Standards and Reference Materials for Laboratory Medicine for Better Patient Care

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in vitro diagnostic medical devices

Laboratory medicine contributes to better patient care

- Screening of populations for early diagnosis
- Confirmation of presence or absence of disease
- Choice of treatment
- Monitoring of therapeutic levels of drugs
- Monitoring of patient care (e.g. diabetes)
  - Self-management of patients
- Safety of blood products
- Compatibility of transplants
- Predisposition for diseases

Spectrum of disciplines

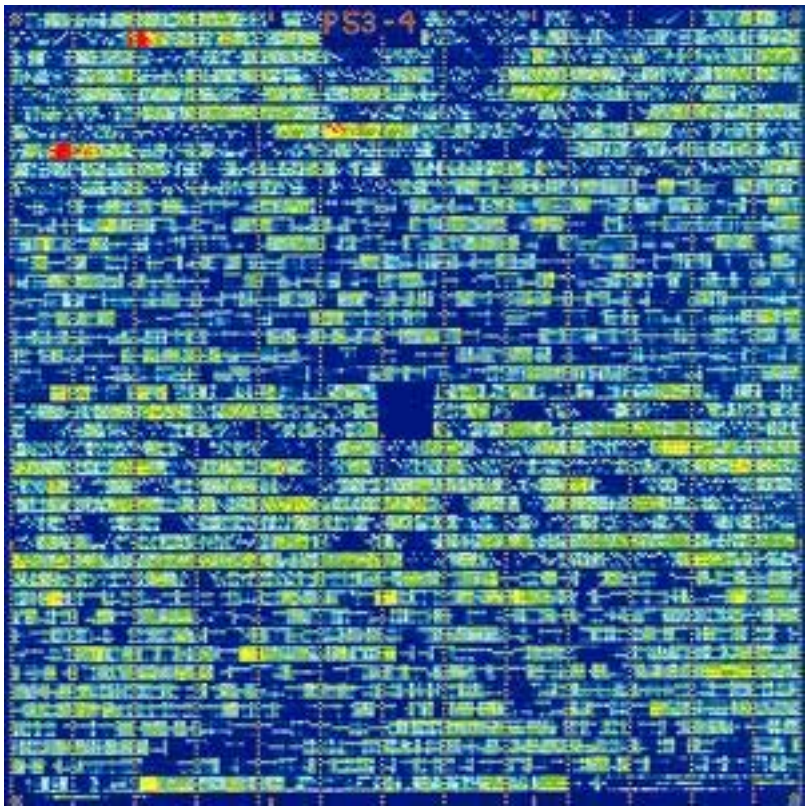
- Clinical Chemistry
- Immunology (hormones, proteins, tumour markers …)
- Serology
- Hematology – Hemostaseology
- Histology
- Microbiology
- Virology
- Nucleic Acid Techniques (DNA, RNA)

