ESSENTIAL HEALTH TECHNOLOGIES

Standardization of *In vitro* Biological Diagnostic Procedures

Existing, new and emerging technologies

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Outline of Presentation

- *In Vitro* Biological Diagnostic Procedures

  Biological Products

  Global measurement standards

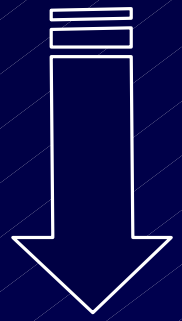
- Existing, new and emerging technologies: approaches to development of standards

- Challenges/Limitations

Definition of Biologicals

Biological sources

Crude, semi purified extracts or purified fractions
of microbial, animal or human tissues



Produced by biological processes

Traditional/ Recombinant DNA
or High technology

Biological product

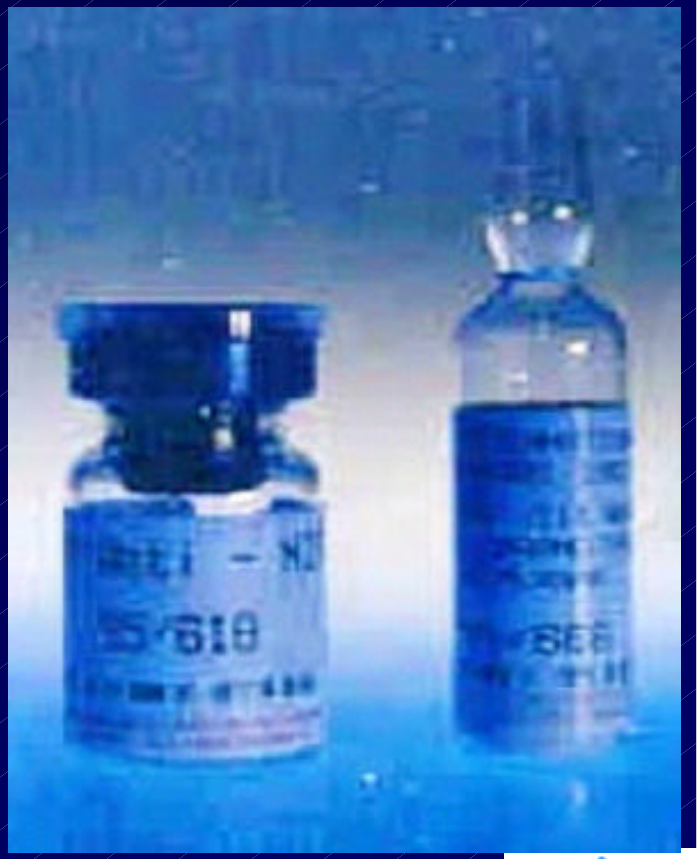
- Complex molecular structure
- Cannot be characterized by physicochemical criteria alone
- Used for diagnosis, treatment or prevention of diseases

Global measurement standards
WHO International Standards
WHO Biological Reference Preparations

