# Laboratorio di Tecnologie Biomediche

## *Introduction to medical devices*

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# Medical Device

- A Medical Device is identified by means of its INTENDED PURPOSE
- Intended to treat, prevent or control physiological characteristics of a living being
  - Disease
  - Handicap
  - Conception
  - Anatomy
  - ...

# Some example of medical device

- Band aids
- Incontinence pads
- ECG
- RMI
- Heart valves from bovine or porcine tissue
- Knee joints
- Hearing aids
- Vessel mesh
- Bone fillers
- Dental implants
- Bone screws both removable or permanent
- Defibrillators
- IV sets
- Syringes
- Eye drops (artificial tears)
- ....and on

# Comments

- Use on humans (or animals on a lower grade of regulation)
- Intended to have a MEDICAL purpose, excluding devices intended for
  - Esthetical purposes
  - Research not aimed to marketing of the device
- Multiple ways of interacting with the human body
  - Implant to NO corporeal interaction (medical SW)
  - Temporary or permanent
  - Acute or chronic
  - Energy or substance exchange
- Clinical effectiveness vs efficacy
- Performance: technical performance + clinical effectiveness (SAFE and EFFECTIVE)

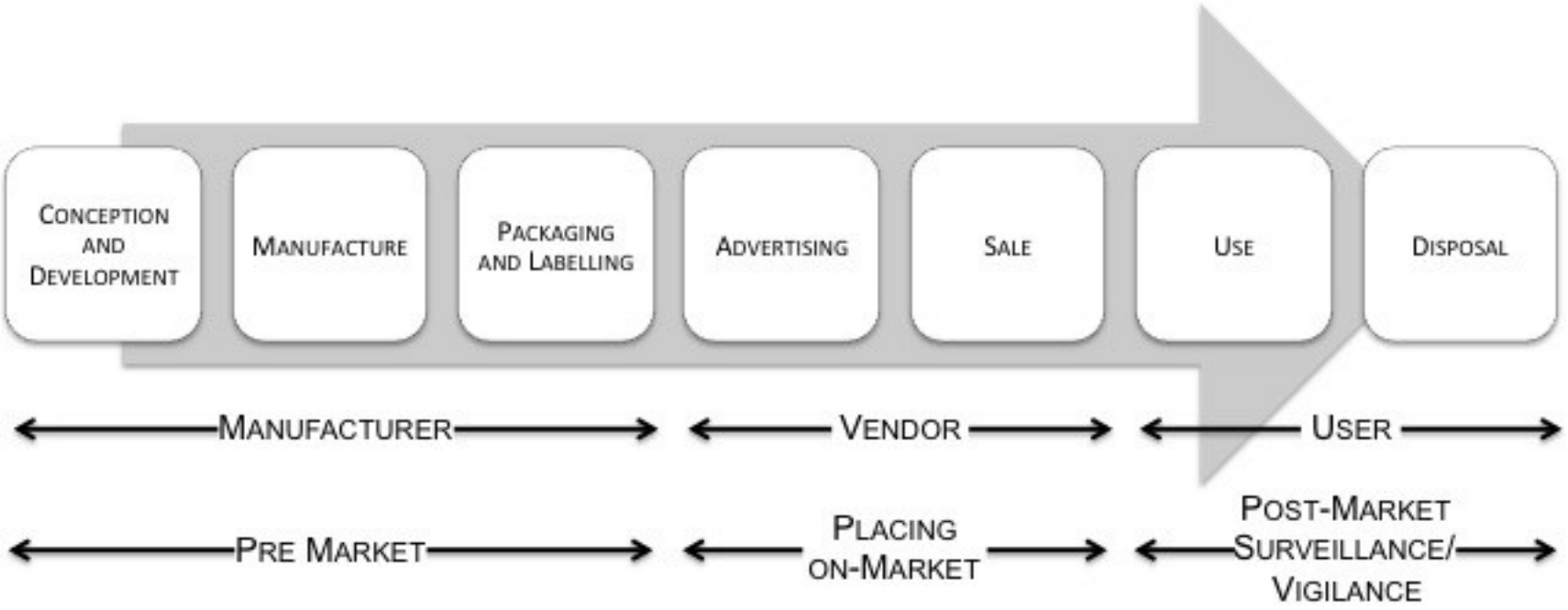
# Medical Device Safety

- Absolute safety cannot be guaranteed
- It is a risk management issue
- It is closely aligned with device effectiveness/performance
- It must be considered throughout the life span of the device
- It requires shared responsibility among the stakeholders

