Medical Devices
An Introduction

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May 24, 2016

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The first step: a shared definition

- 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 examples of Medical Devices

- 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

EC: Medical Device Directive

- The Medical Device Directive is a law that regulates the marketing of Medical Devices in the EC
- 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

Basic requirements in the MDD

- Give proof that the device is safe and effective for the intended use: Technical File
  - SAFE: testing as per standards
  - EFFECTIVE: non inferior to clinical state of the art (clinical trials)
- Give proof that the manufacturer can routinely manufacture device consistently: Quality Management System
  - Controlled manufacturing
  - Lot/ serial number control
  - General management procedures for suppliers, maintenance, calibration
- Continuous control: surveillance
  - On the market
  - Post market clinical trials

Risk based approach

Vulnerability of the human body

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
- Control
  - Higher for higher risk classes
  - From self- declaration to comprehensive device and company audit by Notified Body

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)
- 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

A common trend: risk control

- Devices can be marketed only after extensive testing
  - Bench testing
  - In vitro- in vivo testing
  - Clinical trials
- Medical devices companies are compelled to maintain a Quality Management System
  - GMP
  - ISO 13485
- Devices must be evaluated over time (follow up)
  - by the manufacturers
  - by the competent authorities

Risk subjects

- Manufacturer is compelled to evaluate impact of use of the device:
  - On patient
  - On intended user
  - On bystanders
  - On general environment
- Manufacturer is compelled to evaluate effect of product impact in all life cycle, from manufacturing to disposal

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: Device

- Devices on the market must be SAFE and EFFECTIVE
- SAFE: The risk-benefit ratio must be favorable for the patient (or end user)
  - Expected clinical benefit
  - Side effects
  - Residual risk
- EFFECTIVE: The device must effectively perform clinical actions
  - Intended use defines the expected clinical benefit
  - Clinical benefit must be proven by clinical data
- The patient and end user are always protected, even against continuous research

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

Methods of the MDD

- The device must demonstrate to operate effectively and safely before it is released to the end user
- Detailed checklist of essential requirements that must be fulfilled
- Full responsibility of the manufacturers
- Independent review for medium and high risk devices by appointed Boards

Annex I: how it’s made

- I General Requirements
- II REQUIREMENTS REGARDING DESIGN AND CONSTRUCTION
  - **Chemical, physical and biological properties**
  - **Infection and microbial contamination**
  - **Construction and environmental properties**
  - **Devices with a measuring function**
  - **Protection against radiation**
  - **Requirements for medical devices connected to or equipped with an energy source**
  - **Information supplied by the manufacturer**

General comments

- “Designed and manufactured”
  - Design criteria
  - Product specifications
  - Production control activities
- “Minimize the risk”
  - Evaluation of causes and of probability of risk
  - Control methods
  - Perfection is “impossible” but it is required to implement all possible solutions

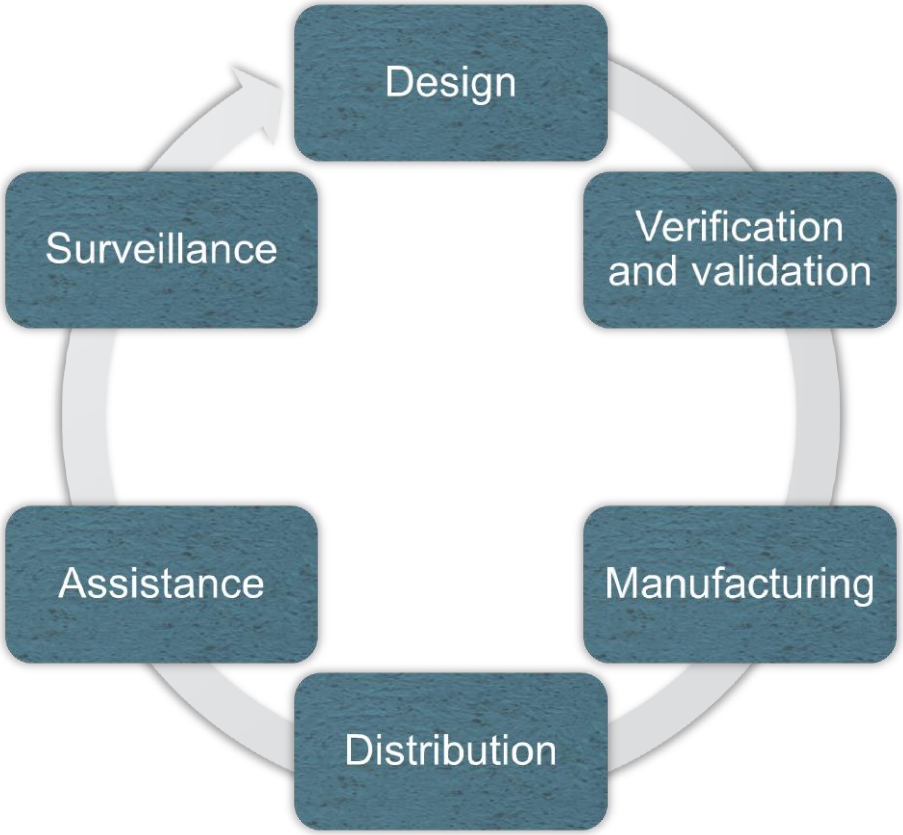
Norms

- 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

Manufacturers obligations

- Design control
- Product and process validation
- Clinical evaluation
- Manufacturing as per Good Manufacturing Practice guidelines
- Retention of records
- Continuous surveillance
- Device database
- Strict control on Post Market information and follow up clinical trials

Device life cycle



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

Quality standard for design

ISO 13485 clause 7

- Clinical and safety requirements: user needs
  - Expected benefit
  - Mechanism of action
- Device technical development
  - Tech drawings
  - Composition
  - SW modules
- Device technical verification and validation
  - Bench test
  - Safety test on animal models (ISO 10993)
  - Design transfer from prototype to industrial scale

Standard for risk management

ISO 14971

- Search of potential harmful events or device malfunctions
- Evaluation of probability and of impact on patient health (severity)
- Search of risk control measures (example: safe design, protections and alarms)
- Evaluation of risk-benefit ratio

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

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

Standard for clinical trials
ISO 14155

- Clinical trials on humans: authorized by Ethics Committee
  - Device with favorable risk- benefit ratio for each participant
  - Good statistical significance
- Difficult study design
  - Placebo? Mock device?
  - Number of participants
  - Data from animal models

Any questions, guys?