WHO Biological Reference Preparations
Global measurement standards

PURPOSE / IMPACT

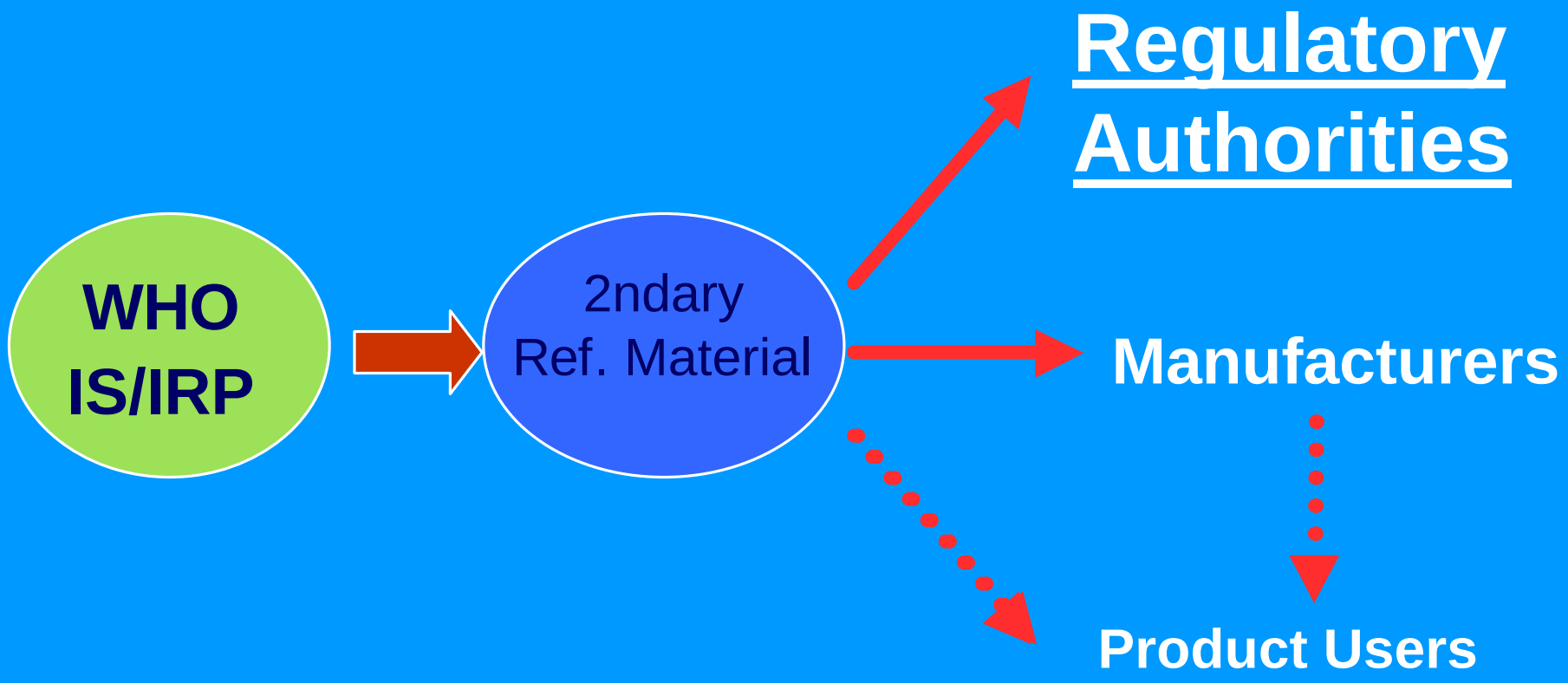
- Tool for comparison of biological measurement results worldwide (unit of measurement/biological system)
- To facilitate transfer of laboratory science into worldwide clinical practice
- To support harmonization of international regulations
- To accelerate transfer technology