# Medical Device Safety

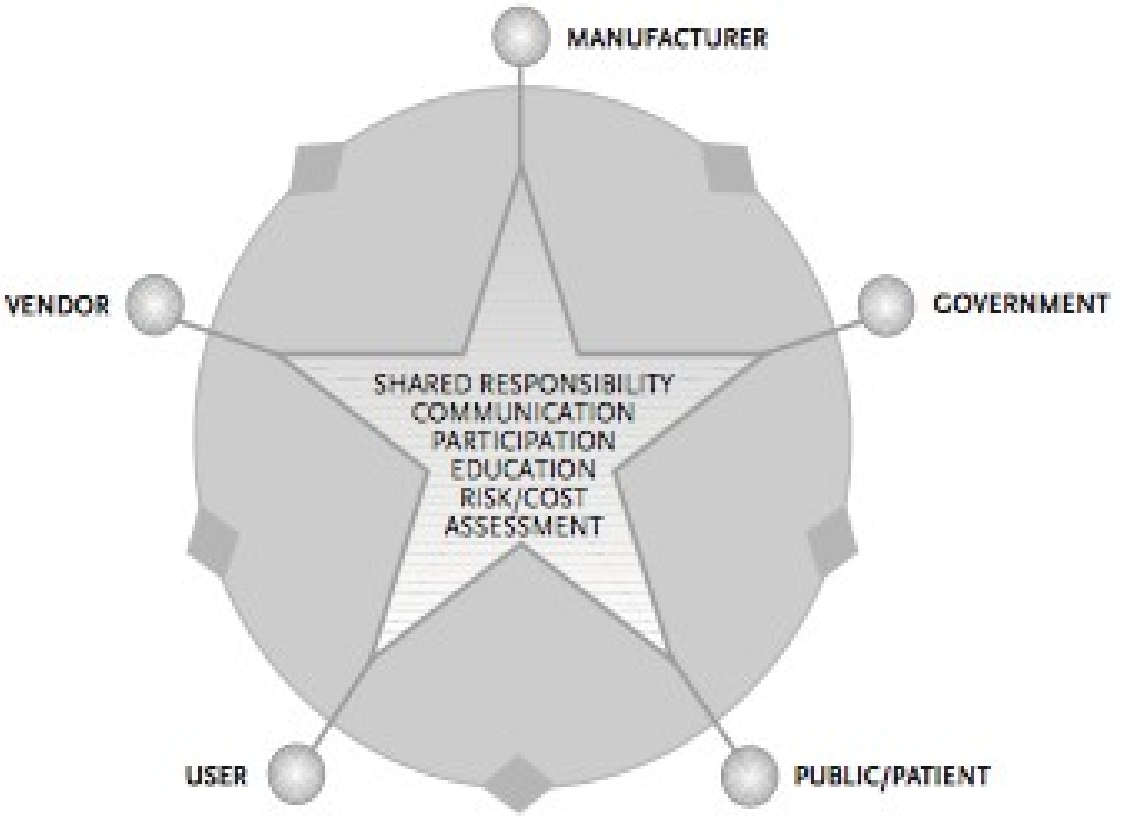
- Risk assessment
  - Potential risks associated with the devices
- Criteria
  - applied to a vast range of different medical devices and technologies
  - combined in various ways in order to determine classification
- Risk management
  - Higher for higher risk classes
  - From self- declaration to comprehensive device and company audit by Notified Body

# Life cycle of a medical device



# Stakeholders

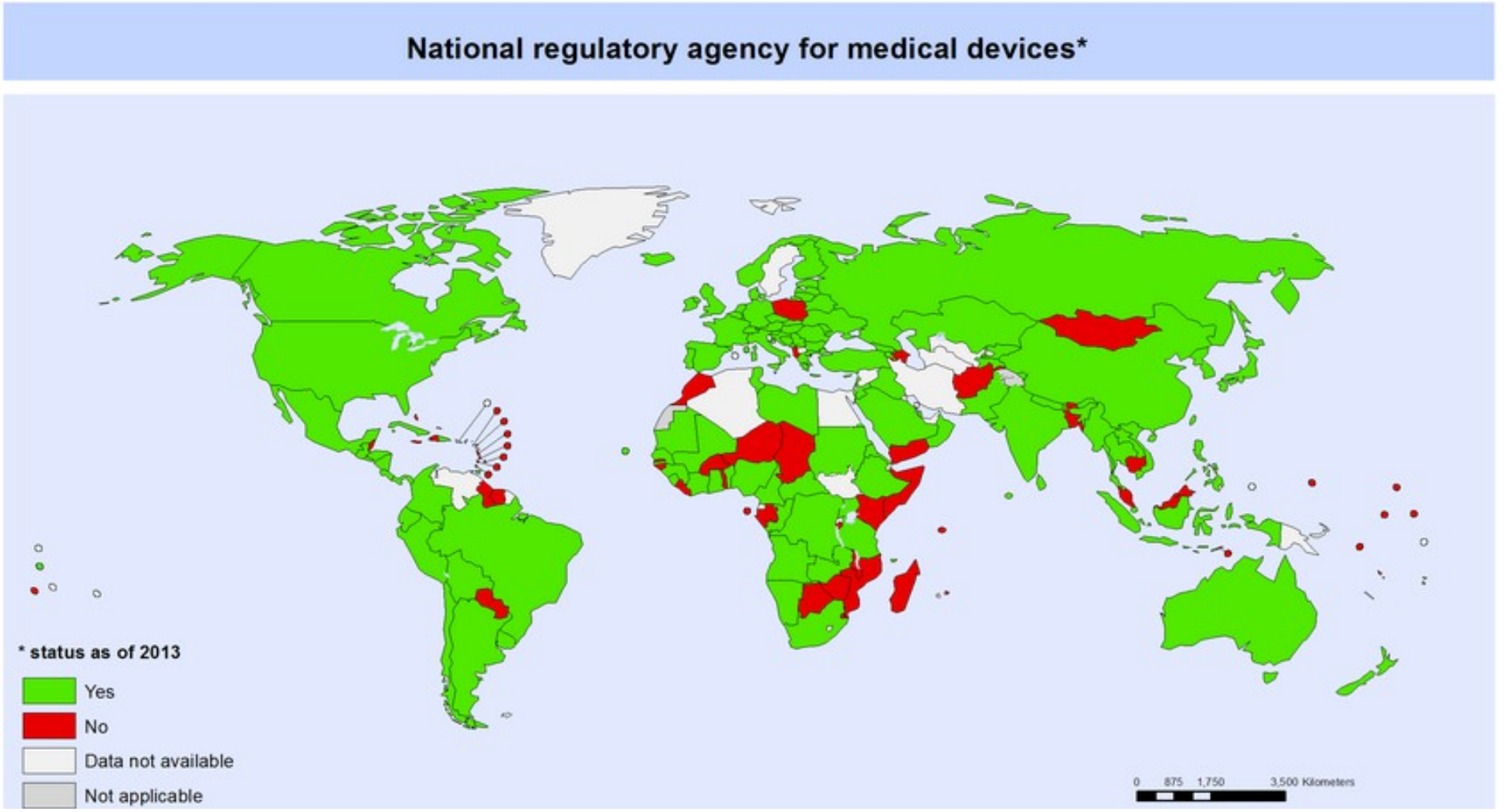
- Manufacturer
- Vendor
- User
- Public / Patient
- Government



