Health Research Authority

REC review of device studies – policy, procedure and ethical issues

Mrs Joan Kirkbride, Director of Operations and Approval – joan.kirkbride@nhs.net

Overview

- Legal / policy requirements for ethical review
- Medical Devices Research Collaboration Group
- Integrated Research Application System (IRAS) for device studies
- Considerations for REC review of regulated and non-regulated studies
- HRA Approval

Requirements for ethical review

Medical Devices Regulations

- Under the Medical Devices Regulations 2002, a **clinical investigation** must have approval from an ethics committee as well as Notice of No Objection from the Competent Authority
- The Regulations do not specify a requirement for approval from a “recognised” ethics committee
- Clinical investigations not involving the NHS (e.g. private ophthalmology clinics) could legally be reviewed by a non-NHS REC but application to NRES is strongly recommended

GAfREC

- ***Previous GAfREC:***

  Requirement for review where a medical device study is research involving NHS patients or their tissue or data.

- ***Updated UK-wide GAfREC (1.9.2011):***

  Also provides for review by RECs of any research where ethical review is a legal requirement

‘Research’ or ‘post-market surveillance’?

- Post-market studies of CE marked devices by the manufacturer are often limited to collection of anonymised data from normal clinical care
- Under NRES guidance, such studies may generally be classified as post-market surveillance and within scope of ‘service evaluation’, not research
- http://www.hra.nhs.uk/documents/2013/09/approval-of-medical-devices-research-version-2-april-2008.pdf
- However, REC review is required where:
  - Selection of treatment is protocol-driven, not based on usual standard of care; and/or
  - Protocol involves procedures additional to usual care (e.g. extra monitoring, scans, samples)

NRES application policy

- No legal requirement for REC to be recognised
- Application to a flagged REC is recommended, but other RECs may review medical device studies
- Flagged RECs are selected mainly on basis of previous experience and local demand
- Lists of flagged RECs are kept under review in the light of pattern of applications and likely demand

Current flagged RECs

- Cambridge Central
- Cambridge East
- London - Dulwich
- London - Stanmore
- North East - York
- North West – GM South
- Northern Ireland – HSC 2
- Scotland A
- South East Scotland 2
- South West - Exeter
- West Midlands - Edgbaston
- West Midlands - South Birmingham
- Yorkshire & the Humber - Leeds West
- Yorkshire & the Humber - Sheffield

Medical Devices Research Collaboration Group

Medical Devices Research Collaboration Group

- MHRA Devices Division
- HRA
- DH R&D
- NIHR CRN Co-ordinating Centre
- R&D Forum
- Association of British Healthcare Industries
- Institute of Clinical Research

Objectives

- Clarify **roles and responsibilities**
- Produce clear and consistent **guidance** for researchers
- Develop streamlined **processes**
- Ensure effective **communications** between review bodies

Joint guidance

- Comprehensive guidance on requirements for approval of devices research: http://www.hra.nhs.uk/resources/before-you-apply/types-of-study/medical-devices-research-2/

- Guidance on REC/MHRA communications: http://www.hra.nhs.uk/documents/2013/09/communications-on-medical-devices-investigations-version1-april-2008.pdf

Medical device studies and IRAS

www.myresearchproject.org.uk

IRAS

INTEGRATED RESEARCH
APPLICATION SYSTEM

IRAS Project Filter

- Modifications introduced to the Project Filter for medical device studies (July 2011):
  - Distinguishes commercial and non-commercial studies
  - More specific categorisation of type of study
  - Disables some questions in Part A for studies of CE marked devices involving no change to normal care

- Aim of changes:
  - More 'intuitive' for applicant in identifying the appropriate category
  - Clarifies type of study for REC/R&D and signposts regulatory/ethics /liability issues
  - Proportionate approach to information required in application

generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

On-line guidance is available wherever you see a hyperlinked word or this symbol displayed. Please read this guidance carefully. For Help with your application, click here.

