



UBORA: Euro-African Open Biomedical Engineering
e-Platform for Innovation through Education

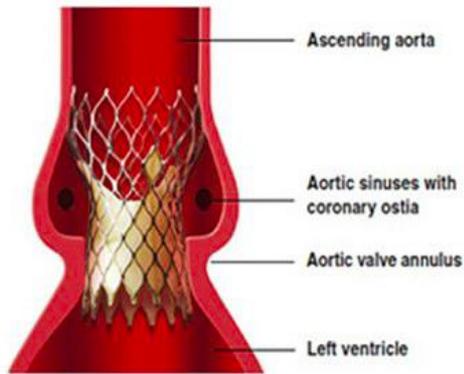
“Biomedical regulation
for product safety and
manufacturing
quality”

Topics:



- Essential Requirements for safety in Europe
 - International standards for the design of medical devices
 - International standards for the manufacturing of medical devices
 - Technical testing and clinical evaluation of newly designed medical devices
-

What do they have in common?



And now?



Tubing connect

Blood gas moni

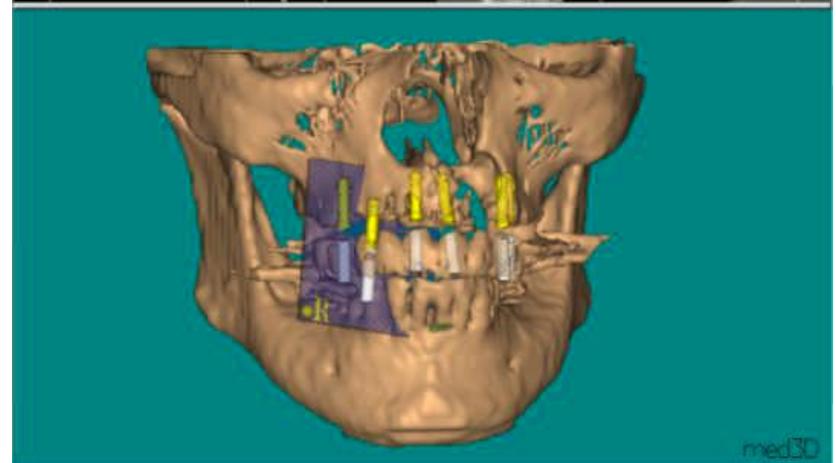
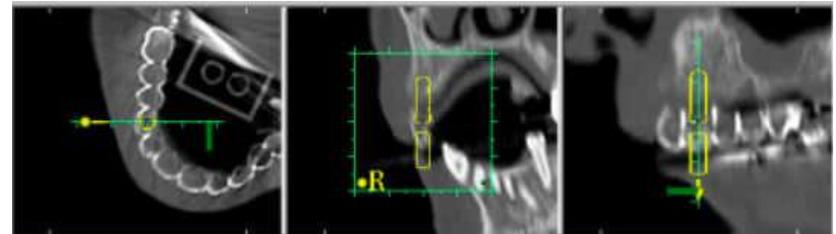
Pressure monito

Water heater

ECMO pump

Artificial lung

Back-up batter



Patient: Michael Haas. Implant in Regio 13, Länge 13,0 mm, Durchmesser 3,8 mm, Typ: Cerlog Cylinder.

Some more examples of Medical Devices



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

So... What do they have in common?



- Use on humans
 - Intended to have a MEDICAL purpose
 - Do not act through the metabolic pathway (drug)
 - 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
-

Legal framework



- A special kind of manufactured product
 - affects the public health
 - In the main part purchased by health organizations
 - Marketed under special, dedicated laws
 - EC: Medical Devices Directive
 - US: Code of Federal Regulation for Good Manufacturing Practices
 - Canada: Canadian Medical Device License
 - ...
-

EU Directive/ EU Regulation



- The Medical Device Directive/ Regulation is a law that regulates the marketing of Medical Devices in the EU
 - Details the device identification
 - Classification
 - Application (custom made, research, marketing...)
 - Defines manufacturers responsibilities and duties
 - Essential Requirements: for safety and performance
 - Surveillance: for continuous control
 - Assigns to local Competent Authorities control over manufacturers
-

EU MDD/MDR



- 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
-

Dividing and organizing...



- Risk classes are defined according to multiple product characteristics:
 - 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
-

Special classes



- Special classes
 - Custom made
 - Clinical investigation
 - Other risk related characteristics require special control
 - Medicinal substance
 - Tissue of animal origin
 - Human blood derivatives
-

Classification and risk



- Class I: lowest risk
 - non sterile gauze, reading glasses, conductive gel
- Class IIa: lower intermediate risk
 - IV set, transfusion sets, ECG
- Class IIb: upper intermediate risk
 - Wound care, blood bag; DAE
- Class III: highest risk
 - Heart valves, medicated stents

Scope of the MDD/MDR



- 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
-

Methods of the MDD



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

Essential requirements



- List of general technical requirements, valid for each class
 - Define the minimum level of safety expected for each class, for example:
 - Sterility
 - Electrical safety and EM compatibility
 - Bio-compatibility
 - Technical features
 - For each device, the compliance is proven by testing according to product- specific standards
-

Standards



- 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 IEC 60601-1
 - For sterile devices ISO 11137 et al.
 - For devices in contact with the body ISO 10993
 - Multiple harmonised and not harmonised norms for technical regulation of product- specific features
-

Where do standards come from?



- International standardization Bodies
 - ISO
 - IEC
 - ASTM
- Some standards have regulatory effect
 - Harmonised standards in EU
 - Recommended standards in USA

Harmonized norms

http://ec.europa.eu/enterprise/policies/european-standards/harmonised-standards/index_en.htm



- The European Commission “approves for regulatory purposes” a recognized standard from a Standards Organization
 - ISO 14971 -> ISO EN 14971 (commented and integrated)
- Solutions for compliance with a legal provision for essential requirements

Compliance to norm allows presumption of compliance to essential requirements for safety

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 for production control
 - GMP
 - ISO 13485
 - Devices must be evaluated over time (follow up)
 - by the manufacturers
 - by the competent authorities
-

Risk subjects



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

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 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
-

Manufacturing quality: the 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
-

Manufacturing flow



Acceptance

- Raw materials quality
- Personnel skills

Manufacturing

- Process repeatability
- Equipment control

Release

- Quality control
 - Quality assurance and traceability
-

Quality standards for production



- For Standard Operation Procedures: ISO 13485
 - Material control
 - Manufacturing
 - Quality control
 - For manufacturing areas
 - Cleanrooms ISO 14644
 - Sterile manufacturing ISO 13408
-

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
-



UBORA: Euro-African Open Biomedical Engineering e-Platform for Innovation through Education

This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 731053