# Standards & regulations

- Standards
  - Recommendations
  - Use is voluntary
  - Available to the public
  - Established by consensus of all parties concerned
  - Based on consolidated results of science, technology and experience
  - Approved and published by recognized standardisation body
- Regulations
  - Legislation
  - Use is mandatory
  - Available to the public
  - Developed by an authority under public observation
  - Provide technical specifications either directly or by reference, e.g. to standards
  - Adopted by an authority

# Standards & regulations



# Standards & regulations

- Efficient regulations system means:
  - Safety for patients and workers
  - Higher quality of devices
  - Reliability in diagnostic exams
  - Healthcare for the whole community

# Standards & regulations

- International regulation agencies for global harmonization
  - WHO, Harmonization Task Force (GHTF, no more active) , International Medical Devices Regulatory Forum (IMDRF)
- International regulation agencies for regulatory harmonization in a specific area
  - Europe, Africa, Asia, …
- National regulation agencies

# Standards & regulations

- WHO promotes and recognizes the guidance provided by the 5 study groups of the Global Harmonization Task Force (GHTF) during the last 20 years.
- WHO is an official observer in the managemer committee of the International Medical Devices Regulatory Forum (IMDRF).

World Health Organization

# Standards & regulations

- The International Medical Device Regulators Forum (IMDRF) was conceived in February 2011 as a forum to discuss future directions in medical device regulatory harmonization (www.imdrf.org)
- It is a voluntary group of medical device regulators from around the world who have come together to build on the strong foundational work of the Global Harmonization Task Force on Medical Devices

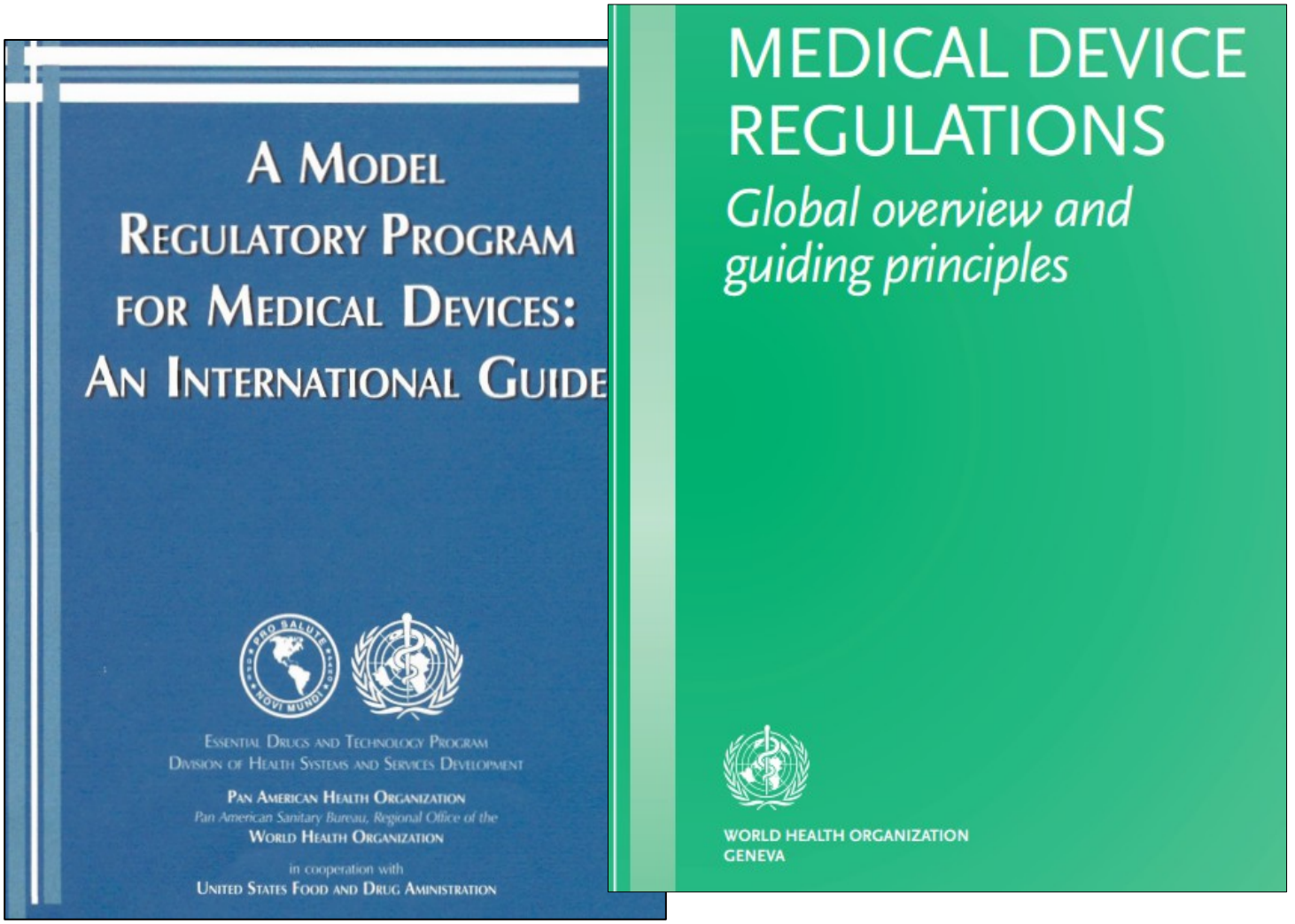
IMDRF International Medical Device Regulators Forum