WHO Biological Reference Preparations

Global measurement standards

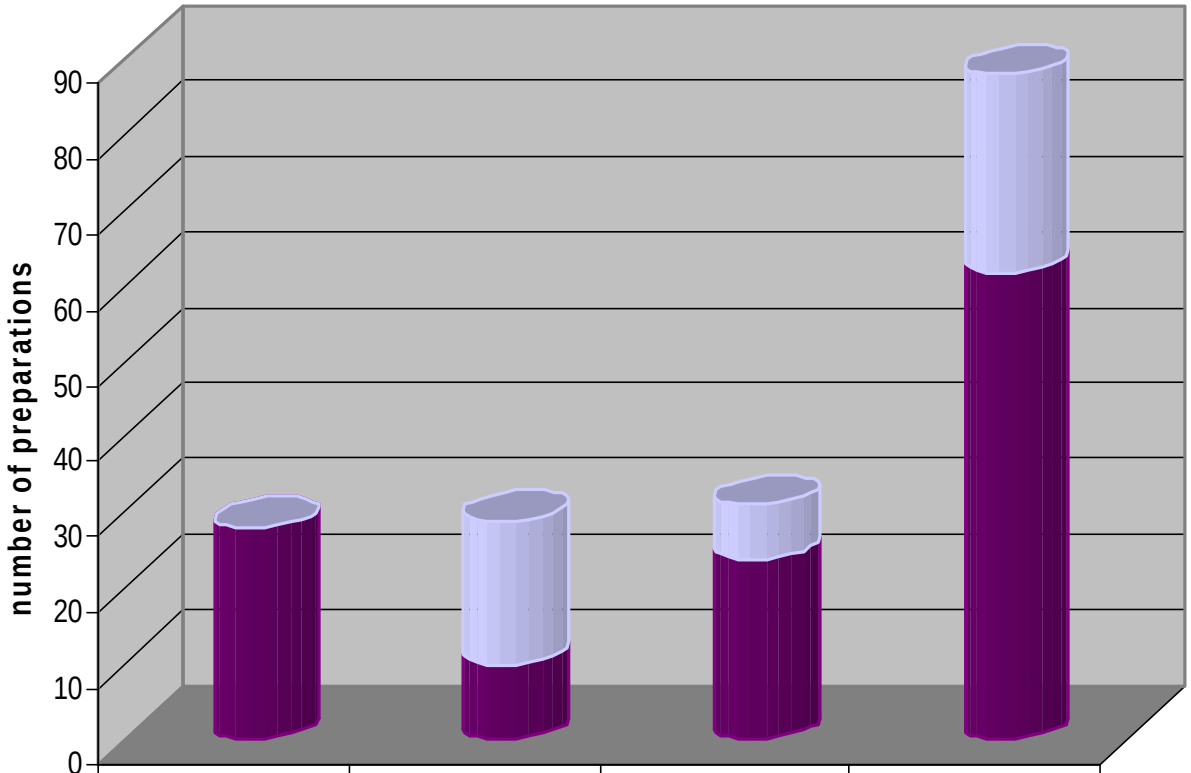
A tool for comparison of results worldwide



WHO Biological Reference Preparations

In vitro Biological Diagnostic Procedures

Priority Drive: Safety



	Blood Safety and General Hematology	Blood Coagulation and Thrombotic Disorders	Immunological Disorders	Total
Therapeutic products	0	19	7	26
In vitro diagnostic tests	28	10	24	62

Medical field application

WHO BIOLOGICAL REFERENCE PREPARATIONS

How are they developed & established?

