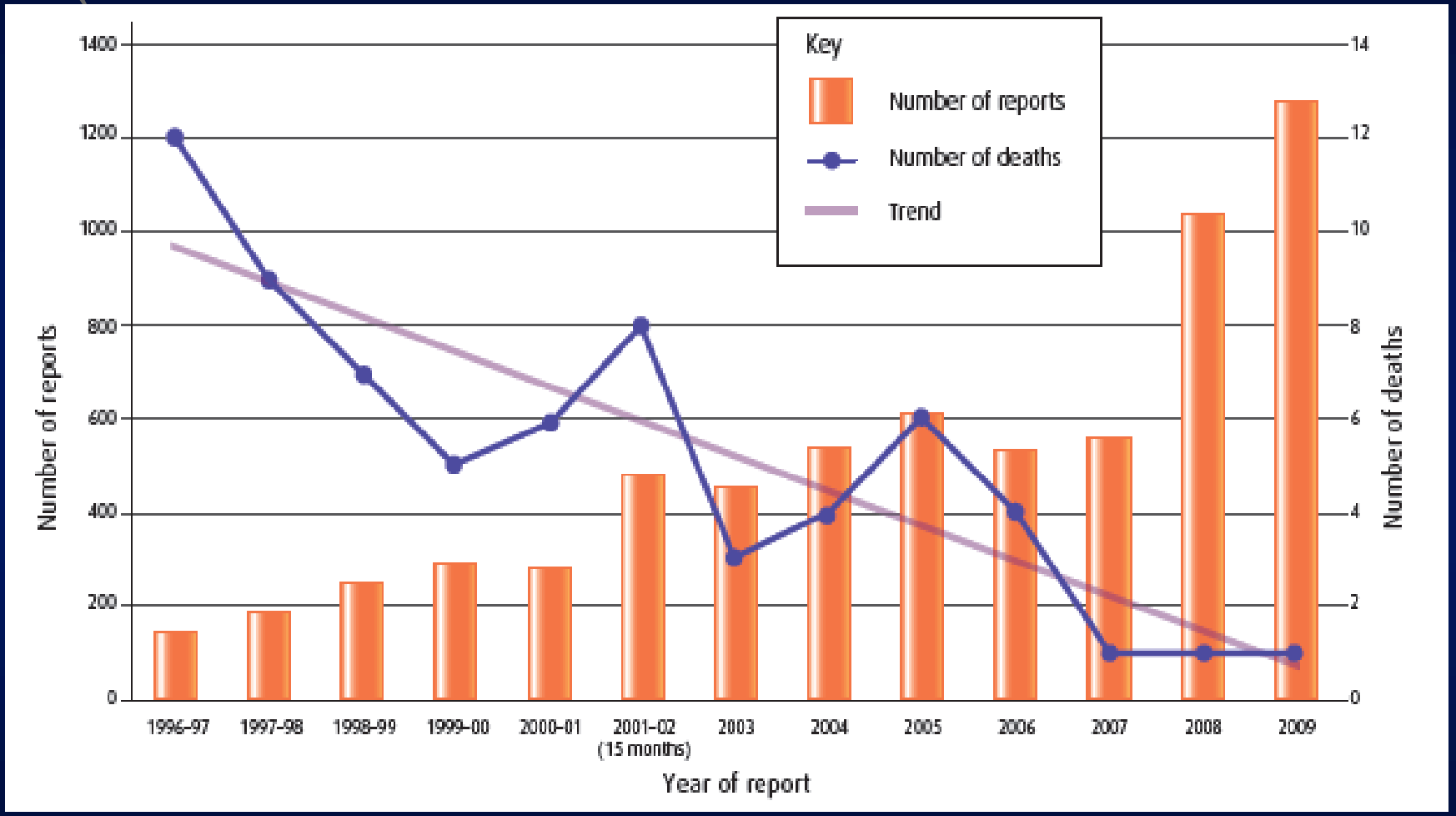
HV and Achievements

AHTR (particularly **ABO incompatible** transfusions) significantly **reduced**:

- *combined and synchronized actions (hBB and clinical wards)* to reduce mix-up:
  - stringent ID checks of the patients
  - clerical controls of the issued BC
  - bedside test

N.B. These dramatic accidents are rare if the bedside test is performed systematically (good compliance), "lege artis" (good material and good technique) and the correct interpretation of the results (good personnel) is guaranteed.