# Standards & regulations

- Europe:
  - European Committee for standardization (CEN)
- USA
  - Food and Drug Administration (FDA)
- South America
  - Latin American Harmonization Working Party (LAHWP)
- Asia
  - Asian Harmonization Working Party (AHWP)
- Africa
  - Pan African Harmonization Working Party on Medical Devices and Diagnostics (PAHWP)
  - NEPAD with African Medicines Regulatory Harmonization Programme

# Standards & regulations

Available in a free pdf version on the WHO website, www.who.int

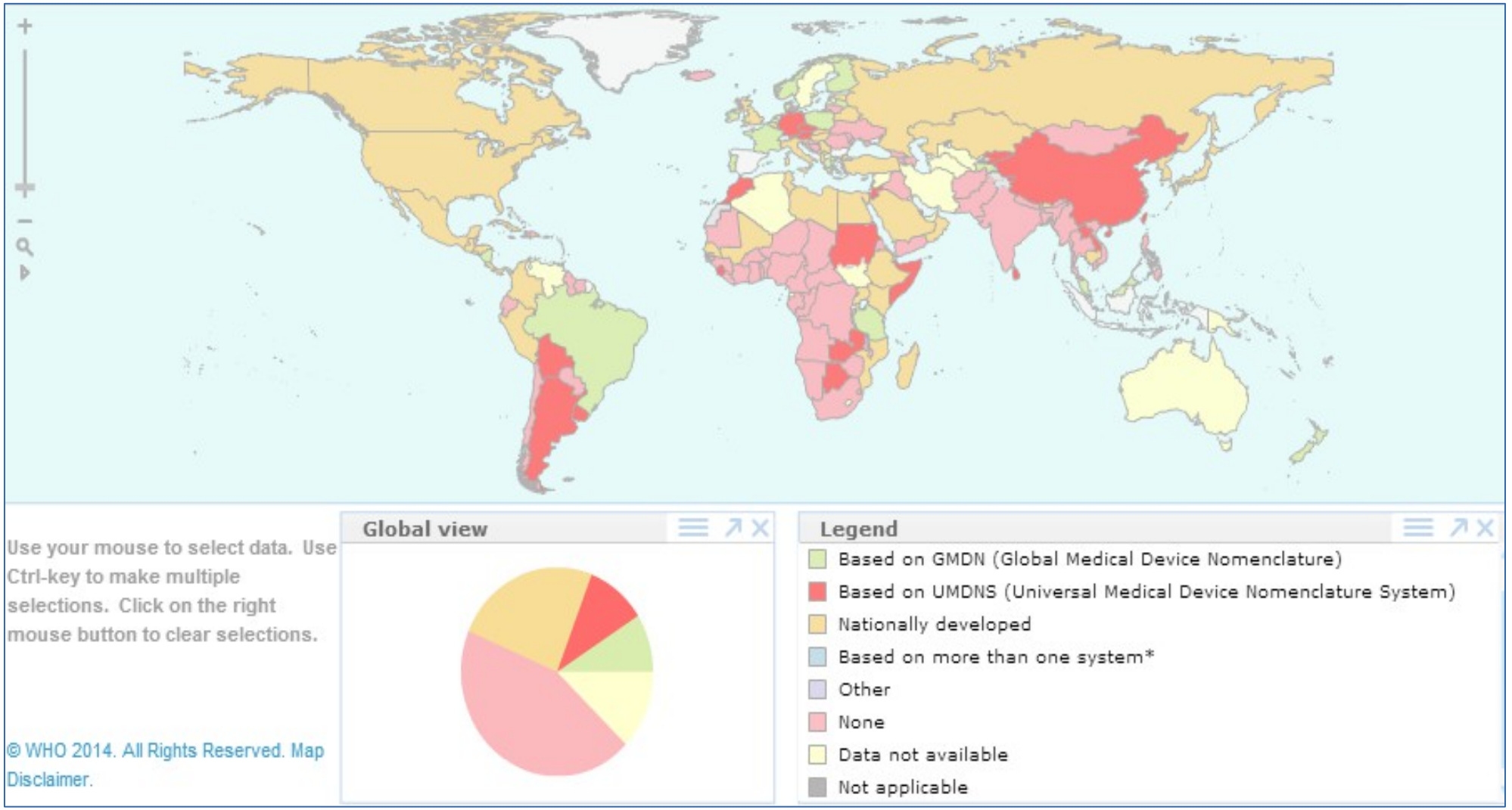


# Standards & regulations

- A nomenclature system is also useful to classif devices and harmonize regulations.
  - GMDN agency: Global Medical Device Nomenclature (www.gmdnagency.com)
  - ECRI institute: Universal Medical Device Nomenclature System (UMDNS) (www.ecri.org)