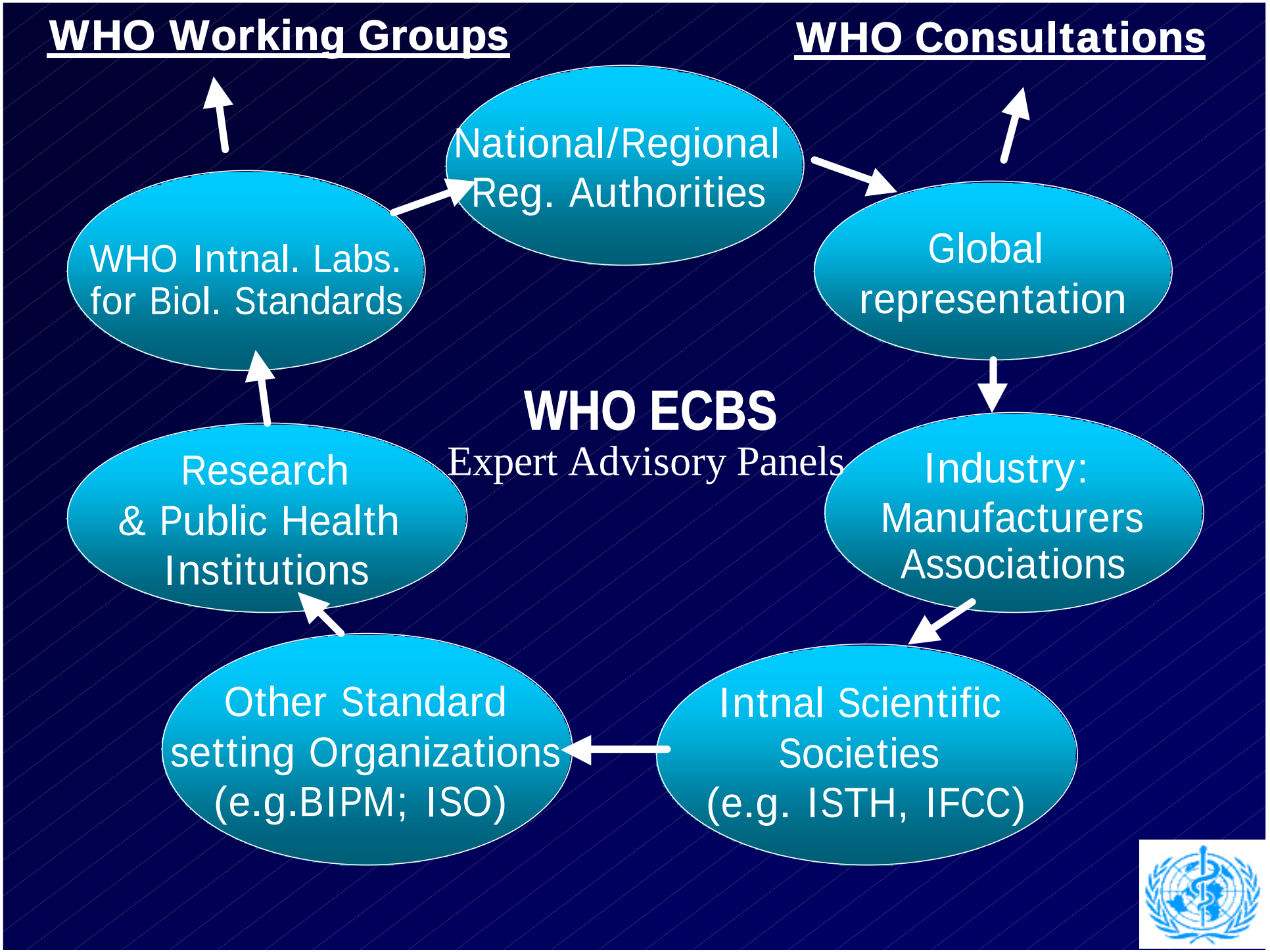
- Candidate materials donated (industry, PHL, academy)
- Freeze-dried materials (when possible)
- WHO Collaborative studies to assign values (not funded)
- Wide international collaboration (WHO Working Groups)
- Established by WHO Expert Committee on Biological Standardization (ECBS)

- Held and distributed, on behalf of WHO, by the WHO International Laboratories for Biological Standards

↗WHO Guidelines for the preparation, characterization and establishment of international and other standards and reference reagents for biological preparations (WHO TRS No. 800, 1990)

WHO Working Groups

- Scientific issues involved in the standardization of the new biological technology/type of product
- Selection & characterization of candidate materials
- Design protocols for WHO Collaborative studies
- Harmonization of procedures & reagents
- Issues concerning the appropriate use of materials


WHO Working Groups
WHO Consultations
National/Regional
Reg. Authorities
WHO Intnal. Labs.
for Biol. Standards
Global
representation
WHO ECBS
Expert Advisory Panels
Research
& Public Health
Institutions
Industry:
Manufacturers
Associations
Other Standard
setting Organizations
(e.g.BIPM; ISO)
Intnal Scientific
Societies
(e.g. ISTH, IFCC)

Existing, New and Emerging Technologies

How do we approach standardization of:

- *Existing* technologies: Replacement of HBsAg IS
- *New technologies* : NAT IS
- *Emerging* technologies: Prion Diseases

“Existing” Technologies

Main Issues:

- Replacement of the subsequent batch in time: Subsequent batches calibrated versus (at least) the previous standard
- Continuity of Unit of biological activity defined by the 1st IS
- Changes in the methodology with time

Replacement of the 1st International Standard for HBsAg: WHO collaborative study

- No drift in the value of the HBsAg measurement standard (expressed in IU) since its establishment 20 years ago
- Appropriate quantity to measure is biological activity (IU) and not protein concentration (ng/ml).
- Global regulatory recognition that all measurement for HBsAg diagnostic tests to be reported in IU and traceable to WHO IS.