Please enter a short title for this project (maximum 70 characters)

Medical devices test project

1. Is your project research?

(•) Yes ( ) No

2. Select one category from the list below:

( ) Clinical trial of an investigational medicinal product
(•) Clinical investigation or other study of a medical device
( ) Combined trial of an investigational medicinal product and an investigational medical device
( ) Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice
( ) Basic science study involving procedures with human participants
( ) Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
( ) Study involving qualitative methods only
( ) Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
( ) Study limited to working with data (specific project only)
( ) Research tissue bank
( ) Research database

If your work does not fit any of these categories, select the option below:

( ) Other study

2a. Is the study sponsored or funded by a device manufacturer or other commercial company?

(•) Yes ( ) No

- ○ Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- ○ Study involving qualitative methods only
- ○ Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
- ○ Study limited to working with data (specific project only)
- ○ Research tissue bank
- ○ Research database

If your work does not fit any of these categories, select the option below:

- ○ Other study

2a. Is the study sponsored or funded by a device manufacturer or other commercial company?

- ◉ Yes ○ No

Please select one of the following:

- ◉ Clinical investigation for CE marking purposes (includes investigation of a CE marked device outside its current intended purposes or in modified form)
- ○ Combined clinical investigation for CE marking purposes and clinical trial of an investigational medicinal product
- ◉ Post-market clinical study of one or more CE marked devices within intended purposes, involving a change to standard care or randomisation between groups
- ○ Registry of a CE marked device in clinical use, involving no change to standard care or randomisation
- ○ Performance evaluation of an in vitro diagnostic device (PEIVDD)

2b. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation?	○ Yes	◉ No
b) Will you be taking new human tissue samples (or other human biological samples)?	○ Yes	◉ No
c) Will you be using existing human tissue samples (or other human biological samples)?	○ Yes	◉ No

3. In which countries of the UK will the research sites be located? *(Tick all that apply)*

- ☑ England

- ○ Study administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
- ○ Study involving qualitative methods only
- ○ Study limited to working with human tissue samples (or other human biological samples) and data (specific project only)
- ○ Study limited to working with data (specific project only)
- ○ Research tissue bank
- ○ Research database

If your work does not fit any of these categories, select the option below:

- ○ Other study

2a. Is the study sponsored or funded by a device manufacturer or other commercial company?

○ Yes ◉ No

Please select one of the following:

- ○ Clinical study of a non-CE marked device where commercialisation of the product is intended
- ○ Clinical study of a non-CE marked device for use within the institution, where commercialisation is not intended
- ○ Clinical study of one or more CE marked devices for an off-label indication
- ◉ Clinical study of one or more CE marked devices for a labelled indication, involving a change to standard care or randomisation between groups
- ○ Clinical study of one or more CE marked devices for a labelled indication, involving *no* change to standard care or randomisation between groups
- ○ Pre-clinical device development or performance testing

2b. Please answer the following question(s):

a) Does the study involve the use of any ionising radiation?	○ Yes	◉ No
b) Will you be taking new human tissue samples (or other human biological samples)?	○ Yes	◉ No
c) Will you be using existing human tissue samples (or other human biological samples)?	○ Yes	◉ No

3. In which countries of the UK will the research sites be located? *(Tick all that apply)*

Study types - commercially sponsored

- Clinical investigation for CE marking *
- Combined clinical investigation / CTIMP *
- Post-market study of CE marked device – involving change to care or randomisation
- *'Registry'* of CE marked study in clinical use – no change to care or randomisation
- Performance evaluation of IVDD

* requires MHRA application by the manufacturer

Study types – not commercially sponsored

- Clinical study of non-CE marked device – commercialisation intended *
- Clinical study of non-CE marked device – commercialisation not intended
- Clinical study of CE marked device for off-label indication
- Clinical study of CE marked device for labelled indication – change to care or randomisation
- Clinical study of CE marked device for labelled indication – no change to care or randomisation
- Pre-clinical device development

* requires MHRA application by the manufacturer

IRAS Part B Section 2 – information on medical devices

- Part B Section 2 is generated for:
  - all studies of medical devices
  - other clinical studies involving an *ancillary device* without a CE mark or used for non-labelled indication

- Sub-section A – common information on the device for all review bodies

- Sub-sections B and C – additional information required by MHRA Devices only for regulated investigations

Project Title: **Medical devices test project**
Section: **Part B Section 2: Medical Devices**
Full project dataset

Part B: Section 2

A. General information

Information in this sub-section will be included in applications to the Research Ethics Committee and NHS R & D offices at the research sites.