# Standards & regulations

## Nomenclature distribution

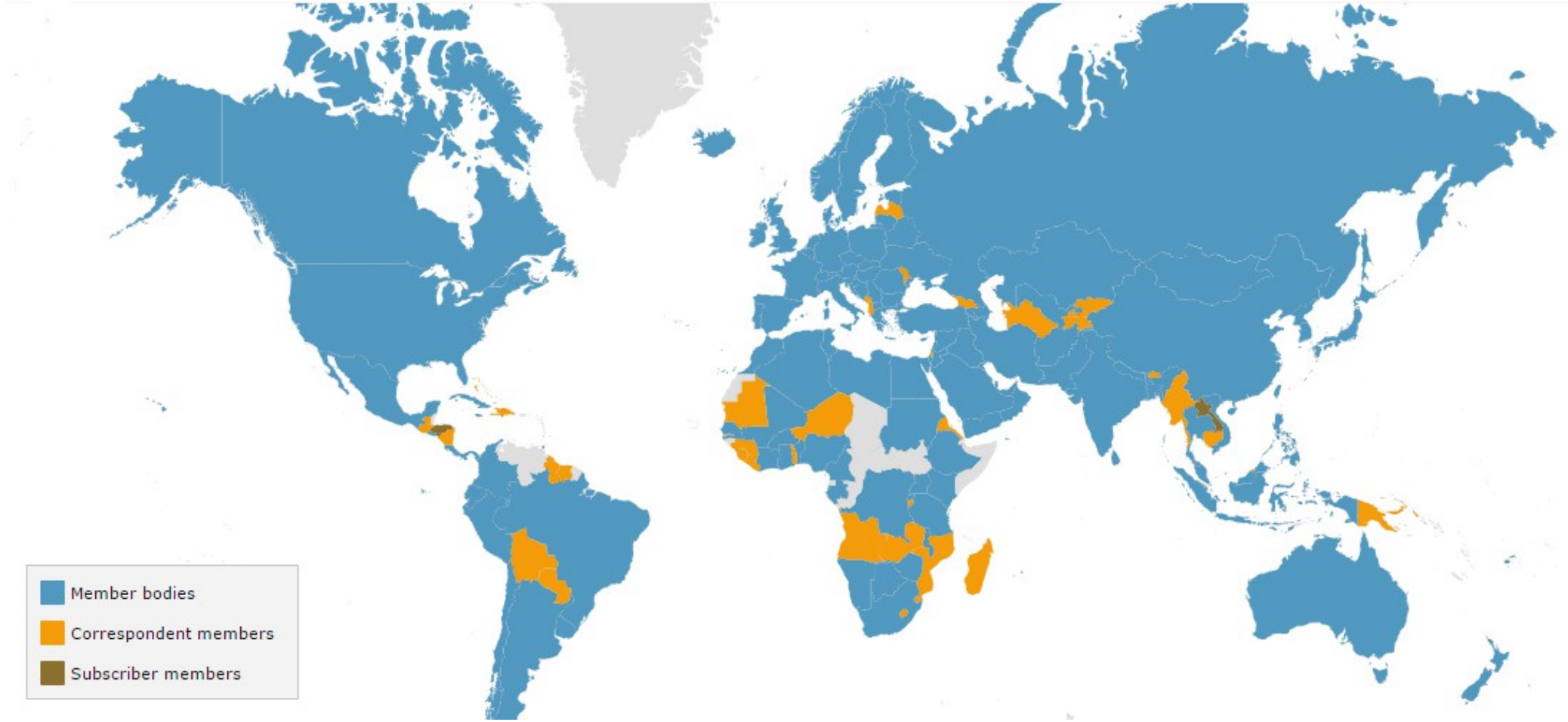


# ISO standards

- Non-governmental membership organization
- The world's largest developer of voluntary International Standards
- Members from 165 countries and 3,368 technical bodies to take care of standard development