“New” Technologies

Priority Drive

- Impact on Global Public Health
- Need for international harmonization of regulations
- Timely standardization of the technology

Nucleic Acid Based Technology (NAT)

Blood safety & Clinical Diagnostic

NEED FOR INTERNATIONAL HARMONIZATION (1995)

- Powerful technology: detection of viral nucleic acid
- Reduction of viral load entering manufacturing processes
- Investigation of removal/partitioning of viral nucleic acid in manufacturing steps
- Clinical safety monitoring
- Tracing of viral transmission by a blood product

WHO Biological Reference Preparations

Standardization of Nucleic Acid based technology
applied in the detection of blood-borne viruses

HCV RNA
HBV DNA
Parvovirus B19 DNA
HAV RNA

HIV-1 RNA
HIV-1 RNA Ref. Panel

Aim

- to provide a tool for inter-laboratory data link
  (analytical sensitivity)

Impact

- Support blood products safety regulations worlwide
- Measurement of viral load: monitoring the disease

Held and distributed by the WHO International Laboratories for Biological Standards
Catalogue available on www.who.int/biologicals

“Emerging” Technologies
Study of Prion Diseases

Priority Drive

- Impact on Global Public Health
- Facilitate the exchange of information and knowledge
- Facilitate development and comparison of diagnostic approaches and assay systems for study of new diseases

Human Prion Diseases (vCJD/CJD)

In progress.....

Development of Reference Panels:
Brain, tissue and blood human derived materials from sporadic CJD & vCJD cases

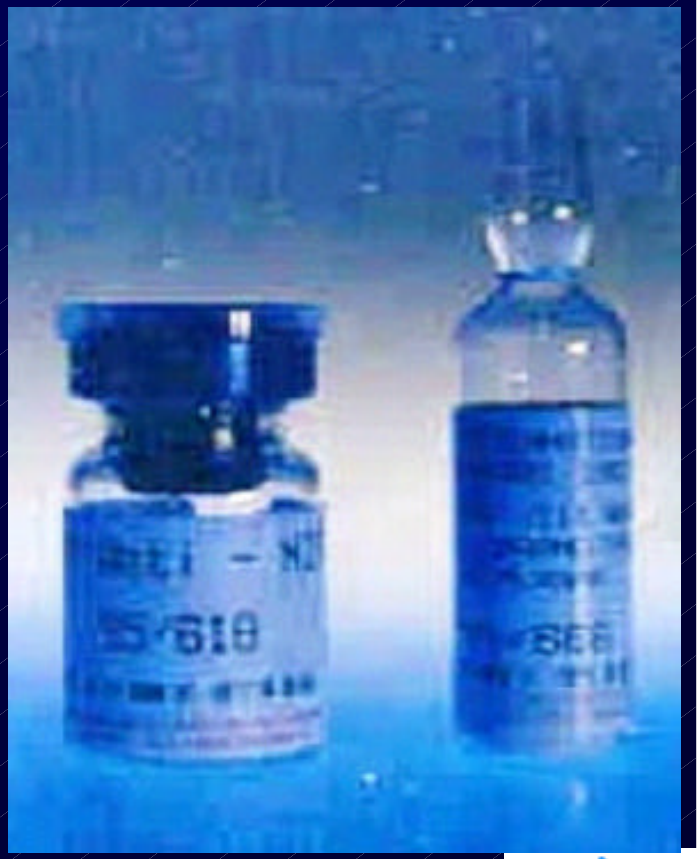
- to facilitate CJD and vCJD diagnostic procedures aimed to identify infected individuals, organs and tissues

- to facilitate risk assessment of pharmaceutical manufacturing processes to remove infective agents