1-1. Is the manufacturer (or other organisation responsible for developing the device) the same organisation named as lead sponsor for this study?

○ Yes ○ No

NHS REC Form
NHS R&D Form

Organisation

Address

Post Code

Fax

E-mail

2. Details of the medical devices to be used in the study

NHS REC Form

NHS R&D Form

Name of the manufacturer:

Manufacturer's trade name for the device:

Device identification name and/or number:

Name:

Number:

Generic name of device and principal intended use(s):

Length of time since device came into use:

Add another investigational device

3-1. Further details of the purpose of the study

NHS REC Form

NHS R&D Form

Does the study involve:

- Investigation of a new medical device
- Investigation of new implantable material
- Use of an existing product outside the terms of its CE market intended purpose
- Use of a modified product
- Use of an existing product within its CE market intended purpose

☐ NHS R&D Form

Does the study involve:

- ○ Investigation of a new medical device
- ○ Investigation of new implantable material
- ○ Use of an existing product outside the terms of its CE market intended purpose
- ○ Use of a modified product
- ○ Use of an existing product within its CE market intended purpose

3-2. Please give further details below including the following:

Description of any new device, materials, method of use or operation with a summary of the intended purpose.

Composition of any new implantable materials, including summary of biocompatibility findings from studies to date.

A summary of any modifications to CE marked devices.

A summary of any proposed changes to the CE market intended purpose.

For all products with CE mark please attach instructions for use.

Non-commercial clinical investigation of non-CE marked product – commercialisation not intended

- No MHRA application in this scenario
- Therefore IRAS generates additional questions for the REC and R&D form on:
  - Manufacturing of the device
  - Safety and performance testing
  - Plans for further development
- A signed declaration is required from the Head of Clinical Engineering or equivalent at the institution to provide additional assurance

For all products with CE mark please attach instructions for use.

4. Please describe the arrangements for manufacture of the investigational device. *Include details of the quality assurance system in place within the legal entity. Give details of any collaboration with a commercial manufacturer or other sub-contractor and enclose a copy of the contract.*

5. What safety and performance testing has been undertaken on the investigational device and its constituents? *Please give summarised details of appropriate tests (including outcome i.e. pass/fail), e.g. mechanical, electrical, biological, toxicological, sterilisation.*

- ☐ NHS REC Form
- ☐ NHS R&D Form

6. Please describe the sponsor's plans for further development and use of the device. *Indicate whether the plans include making it available (whether for a fee or not) to other legal entities or working with a device manufacturer or other company to commercialise the product.*

- ☐ NHS REC Form
- ☐ NHS R&D Form

6. Please describe the sponsor's plans for further development and use of the device. *Indicate whether the plans include making it available (whether for a fee or not) to other legal entities or working with a device manufacturer or other company to commercialise the product.*

NHS REC Form
NHS R&D Form

7. Declaration

This declaration should be authorised by the head of clinical engineering or equivalent at the institution developing the device.

I confirm that the information provided in this section is accurate to the best of my knowledge. I take full responsibility for ensuring that the device has been manufactured to the standards expected of an equivalent CE marked device and that all relevant testing to demonstrate compliance with these standards has been undertaken.

Name: .....

Post: .....

Organisation: .....

Date: .....

