MHRA
Regulating Medicines and Medical Devices

Regulation of Medical device studies and the role of the MHRA

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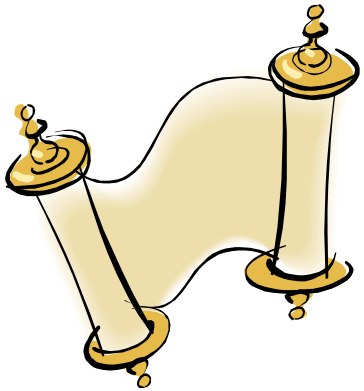
Directives for Medical Devices

3 Directives:

- Active Implantable Medical Devices (90/385/EEC)
  Powered implants
- Medical Devices (93/42/EEC)
  Most other devices
- In Vitro Diagnostics (98/79/EC)
  In Vitro Diagnostic Products



Risk Classification

- **Low Risk – Class I**

  Plasters, Walking Sticks, Wheelchairs, Stethoscopes, Medicine Spoons, Administration Sets, Syringes, Re-usable Surgical Instruments

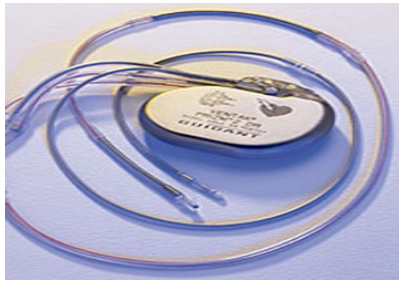
- **Medium Risk – Class IIa and IIb**

  Needles, Dental Filling Materials, Contact Lenses and Solutions, Diagnostic and Monitoring Equipment, Condoms, Infusion Pumps, Blood Bags, Haemodialysis Concentrates, Hearing Aids, Ventilators, Incubators, Surgical Lasers, Anaesthetic Machines, Nebulisers

- **High Risk – Class III and active implantables**

  Pacemakers, Cochlear Implants, Breast Implants, Devices containing Medicinal Substances, Devices containing Animal Materials, Cardiovascular and Devices, Neurological Implants, Absorbable Sutures

EU REGULATORY SYSTEM



compliance ERs
safety, performance

CE

European market

Notified Body

- *quality systems*
- *design dossier*
- *clinical data (literature, C/I)*

accredit
audit

investigation
action

Competent Authority

post market surveillance
serious adverse events

EU MARKET

compliance with all Essential Requirements covering safety and performance

ESSENTIAL REQUIREMENTS

"the devices must be designed in such a way that….they will not compromise the clinical condition or SAFETY of patients……provided that any RISKS which may be associated with their use constitute acceptable RISKS when weighed against the benefits…"

…..devices must achieve the performance intended by the manufacturer…..

MDD: Annex 1

Clinical data requirements

- *Characteristics and performances referred to in ERs, evaluation of the side-effects and of the acceptability of the benefit/risk ratio must be based on clinical data*

- All classes of device need clinical data

- Clinical Investigations shall be performed for Class III and implantable devices unless justified to rely on existing clinical data.

- Must justify where clinical data is not used

CLINICAL DATA

"…..clinical data must be based on either a compilation of the relevant scientific literature…..or the results of all the clinical investigations….."

MDD: Annex X

INDICATIONS C/I

- *new device*
- *new function*
- *new feature*
- *modification*
- *new material*
- *new manufacturer*
- *ex vivo cannot mimic clinical situation*

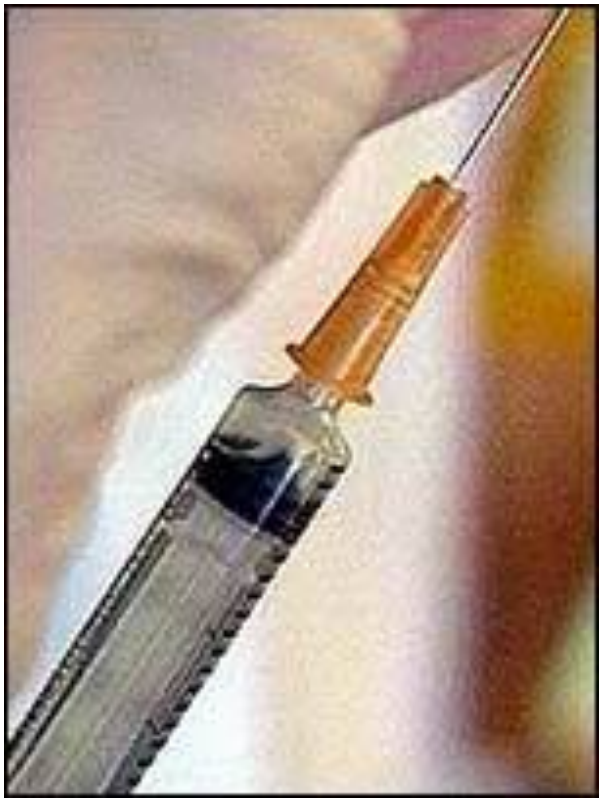
Study design - Key points

- Safety and Performance NOT Efficacy

  Therefore often:
  - » - Small sample sizes
  - » - No comparators
  - » - Simple stats
  - » - Short follow-up or continue Post Market

- No phases
- Difficult to blind
- Learning curve for users
- First clinical use maybe post market

MHRA approval required?