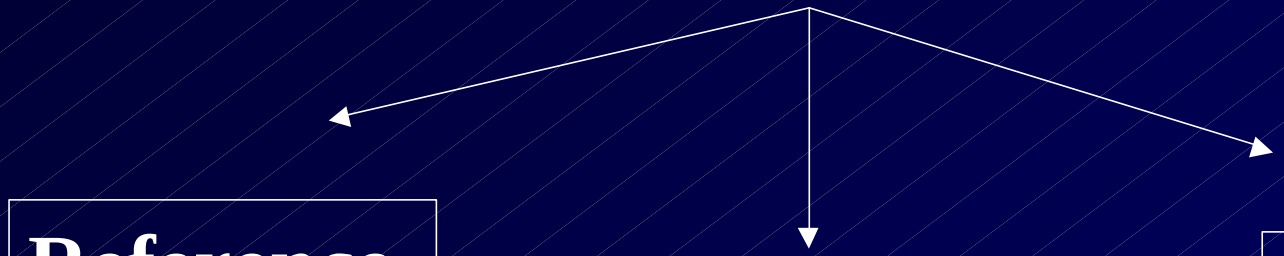
Challenges/Limitations

Challenges (I)

- Biological standardization is a specilized scientific exercise with rapid development
- Need to address existing, new and emerging technologies with impact in public health
- Need to keep pace with new approaches in standardization
- Coordination with other standard setting organizations (e.g. ISO)



The Reference system (ISO/DIS 17511)
(Intnal Conventional Reference Materials)



Reference material

Reference method

Reference laboratory

The application of the reference system is intended to provide:

traceability & quantification of uncertainty

The Reference system (ISO/DIS 17511)
(Intnal Conventional Reference Materials)

Difficulties, based on scientific issues, have been identified in implementing the ISO 17511 for the development of biological reference materials as defined by WHO and in the biologicals field. This needs to be resolved.

More collaboration and communication needed

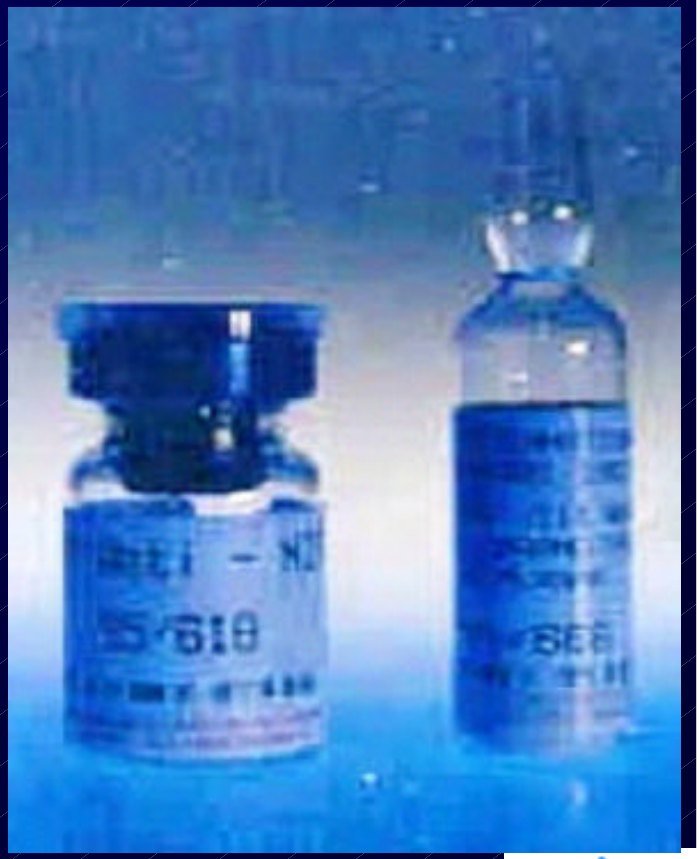
New Initiative

Use of the global measurement standards in the regulation and quality control of *in vitro* biological diagnostic procedures (high risk IVDs):

- WHO Consultation of regulatory authorities, manufacturers & standard developers (May 2004)

Challenges/Limitations (II)

- Proliferation of tests in the biological field: **international-global issue**
- Need for standardization essential to the regulation and quality control of those tests
- Need to assure access to appropriate reference materials by developing countries
- Need to promote appropriate use of biological reference materials



WHO Biological Reference Preparations
WHO Catalogue

- Web site address:

http://www.who.int/biologicals

Essential Health Technologies
Health Technology and Pharmaceuticals Cluster
World Health Organization