# ISO standards

## ISO Members

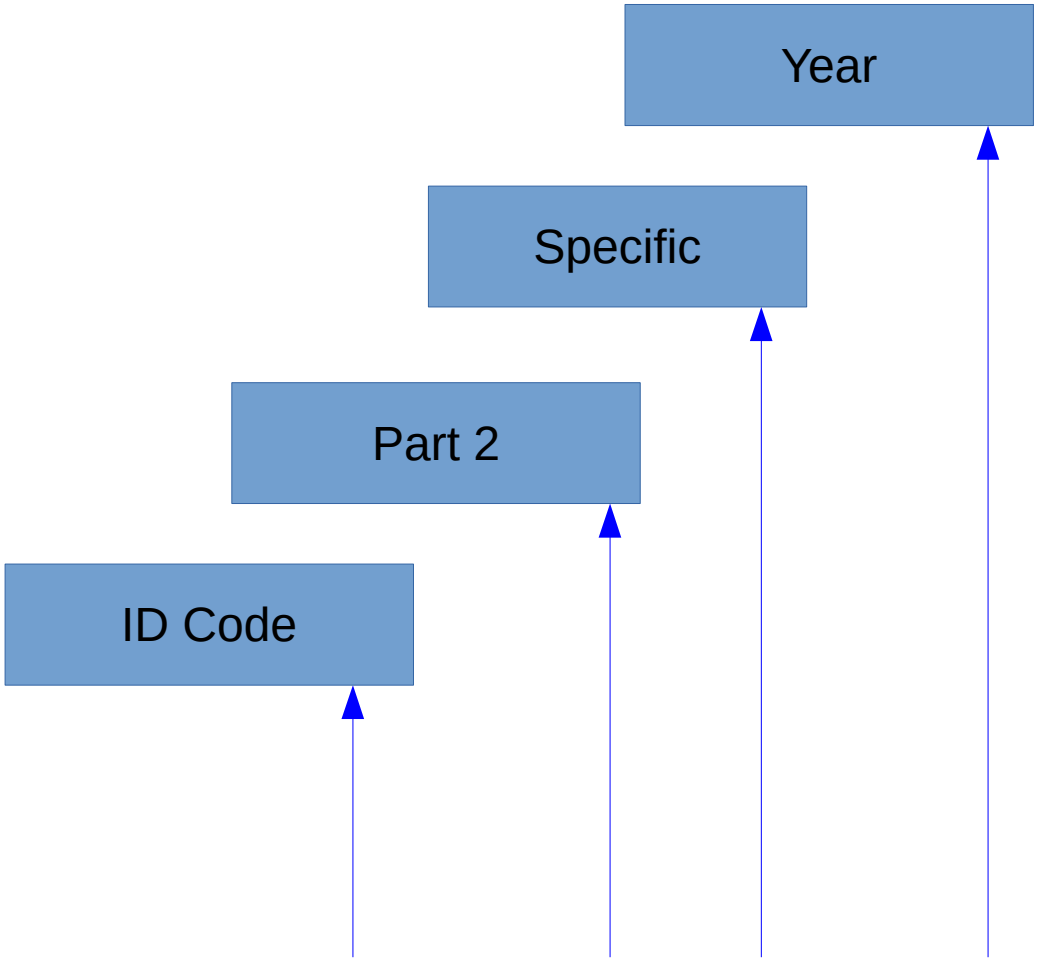


# ISO standard

- Typical ISO standard structure:
  - Definition of application field
  - Definition of technical terms used in the document
  - Regulatory references
  - Technical regulations
  - Technical tables and appendixes
- ISO standards are not free

