



Conducting Device Studies in South Africa

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Bringing your projects to a higher level.

Objectives

- Definitions
- Regulations governing medical devices
 - Overview of global regulations
 - South African regulations
- Monitoring issues
 - Essential Documents
 - Informed consent
 - Device handling, use and accountability
 - Investigators
 - Subject follow-up
- Safety reporting

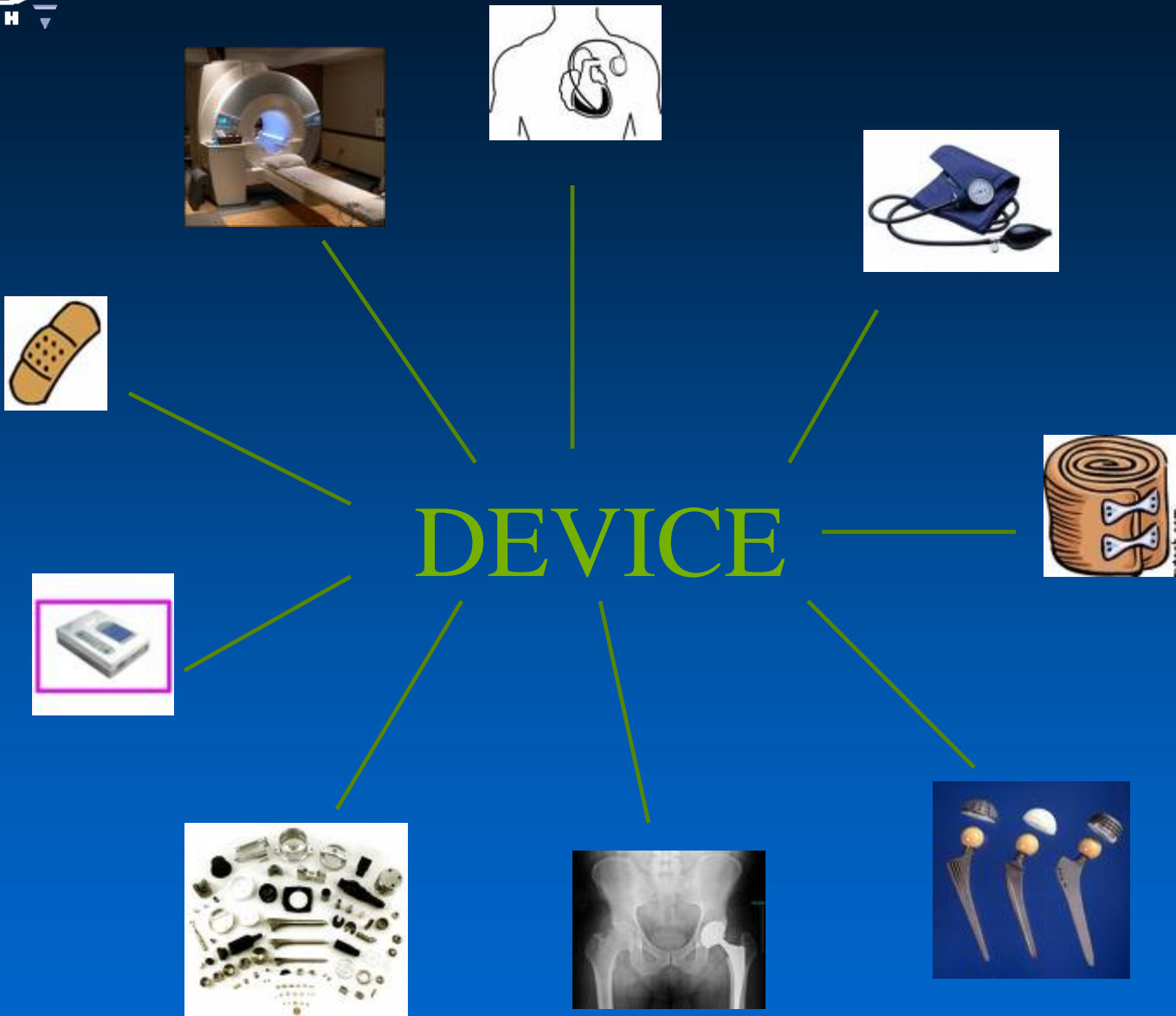


ISO Definition of Medical Device

- Any instrument, apparatus, appliance, material or other article, whether used alone or in combination, (including the software necessary for its proper application) intended to be used on humans for:



- diagnosis, prevention, monitoring treatment or alleviation of a disease, injury or handicap: *MRI units, implantable radioactive pellets for prostate cancer*
- investigation, replacement or modification of anatomy or physiological process: *joint replacements, pacemakers*
- Control of conception: *condoms, IUDs*



Medical Device Regulations

- FDA
 - 21 CFR Part 812 Investigational Device Exemptions
- EU Directives
 - Council Directive of 1993 concerning the approximation of the laws, regulations, administrative provisions and directives of the Member States relating to active implantable medical devices
 - Council Directive of 1990 on the approximation of the laws, regulations, administrative provisions and directives of the Member States relating to active implantable medical devices
- ISO 14155-1 & 14155-2
 - Clinical investigation of medical devices for human subjects
 - Part 1: General requirements
 - Part 2: Clinical investigation plans

**What's
missing
???**



South African Regulations



- Medicines and Related Substances Amendment Act No.72 of 2008
- SA GCP Guidelines (2006):



- *“These guidelines have **not specifically addressed** clinical trials on complementary medicines, traditional medicines, non-pharmacological interventions including surgical procedures, **medical devices** and X-rays. However, these guidelines are such that, in the absence of alternatives, the basic principles outlined in this document may be used to guide any research involving human participants.”*