Development of technology - pregnancy testing

1960

1980

Development of Nucleic Acid Technologies



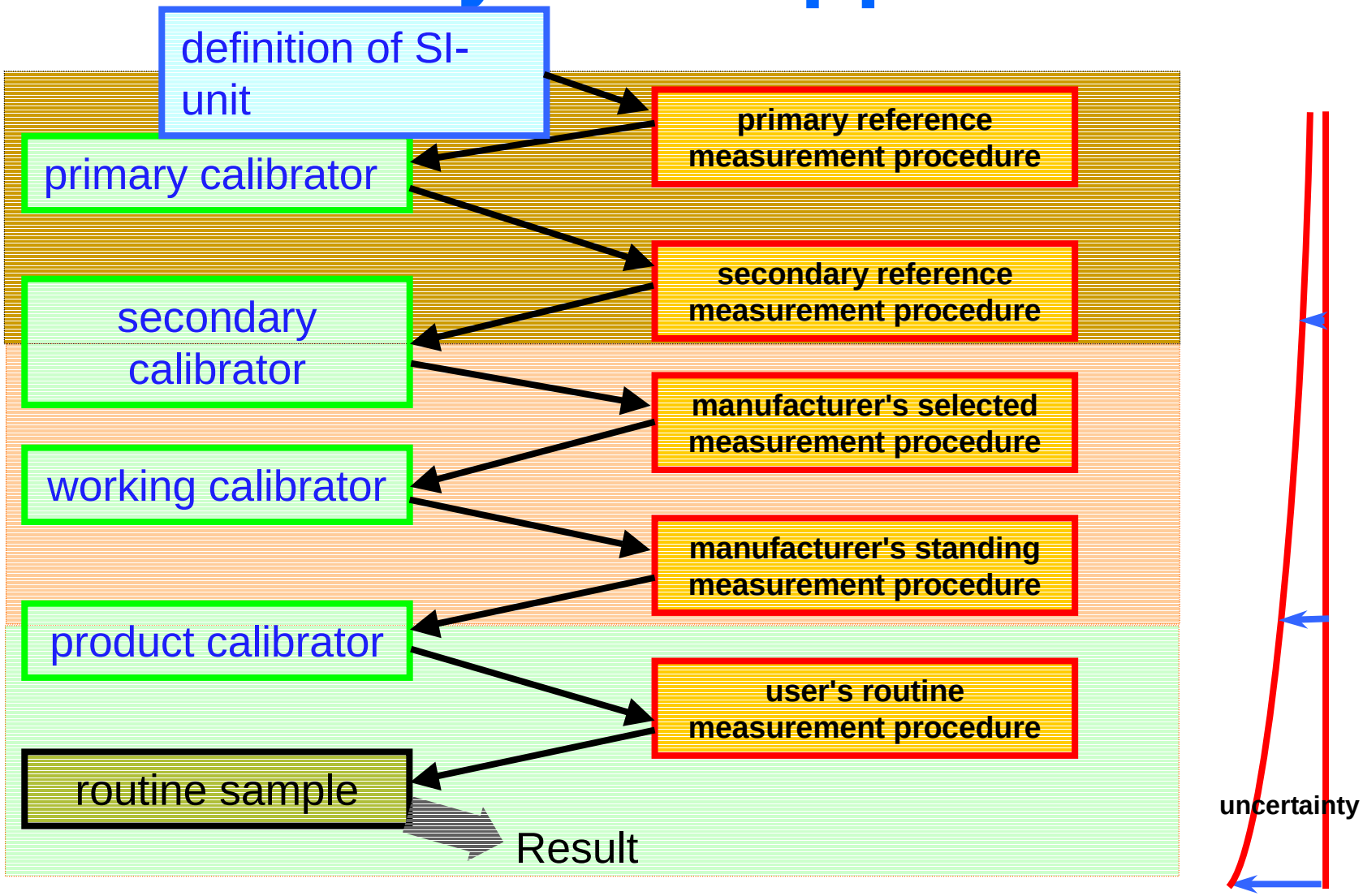
The Directive 98/79/EC on *in vitro* diagnostic medical devices

- The Directive regulates the development and marketing of in-vitro diagnostics. It addresses mainly manufacturers of in vitro diagnostics, but has implications for the users as well
- It specifies requirements on the quality and safety of products intended to be placed on the market in the European economic area
- Amongst other requirements it aims at comparable results for patient data across methods, time and geographical region