Did HV work? … take the example of UK-SHOT



Total reports and total deaths definitely due to transfusion (1996 – 2009)

HV and Achievements

HV has had a significant impact on the **mentality** of those involved in blood transfusion.

Increased awareness of the real transfusion risks:

- demands for consultation from experts by hospital staff increased
- reporting of AR/AE intensified
- errors and near-misses reporting increased, advents diminished
- risk management intensified
- transfusion practice rationalized, good clinical practice applied
  → *Jonathan Wallis, UK*
- number of blood transfusions decreased.

- combination of *different interventions at different levels*

N.B. This contributed also to the decrease in mortality due to blood transfusion.

HV and Achievements

HV integrated in the **QMS** (especially in the BE).

→ *Tom Vuk, Croatia*

HV as a quality tool is leading to:

- errors and near misses dropping (despite increase in notifying)
- non-conformities of blood components decreasing
- complaints of customers in the hospital diminishing
- errors in the processes better managed and followed up.

N.B.

Speaking about achievements in the context of HV, it should not be forgotten that improvements are not always measurable (for different reasons)

Specific outcomes may not yet be assessable (f.ex. when actions have been taken only recently)

→ *the benefit of HV may be even higher than we can assess today.*

HV and Global Achievements

1st global achievement of HV:

- *documentation* of risks and side effects

- *quantification* of them (or at least an order of magnitude)
  - special interest in the context of TTI of viruses (HIV in first place, but also for HBV, HCV, HTLV,...): *over*-estimated
  - TTI due to bacteria: *under*-estimated

HV and Global Achievements

2nd global achievement of HV:

- *discovery and re-discovery* of important entities (infection, disease, situation,...) before, during and after *transfusion*, but also in the context of *donation*:
  - *known risks* and problems before structured HV was organized
  - *"new" entities* (associated with donation respectively transfusion): "painful arm", TRALI
  - *wide range of expression characteristics* as IBCT - from absence of symptoms after transfusion of the wrong BC to lethal outcome due to massive haemolysis of ABO incompatible red cells
  - other pathologies were described before HV was organized but the *link* to blood transfusion was less obvious and not recognized: TACO, TA-GVHD, under-transfusion,...