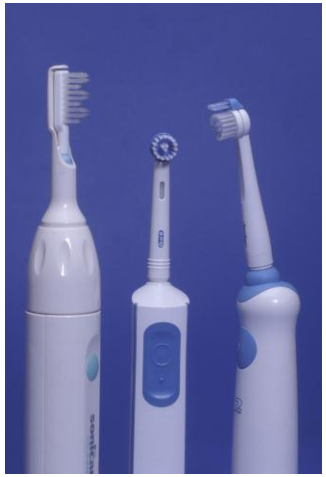
There are no further questions in this section. Please continue to the next section or return to the Navigate page.

Considerations for ethical review

The Directive defines medical devices as:

- **any** instrument, apparatus, appliance, material or other article, whether used alone or in combination, including the software necessary for its proper application intended by the manufacturer to be used for human beings for the purpose of:

- Diagnosis, prevention, monitoring, treatment
- Or alleviation of disease.



General points on risk and protection of participants

- Proportionality – enormous range of device types
- Identify and quantify the risk
- Separate risks related to the intervention/procedure and the research from the risk of the device itself
- The participant may also be the device user

Regulated studies

Regulated studies - conflicts of interest

- The inventor may be the researcher and a director of the ‘Company’ owning the IP
- Is this acceptable? How can the risks be mitigated?

Roles and responsibilities – regulated studies

MHRA

- Safety of device
- Design features and materials
- Pre-clinical testing and supporting data
- Sterilisation
- Study endpoints
- Investigator qualifications and training
- Safety monitoring and reporting

REC

- Recruitment / consent
- Participant information
- Other study procedures (e.g. scans, tissue samples)
- Confidentiality
- Incentives and payments
- Conflict of interest
- Insurance and indemnity
- Patient involvement in design
- Publication of results
- Follow-up treatment
- Any other ethical issues

Communicating with MHRA on regulated studies

- Any safety concerns (either on initial application or during the study)
- Prior consultation with MHRA is recommended before giving an unfavourable opinion on safety grounds, or suspending/terminating a favourable opinion
- Reporting possible serious breach or non-compliance

Non-regulated studies

CE marked devices used within intended purpose

- CE Marking provides assurance that the device meets the Essential Requirements under the Directives, i.e. safety and performance has been adequately demonstrated
- Under the Consumer Protection Act 1987, “strict liability” applies for harm resulting from defects in the product, i.e. fault does not have to be proved
- Manufacturer will have product liability insurance

Responsibilities - studies of CE marked devices within label

Assured by CE Marking

- Safety and performance of device, based on pre-clinical testing and where appropriate clinical investigation data
- Manufacturing quality
- Sterilisation
- Product liability insurance

Reviewed by NHS R&D office

- Investigator qualifications and training

REC review

- Design and statistics
- Recruitment / consent
- Participant information
- Other study procedures (e.g. scans, tissue samples)
- Confidentiality
- Incentives and payments
- Insurance and indemnity
- Patient involvement in design
- Publication of results
- Follow-up treatment
- Any other ethical issues

Evidence of CE marking

- Part B Section 2 includes details of the intended uses
- The REC should check that these are compatible with the uses proposed in the study and the device has not been modified
- Documentary evidence of CE marking is not required

Post-market studies – could safety considerations arise?

A post-market study could be the first clinical use of a device

--- *exceptionally*, if a REC has serious safety concerns it could seek advice from MHRA

e.g. an implant or other higher risk product which has obtained a CE Mark based solely on pre-clinical data

Conclusions

- Prepare for ethical review meticulously:

  http://www.hra.nhs.uk/research-community/applying-for- approvals/

  http://www.mhra.gov.uk/Howweregulate/Devices/

HRA Approval

- HRA Assessment + Favourable Ethics Opinion = HRA Approval in England
- UK wide compatibility
- Single application form provided by IRAS

ProtectiUK wide compatibility

Key principles

- Agreeing standards and templates is key – so HRA can provide clear, consistent expectations for assessment
- Assessors will be a dedicated HRA staff resource
- Expertise for technical assurances will be coordinated by the HRA and provided by NHS staff
- Individual components/ standards will deliver early improvement
- HRA Approval will be rolled out by study type; ambition for all study types by end of 2015

Thank you for listening