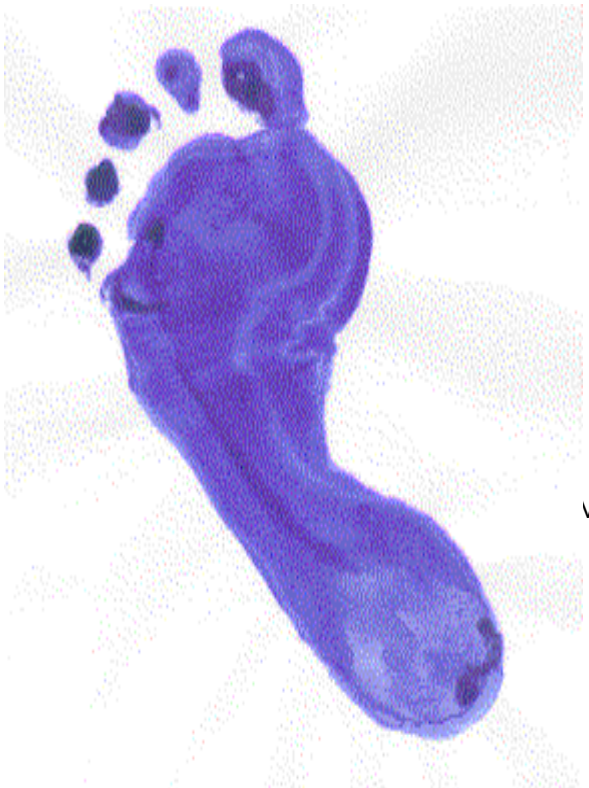
Mandated standards

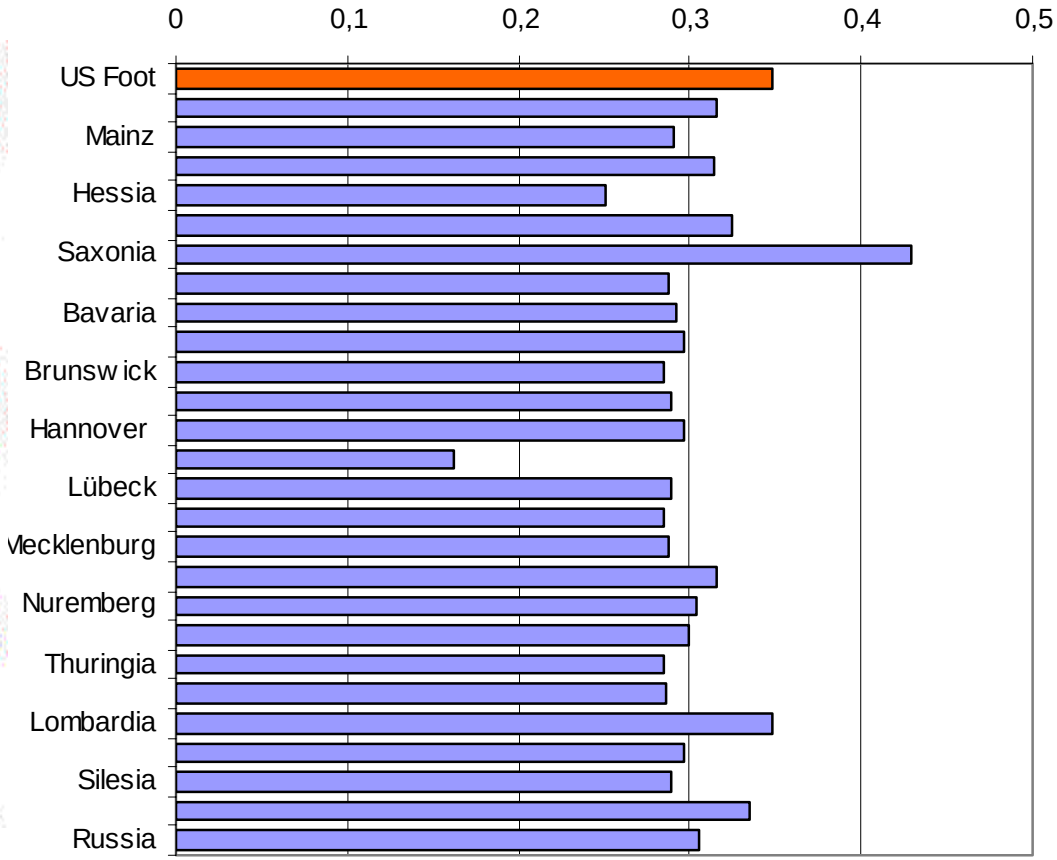
- To support the directive CEN/TC 140 was charged with the development of appropriate standards
  - Labelling and performance evaluation
  - Quality systems and quality management
  - Biological staining and culture media
  - Reference systems
  - IVDs for self-testing
  - External quality assessment
  - Specimen containers

Traceability - the approach



The importance of reference systems





Traceability

- For implementation of the concept in its complete form, i.e. traceability to the highest metrological order we need
  - a clear definition of the analyte
  - a description of the reference measurement procedure
  - a suitable reference material
- There are some 1500 different analytes which are determined in clinical laboratories - but only for some 60 of them these requirements are met on an international level
- In many cases there are no reference materials available in a suitable matrix

The importance of WHO biological standards

- They are most widely used as reference material to calibrate IVD-products
- However, they do not necessarily guarantee identical findings in patient results in all cases, even when different manufacturers claim traceability to the same preparation
- There are considerable lot-to-lot variations which make them unsuitable for calibration of in vitro diagnostic procedures
- But they are the only reference materials presently available

Pragmatic solutions are required

- **Physicians need consistency of results**
- **In many cases the measured analyte is in fact a mixture of many substances (Isoforms). Immunological procedures will differ, because usually different epitopes are addressed**
- **Carefully selected panels of human samples are the most appropriate surrogates**
- **In nucleic acid testing the use of synthetic material representing the genetic sequence are under investigation**

Industry supports the traceability concept

- It is a legal requirement (IVD-Directive and national transposition) in EU-countries
- It is accepted not only in Europe, but also in other countries
- It is promoted by IFCC and other scientific organisations
- It will provide the basis for direct comparability of patient results over geographical regions and time and thus provide a benefit to patients and physicians
- It will allow manufacturers to base their calibration on internationally harmonized reference systems and will permit global marketing of products

Standards provide a suitable framework – WHO support is needed

- The organization is globally present and has access to suitable samples
- Its scientific and educational expertise could provide invaluable assistance
- By taking into account the requirements and needs of laboratory medicine for appropriate reference materials and panels it would contribute to better healthcare
- This would benefit patients, physicians, licensing authorities and manufacturers

Requirements for reference materials

- Values assigned by appropriate procedures
- Homogeneity
- Stability
- Commutability
  - nature of matrix
  - nature of constituents (e.g. Isoenzymes, Isoforms)
  - processing (stabilisers, additives, lyophilisation, freezing / thawing)

In many cases only surrogate materials are feasible - carefully selected panels of human samples are the most appropriate surrogates

JCTLM - Joint Committee on Traceability in Laboratory Medicine

- Organized by **BIPM** (Bureau International des Poids et Mesures) **and IFCC**
- **Supported by interested constituencies (IRMM, NIST, metrological institutes, scientific organisations, reference laboratories, industry etc.) on a global scale**
- **Exchange of information and establishing a network**
- **To set priorities for projects**
  - **medical relevance**
  - **possibility of improvement**
  - **resources**