- Hazardous Substances Act, 1973

- Section 4(1)(b): import of electromedical products

- e.g. ultrasound, PET scanners, ventilators, cardiac pacemakers, infusion pumps, haemodialysis devices, ECGs, EEGs, EMGs, audiometers



Starting Up Device Trials in SA

- Notify MCC
- Apply to ECs
- Register study on SANCTR
 - “The South African National Clinical Trials Register covers the full spectrum of clinical trials including trials on pharmaceuticals, devices, surgical procedures
- Obtain approval from hospital management, if applicable
- Potential stumbling blocks



Insurance



Medical aid funding for study procedures

Monitoring Issues

- Essential Documents
 - Protocol vs Clinical Investigational Plan (CIP)
 - Investigator's Brochure vs Report of Prior Investigations
 - Non-clinical, clinical and engineering/laboratory data
- Informed consent
 - Explanation of the procedure/treatment can be complicated
 - Long lists of potential risks in the ICF incl. risks associated with anesthesia and the surgical procedure
 - Final eligibility possibly only determined once patient is on the operating table
 - Standard hospital consent form required to be signed in addition to trial ICF



Monitoring Issues



- Device handling, use and accountability
 - Documentation of the procedure
 - Important to use source document templates
 - Remember to record all anaesthetic medications and postop medications
 - Documentation in the delegation log of all staff who will be handling devices & doing accountability
 - Sponsor sales representatives, theatre staff, scrub sisters
 - Documentation of device failures/malfunctions, replacements and returns
 - For implantable devices: use and return of instruments used to insert the device also needs to be documented
 - Storage: size and shape of device may pose a problem

Monitoring Issues

- Investigators
 - Availability: theatre schedules
 - GCP training
 - Previous trial experience
 - Device/procedure training (animals, cadavers)



- Subject follow-up
 - With implants, if patients feeling better they may not come back for follow-up visits
 - Differentiate between ‘standard of care’ & protocol specific follow-up visits

Safety Reporting

- Terminology:

adverse device effect vs adverse drug reaction



anticipated/
unanticipated

- report of prior investigations
- CIP
- ICF



expected/
unexpected

- IB

Safety Reporting: FDA

- 21 CFR 812
 - No definition of adverse event, serious or non-serious
 - Unanticipated adverse device effect (UADE)
 - Any serious adverse effect on health or safety or any life-threatening problem or death caused by or associated with a device if the effect wasn't previously identified in the investigational plan
 - Investigators must submit reports of UADEs to the sponsor and IRB asap but not later than 10 working days after first learning of the effect
 - Addresses adverse effects that are serious, related and unanticipated
 - Does not address non-serious, non-related or anticipated adverse events
 - **Do these not need to be reported????**



Example

- Patient who has had a hip replacement develops a life threatening case of pneumonia 2 weeks after the surgery. Pneumonia isn't listed in the report of prior investigations. Is this reportable?

? Serious ✓

? Unanticipated ✓

? Related ???



Safety Reporting: ISO 14155-1

- Adverse event (AE):
 - Any untoward medical occurrence in a subject
 - No relationship is implied
- Adverse device effect (ADE):
 - Any untoward and unintended *response* to a medical device
 - Includes events resulting from
 - insufficiencies or inadequacies in the instructions for use or operation of the device
 - user error



Safety Reporting: ISO 14155-1

- Serious adverse event (SAE):
 - Adverse event that leads to or results in:
 - death
 - life-threatening illness or injury
 - permanent impairment of a body structure or function
 - hospitalization or prolongation of existing hospitalization
 - medical/surgical intervention to prevent permanent impairment to a body structure or function
 - foetal distress, foetal death, congenital abnormality or birth defect

- Serious adverse device effect (SADE):
 - ADE that results in any of the consequences characteristic of an SAE or that might lead to any of the consequences if
 - suitable action is not taken
 - intervention is not made
 - if circumstances are less opportune

Safety Reporting: ISO 14155-1

- Responsibilities of the sponsor:
 - ensure that all AEs and ADEs are reported and reviewed with the investigators
 - SAEs and SADEs are reported to the relevant authorities, ECs and/or safety monitoring committees
 - inform all PIs of all SAEs and SADEs that have been reported to the sponsor based on perceived risk
- Responsibilities of the investigator:
 - inform EC about any SADEs
 - inform the sponsor about all AEs and ADEs in a timely manner



Safety Reporting: ISO14155-2

- CIP must include/provide:
 - procedures for recording and investigating AEs, ADEs and/or outcomes
 - emergency contact details for reporting SAEs & SADEs
 - details of foreseeable AEs & ADEs, their likely incidence and the methods to be used for their management
 - details of the procedures for reporting all AEs and ADEs to the sponsor, ECs and regulatory authorities, according to applicable regulations, including a specification of the types of events



Something to think about.....



A patient is undergoing a knee replacement using a revolutionary new replacement device. The femoral part of the implant has already been inserted but when the surgeon tries to insert the tibial implant, the instrument used for inserting the device breaks and there isn't another instrument available to finish inserting the device. So the surgeon removes the femoral implant and inserts a standard replacement device instead. There are no other complications during the surgery and the patient recovers as would be expected.



Is this reportable?

References

- ISO 14155-1:2003(E)
- ISO 14155-2:2003(E)
- Title 21 of the Code of Federal Regulations (CFR), Part 812
- Lee Truax-Bellows. Adverse Event Differences Between Investigational Devices and Drugs- Perceived or Actual? Monitor June 2008; 19-23