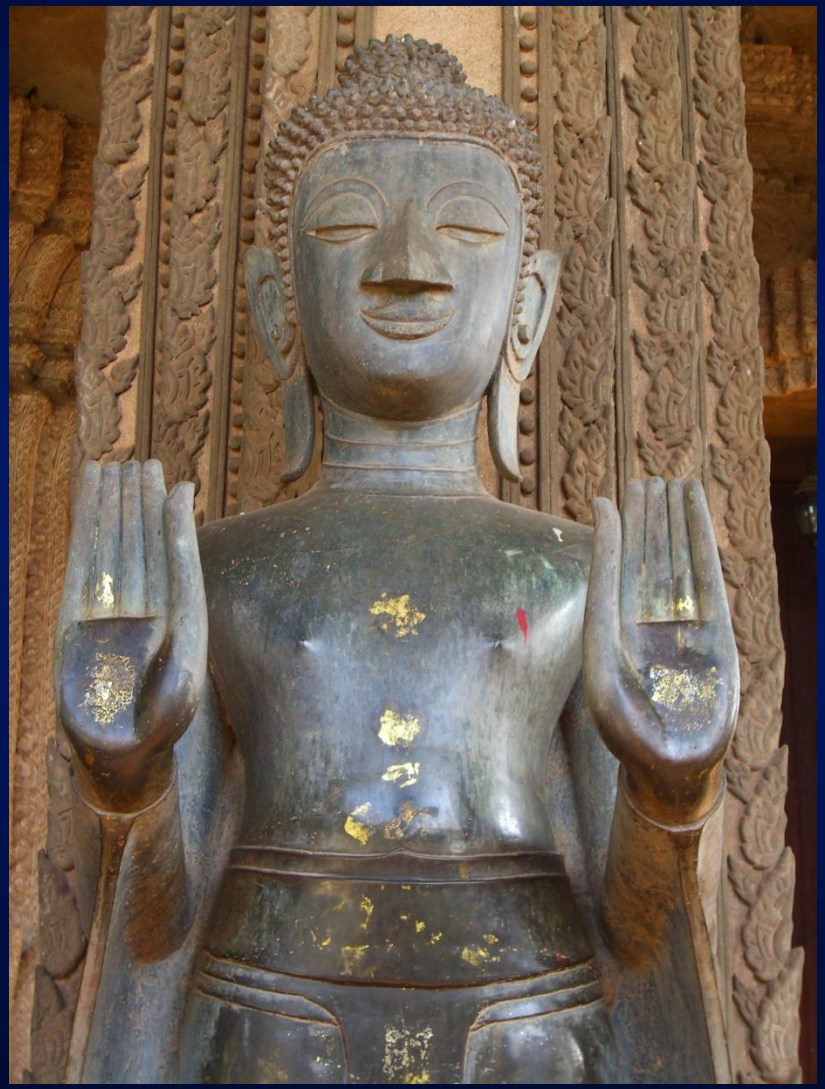
HV and Global Achievements

3rd important achievement of HV:

- *closing a gap* in the Quality cycle of "Plan, Do, Check, Act" with significant improvements in different activities:
  - many different actions and measures were taken to reduce or eliminate risks and problems
  - HV is considered as a quality tool and as such is integrated into QA, QM and QMS.

N.B. In general, integration was easier in BE than in hospitals and it is not really surprising : BE are production sites, operate under GMP rules and have a higher overall level of quality culture.

Not all is finished in HV - some projects are underway … a non-exhaustive list



Global Standardization to be continued

IHN/EHN and **ISBT Working Party on HV*** have made two important contributions in this context:

1. standardisation of definitions of adverse reactions and adverse events (AR/AE) in **patients**

2. standardisation of adverse events / complications in **donors**

ISTARE

(International Haemovigilance Database for the Surveillance of Adverse Reactions and Events in donors and recipients of blood components)

- will be further developed and extended will be used effectively in the future (publications, benchmarks,…)
- data validation is a crucial aspect

→ *Dina Politis, GR/HE and her group*

N.B. There is an urgent need for skilled and experienced individuals for HV data validation and analysis; several organisations have shown interest in collaboration with ISTARE

Donor Vigilance

needs to be further developed (is still missing in some systems)

risks are not properly quantified

very serious (rare) risks may be under-estimated

→ *Peter Tomasulo and Hani Kamel, US; Mat Kuehnert, US*

- Ischaemia → *Marc Germain, CAN*
- Iron depletion → *Gilles Delage, CAN*
- Late fainting (and resulting accidents)
- Nerve injury

N.B. Specific challenges in apheresis (activation of biological systems, loss of immune competent cells, serious AR, …)

Rare (but very serious) Adverse Events (2005)

(courtesy of Jan Jorgensen, DK)

Different types of reactions	*8,2 million manual WB donations*
Death	3
Skin infection	1
AMI	1
Seizure	21
Cardiac arrest	3
RDS	3
Accidents	4
Car accident	1

Clinical Use

We need to better understand why:

- a specific BC is tx and not another one
- a disease needs tx and not another one
- a country/region/institution has a tx pattern different to another

→ *Jonathan Wallis, UK; Erica Wood, AUS; Ginette Labonté, CAN*

Specific questions:

- paediatric cases → *Paul Bolton-Maggs, UK*
- multi-tx patients (large volume of different BC)
- chronically tx patients (long term treatment w. a single type of BC)

Errors and near-misses

An opportunity to detect symptoms of weakness in systems and sub-systems

→ *Jeannie Callum, Cindy Hyson and Ann Wilson, all from CAN; Paula Bolton-Maggs, UK*

Some other areas need to be explored or revisited:

- emerging, submerging and re-emerging pathogens

  → *Roger Dodd, US*

- other tx risks:

✓ relevance of under-transfusion,

✓ role of BC age at transfusion,

✓ impact of transfusion on immune functions,

✓ hazards of alternatives to transfusion,…

Hot vs. cold HV; most cases were of the domain of MD-VGL

Rapid alert and early warning

Challenges ahead: control and use HV data

Further integration of ***HV into QMS*** (BEs, HCIs):

- starting with developing QI for HV in BEs (ISO9001:2000, cGMP,…)