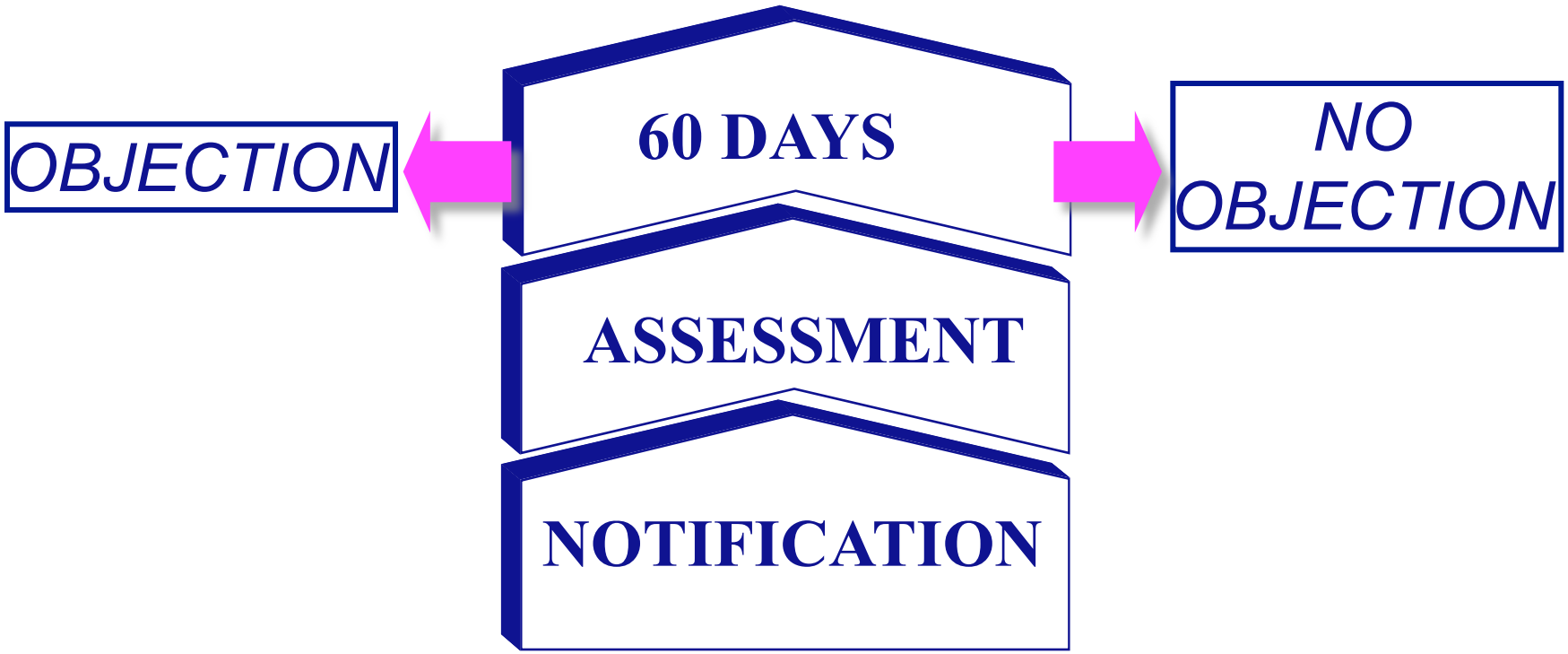


- non CE marked device
- *in-house manufacture*
- *off-label use*
- *drug/device combinations*
- *CE marked devices*
- *in vitro diagnostics*

MHRA submission

- IRAS
- MHRA guidance: http://www.mhra.gov.uk/Howweregulate/Devices/Clinicaltrials/index.htm
- Daniella.smolenska@mhra.gsi.gov.uk

HANDLING BY CA



GROUNDS OBJECTION

"….unless the Competent Authority have notified him within that period of a decision to the contrary based on considerations of public health or public policy….."

MDD: Article 15

GENERAL INFORMATION

- *SAFE manufacturing procedures*
- *ADEQUATE pre-clinical data*
- *SAFE protocol parameters*
- *estimation of RISKS*
- *how RISKS have been addressed*
- *ethics committee opinion*

SPECIFIC INFORMATION

- *protocol, patient information, investigator's brochure, statistics*
- *background, history previous models*
- *design*
- *materials*
- *electrical safety*
- *microbiological safety, sterilisation*
- *toxicology*
- *safety animal tissues*
- *drug component safety, usefulness*
- *risk assessment*

GROUNDS OBJECTION

10-15%:

- *lack relevant clinical end points*
- *clinical parameters insufficient/ inappropriate*
- *inadequate pre-clinical testing/ assessment*
- *inadequate toxicological testing/ analysis*
- *no sterilisation validation*
- *inadequate electrical testing*
- *risks outweigh benefits*

FINAL LETTER

No grounds for objection:

- *comments*
- *adverse event reporting*

grounds for objection:

- *details*
- *meeting*
- *how to reapply*

FURTHER CA FUNCTIONS

- *approve modifications*
- *adverse incident investigation*
- *final report*

ADVERSE EVENT REPORTING

- *all “serious” adverse events*
- *device, non-device related*
- *timelines*
- *all centres (UK, global)*

?discontinue study

Questions?