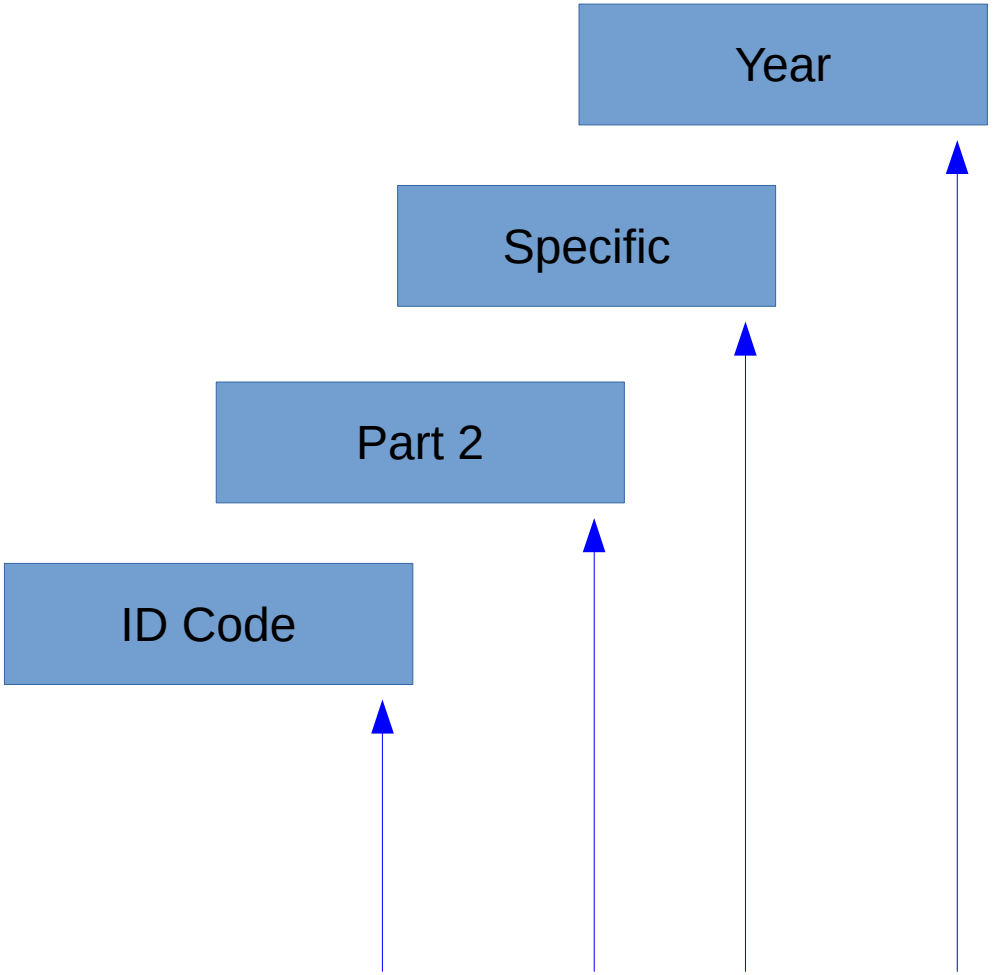
# Identification of a standard

- CAN/CSA-Z386-94 means a standard developed in 1994 by the Canadian Standards Association (CSA, one of four accredited Canadian standards development organizations) and designated by the Standards Council of Canada (SCC) as a Canadian national standard.
- ANSI/AAMI/ISO 15223:2000 means the international standard ISO 15223 (established in 2000) adopted by the Association for the Advancement of Medical Instrumentations in the United States, which in turn is designated by the American National Standards Institute (ANSI) as an American national standard.
- **UNI EN ISO 9001** indicates an Italian national standard (UNI) which is an adoption of a European standard (EN), which is itself an adoption of the International Standard ISO9001.




# ISO 80601-2-56:2009

Medical electrical equipment -- Part 2-56: Particular requirements for basic safety and essential performance of clinical thermometers for body temperature measurement




# ISO 80601-2-12:2011

Medical electrical equipment -- Part 2-12: Particular requirements for basic safety and essential performance of critical care ventilators

- **European Medical Device Directive (MDD)**

More detailed slide-show at
http://www.centropiaggio.unipi.it/course/material/direttiva-dispositivi-medi

# Medical device directive (MDD)

- The MDD is a law that regulates the marketing of Medical Devices in the European Community
- Details the device identification
  - Classification
  - Application (custom made, research, marketing...)
- Defines manufacturers responsibilities and duties
  - Essential Requirements for safety and performance
  - Surveillance
- Gives powers to the Local Authorities to control the putting on the market of the devices

# Risk classes: criteria

- Intended use
  - central circulatory or nervous systems increase class
- Duration of use
  - duration increases class
- Kind of contact with the body
  - not invasive,
  - invasive,
  - implantable
- Energy supply
  - Active or not active

# Classification and control

- Class I:
  - self declaration of compliance by manufacturer
  - band aids, ready-made reading glasses, surgical masks and gloves
- Class IIa and IIb:
  - preliminary and annual audit by Notified Body on Technical File and on Manufacturing
  - Haemodialysis lines and machines; ECG; ventilators; needles of syringes; scalpels; tracheal tubes; ultrasound fetal heart detectors
- Class III:
  - preliminary and annual audit by Notified Body on Design file, Technical File and on Manufacturing
  - Bovine heart valves; deep brain stimulators for Parkinson; bone implants with antibiotic; Coronary drug eluting stent; cerebrospinal drains

# Special classes

- Custom made:
  - self declaration + clinician prescription
  - Glasses; dentures; most orthoses
- Clinical investigation:
  - Special authorization by CA and EC
  - Devices not yet legally approved, innovative
- Compassionate use:
  - special authorization by CA and EC

# EU MDD

- Legally binding indications on how to:
  - Design
  - Test and Validate (according to applicable Norms)
  - Manufacture
  - Control
  - Surveillance and return information
- No Medical Device can be used without prior CE Marking
  - Exceptions for devices under (phase three) clinical investigation
- The National Authorities collect information for the European Database

# Scope of the MDD: QMS

- Quality of products must be consistent over time
  - Manufacturer responsibility
  - Control by Notified Body for higher classes
- Quality is the output of a complete management system
  - Design
  - Manufacturing
  - Control and product release
  - Connected activities: maintenance, training, environmental control and cleanliness, sterility

# Annex 1 of MDD – essential requirements

| No. | Scope |
|---|---|
| | **Part I - General Requirments** |
| 1 | Risk reduction, acceptable risk/benefit |
| 2 | Safety and risk controls |
| 3 | Intended performances |
| 4 | Lifetime of the device |
| 5 | Transportation and storage |
| 6 | Side-effects must continue acceptable risk |
| 6a | Clinical evaluation |
| | **Part II - Design and Construction Requirements** |
| 7 | Chemical, Physical, Biological Properties |
| 8 | Infection and Microbial Contamination |
| 9 | Construction and Environmental properties |
| 10 | Properties for devices with measuring function |
| 11 | Protection against radiation |
| 12 | Protection against Electrical, Mechanical, Thermal risk, Energy supplies or Energy substances |
| 13 | Information supplied by manufacturer |

# Device dossier

- Technical document required by authorities to prove compliance to Essential Requirements
- Descriptive and proof of compliance
  - Tech features (drawing, composition,...)
  - Risk management
  - Bench, in vitro, in vivo testing
  - Clinical data

# Norms

- Device lifecycle is regulated as per:
  - ISO 13485 for Quality Systems
  - ISO 14971 for Risk Management
  - ISO 14155 and various guidelines for Clinical Investigations
- Each product category is then regulated by technical norms
  - For electro medical devices
  - For sterile devices
  - For devices in contact with the body
  - Multiple harmonised and not harmonised norms for technical regulation