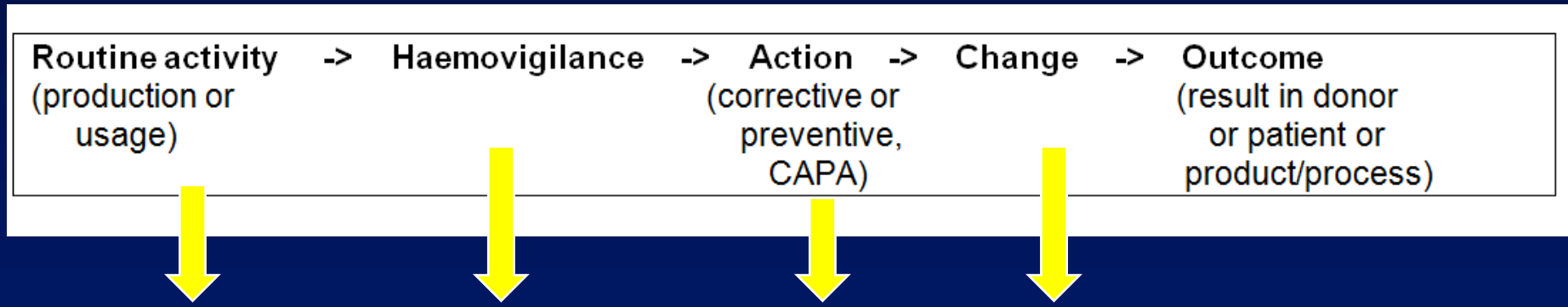
→ *Tom Vuk, CRO*

and

- adding QI for Hospitals (HTC, hBB, wards,…)

Quality cycle applied to the Blood Chain

Do Check Act Plan



Abundant variation in:
Techniques
Materials
Personnel (skills, experience)
Organisation
QM
…

Observations
Reports
Data sets
Surveys
Studies
Inquiries
…

Modification of:
Techniques
Material
Equipment
Organisation
Procedures
…

Single
Multiple
Combined

Obvious
Measurable
Invisible
Very rare
Inexistent

Challenges ahead: continue or merge

HV or Bio-Vigilance

↗ That is the question … or only a question!

Pros and Cons

→ *Michael Strong, US; Jo Wiersum, NL*

US, EU – common framework

linking into Patient / HC safety

→ *Alexis Harvey and Barbie Whitaker, US*

Challenges ahead: know what happens and where it happens

Worldwide Registry of systems for extended HV:

- National
- By Region (EU, Arab, Latino America, SEA,…)
- Global

A regional layer may be useful as significant differences exist in HC systems, medical practice, culture and language,…

Challenges ahead: bringing HV to developing countries

Developing countries :

HV has its best added value, its maximum impact for different reasons (severe AR/AE, high seroprevalence of TTIs, weak QM,…)

→ *Luiz Amorim, Brasil; Ananda Gunasekera, Sri Lanka**

Unified effort needed:

- WHO*, IFRCS, GF-ATM, PEPFAR, …
- IHN*, ISBT, national societies,…
- Bi-/multi-lateral cooperations*

World Health Organization

WHO strategy for safe blood transfusion

Stratégie de l'OMS pour la sécurité transfusionnelle

Voluntary blood donation

Testing of all donated blood

Safe and rational use of blood

Haemovigilance

Quality systems

National coordination of blood transfusion services

Global Consultation on Universal Access to Safe Blood Transfusion in June 2007 in Ottawa (coincided with the global launch of World Blood Donor Day)

→ working in collaboration with the Public Health Agency of Canada, Health Canada, Canadian Blood Services, and Héma-Québec:

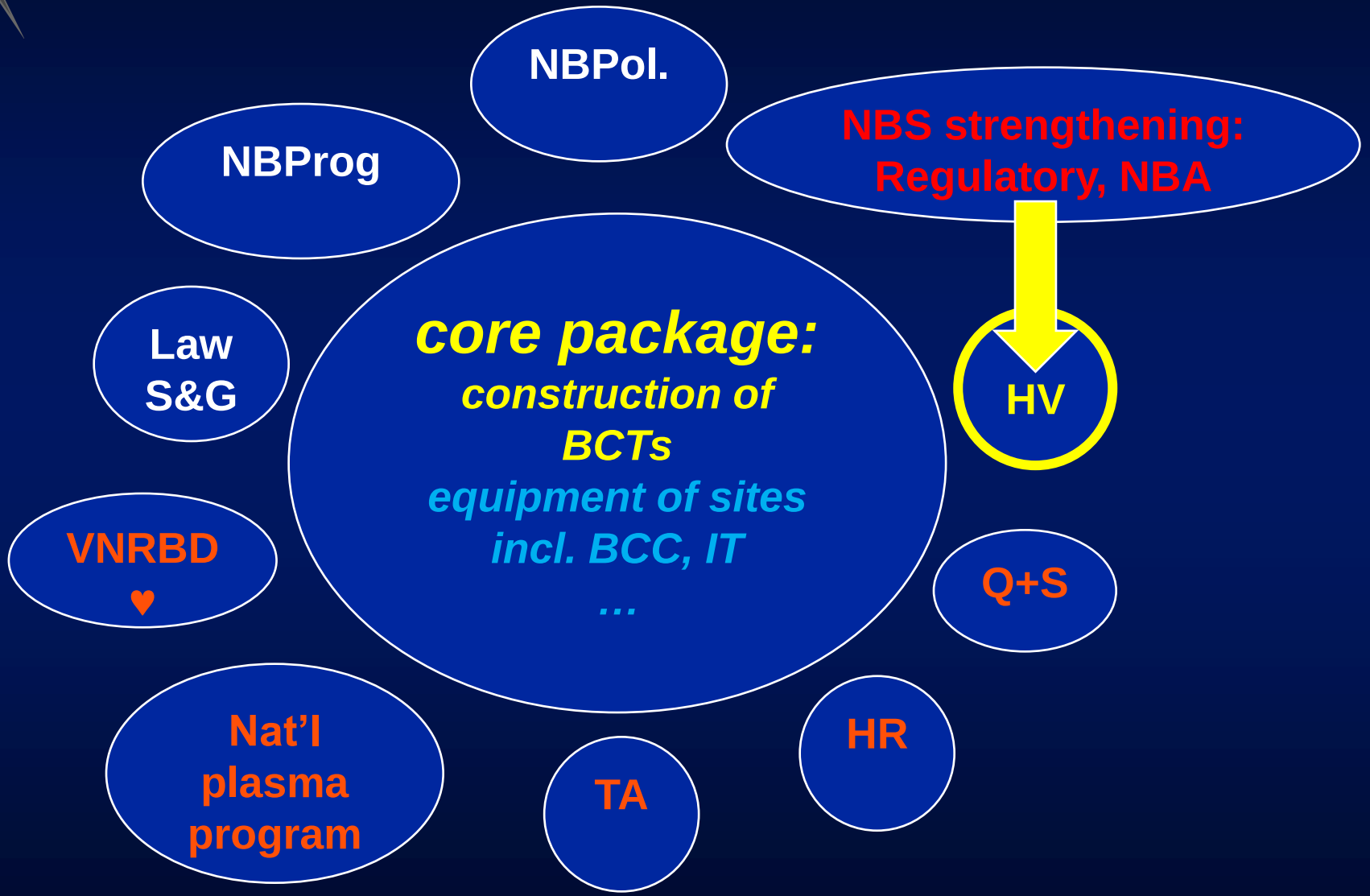
One of the key recommendations made by the participating experts was for WHO:

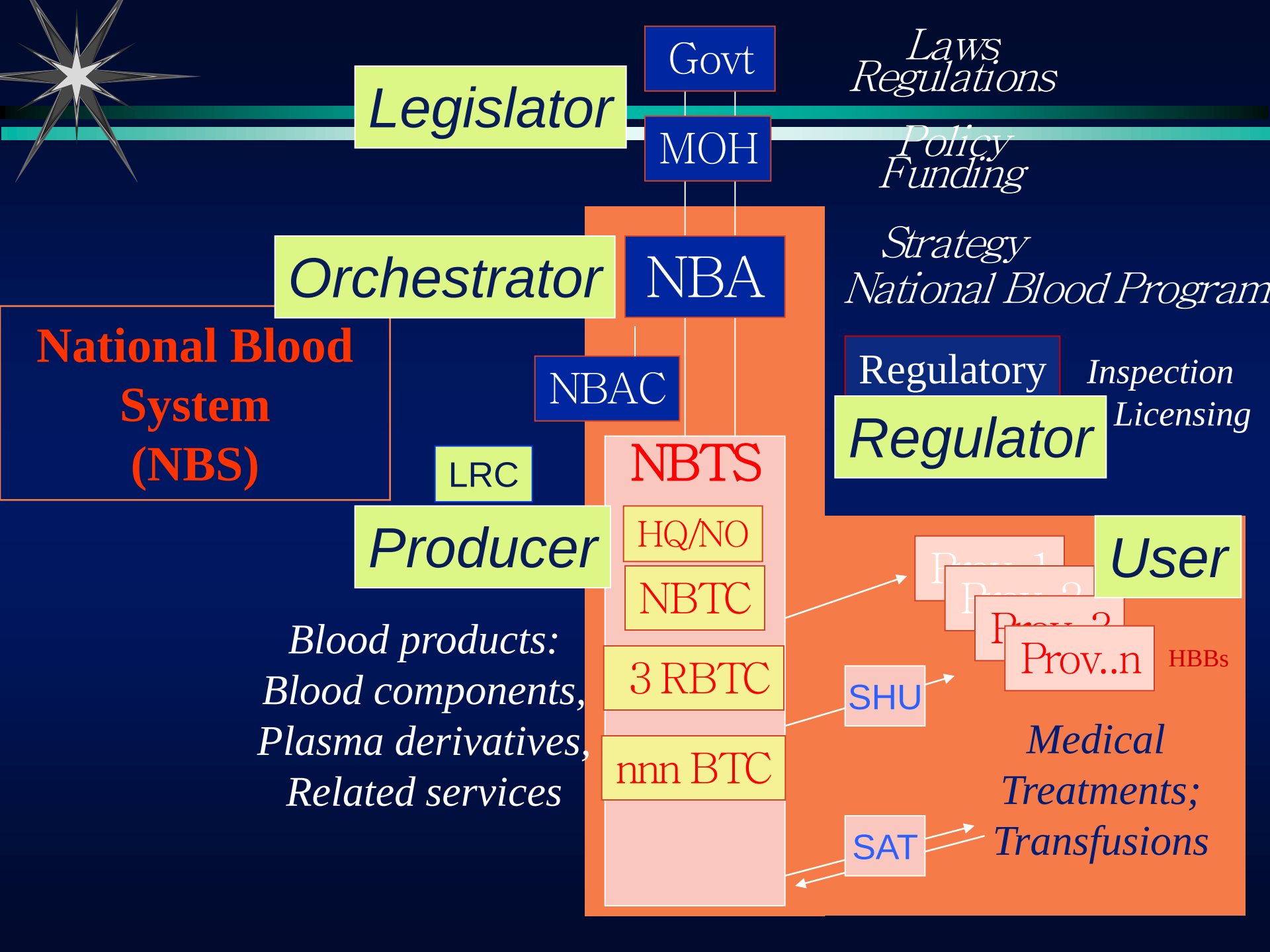
“to develop a global hemovigilance, surveillance and alert network, which would provide a platform to countries for sharing key information on blood safety and availability issues and build a timely response in addressing emerging threats.”

→ new global consortium = GloSCH

with founding members being WHO, ISBT, EHN/IHN, Government of Canada, and USPHS (Public Health Services of the United States of America).

Bi- / Multi-lateral Cooperation Blood Projects




Govt
Legislator
Laws
Regulations
MOH
Policy
Funding
Orchestrator
NBA
Strategy
National Blood Program
National Blood System (NBS)
NBAC
Regulatory
Regulator
Inspection
Licensing
LRC
NBTS
Producer
HQ/NO
NBTC
User
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nnn BTC
Prov..n
HBBs
SHU
SAT
Blood products:
Blood components,
Plasma derivatives,
Related services
Medical
Treatments;
Transfusions

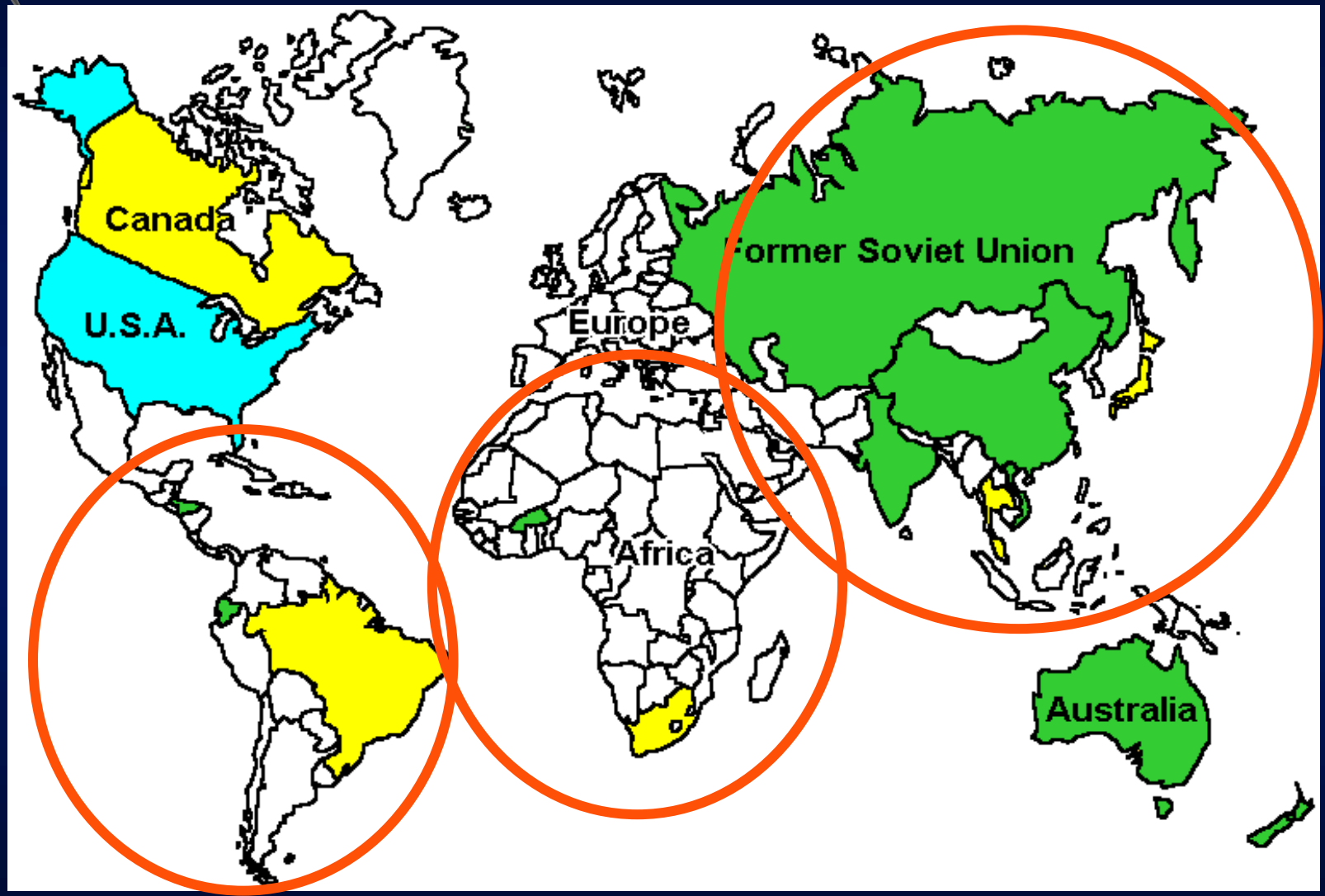
Globalization:

Embracing not only developing countries

But also transitional and developed countries

… including BRIC(S) countries

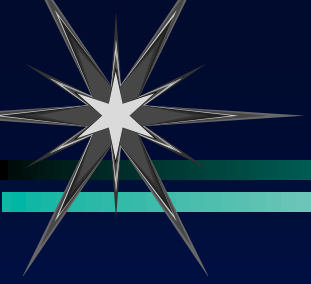
Haemovigilance: … a global affair



... Still a long way to go for HV!

Many thanks !

Grands mercis !



- *Invitation by Pierre ROBILLARD(e-mail 02.2012), Montreal, Canada*
- *Haemovigilance: Where are we in 2012?*
- *14th IHS International Haemovigilance Seminar in Montreal*
- *April 25-27, 2012*
- *14:00-15:00 >>>60 minutes*
- *60-90 slides*