# Standard for biocompatibility

- **ISO 10093**
- Assessment of device impact on human body in terms of risk of bio-incompatibility
- Device identification: materials, manufacturing methods, sterility level
- Evaluation of available information
- Planning of test to collect new information
  - Material characterization
  - In vitro
  - In vivo

# Standard for biocompatibility

- **ISO 10093**
- Recognized world-wide, if applied by:
  - certified labs (ISO 17025 or similar accreditation)
  - According to Good Laboratory Practices

# Standard for biocompatibility

- **ISO 10093**
- Evaluation of available information (source of data – clause 4.1)
  - Review and evaluation of existing data from all sources
    - Literature
    - Company data on similar devices
    - Supplier declarations
  - Selection and application of additional tests

# Standard for biocompatibility

- **ISO 10993**
- Device identification:
  - MDD: classification by the intended use
  - ISO 10993: classification by the kind of body contact
    - Nature
    - Duration

# Standard for biocompatibility

- **ISO 10993**
- Nature of body contact (clause 5.2)
  - Surface
    - skin, (band-aids, electrodes)
    - mucose, (contact lenses, intra vaginal devices,...)
    - breached surface (wound dressing)
  - External path
    - indirect blood path (IV sets)
    - tissue as path (laparoscopes, draining tubes)
    - blood circuits (ECMO)

# Standard for biocompatibility

- **ISO 10993**
- Nature of body contact (clause 5.2)
  - Implant devices
    - Tissue (filling gel, pacemakers)
    - Bone (replacement joints, bone cement)
    - Blood (heart valves, stents)

# Standard for biocompatibility

- **ISO 10993**
- A: Limited - 24h or less
  - Needles
  - Internal defibrillation electrodes
- B: Prolonged – 24h to 30 d
  - catheters
- C: Permanent – 30d plus (even intermittent)
  - Implants
  - Repeated use devices

# Standard for biocompatibility

- **ISO 10993**
- Biological testing:
  - Only if no past data are available
  - On the (sterile) final product, form commercial manufacturing
  - Test planning as per annex A
  - Test protocol to identify correct procedures
  - VS positive or negative control
  - According to GLP and/or ISO 17025
  - The test results should be reproducible (intralaboratory) as well as repeatable (interlaboratory) and robust.

# Standard for biocompatibility

- **ISO 10993**

Table A.1 — Evaluation tests for consideration

| Medical device categorization by | | | Biological effect | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Category (nature of body contact, see 5.2) | Contact (nature of body contact, see 5.2) | Contact duration (see 5.3): A – limited (≤ 24 h); B – prolonged (> 24 h to 30 d); C – permanent (> 30 d) | Cytotoxicity | Sensitization | Irritation or intracutaneous reactivity | Systemic toxicity (acute) | Subchronic toxicity (subacute toxicity) | Genotoxicity | Implantation | Haemocompatibility |
| Surface device | | A | X [a] | X | X | | | | | |
| | | B | X | X | X | | | | | |
| | | C | X | X | X | | | | | |
| | Mucosal membrane | A | X | X | X | | | | | |
| | | B | X | X | X | | | | | |
| | | C | X | X | X | | X | X | | |
| | Breached or compromised surface | A | X | X | X | | | | | |
| | | B | X | X | X | | | | | |
| | | C | X | X | X | | X | X | | |
| External communicating device | Blood path, indirect | A | X | X | X | X | | | | X |
| | | B | X | X | X | X | | | | X |
| | | C | X | X | | X | X | X | | X |
| | Tissue/bone/dentin | A | X | X | X | | | | | |
| | | B | X | X | X | X | X | X | X | |
| | | C | X | X | X | X | X | X | X | |
| | Circulating blood | A | X | X | X | X | | | | X |
| | | B | X | X | X | X | X | X | X | X |
| | | C | X | X | X | X | X | X | X | X |
| Implant device | Tissue/bone | A | X | X | X | | | | | |
| | | B | X | X | X | X | X | X | X | |
| | | C | X | X | X | X | X | X | X | |
| | Blood | A | X | X | X | X | X | | X | X |
| | | B | X | X | X | X | X | X | X | X |
| | | C | X | X | X | X | X | X | X | X |

[a] The crosses indicate data endpoints that can be necessary for a biological safety evaluation, based on a risk analysis. Where existing data are adequate, additional testing is not required.

# Manufacturing quality

- **EU GMP ISO 13485**
- The device shall be manufactured consistently to the Device Dossier
  - Equivalent to the prototype
  - Constant level of quality
  - Full traceability
- Standard operation procedures for Company management
  - Industrial processes
  - Equipment
  - Personnel

- **Exercise**

# Exercise

- Identify 4 medical devices and for each one indicate:
  - Intented use
  - Class (I, IIa, IIb, III), and the ISO standard
  - Risk level (low, medium, high)
  - Nature of contact (surface, external path, implanted)
  - duration of contact (limited, prolonged, permanent/repeated use)
  - At least two important manufactures
  - Estimated cost

# Find your reference Standard

- www.iso.org
- Store
- Standard catalogue
- 11 Health care technology
- 11.040 Medical Equipment
- Select the category

# Search your Standard

- www.sba.unipi.it
- Banche dati
- Norme tecniche CEI / Norme Tecniche EN
- Register
- Search your ISO