Preparation for an MHRA GCP Inspection including Training on New and Up-dated SOPs 2015

MHRA

Medicines and Healthcare products Regulatory Agency

NHS Grampian & University of Aberdeen
MHRA GCP Inspection
2015

Welcome & Introduction
Professor Phil Hannaford & Dr Juliette Snow

Medicines and Healthcare products Regulatory Agency
Background - Why Inspect?

• The MHRA's primary objective is to safeguard public health by ensuring that all medicines on the UK market meet appropriate standards of safety, quality and efficacy ie to ensure safety of patient.

• To ensure adherence to principles of GCP both guidelines and regulations.

• To ensure compliance with the laws, rules and regulations of both the EU and UK.
Types of GCP Inspection

• Statutory inspections
  – Scheduled, where organisations are notified in advance
  – Systems based
• ‘Triggered’ inspections
  – Ad hoc inspections
• Requested inspections
  – MAA related
Co-Sponsor Inspection

• UoA & NHSG co-sponsor clinical trials of investigational medicinal products (CTIMPS)
• Roles & responsibilities of each party is set out
  – Joint working protocol
  – Framework Agreement for the co-sponsorship of non-commercial CTIMPs
• Oversight of Sponsorship delegated to Head of School of Medicine (UoA) and R &D Director (NHSG)
What processes do the MHRA inspect?

University/NHSG systems that support conduct of CTIMPs in compliance with regulations and GCP

- **Study start up** – Contracts; 3\(^{rd}\) parties; sponsorship, regulatory approvals; establishing a TMF
- **Study conduct**- consent; management of CTIMPs, amendments ;annual reports; Project management- PMG, TSC, DMC
- **Quality systems** – monitoring, training, SOPs
- **Pharmacovigilance & Serious Breaches**
- **Data** management, IT systems & statistics
- **Study close out**: archiving, publications
What sites will the MHRA inspect?

- Archiving facilities
- UoA Laboratories involved in CTIMPs
- Pharmacy
What will the MHRA inspect?

- CTIMPs that have been active in past 3 years
- **14 Co-sponsored CTIMP studies**- 11 closed, 3 active
- 146 Hosted by NHSG
- MHRA will choose ? to look at in depth

However... MHRA can change their minds before the visit or decide to look at other studies during the visit, therefore we must all be prepared!
Aims of this session

Brief researchers on what the inspectors will be looking at in your CTIMP study:

• Describe up-dated and new SOPs
• Prepare researchers for interviews with inspectors

UoA-NHSG-SOP-018-V2 Preparation and Participation in Inspection by the MHRA
Once notified of Selected CTIMPS:

- Circulate commonly asked questions
- Individual study specific training with key individuals
- Monitors will review TMF
- Mock MHRA interviews
MHRA GCP Inspection
2015

Medicines and Healthcare products Regulatory Agency

Introduction to NHSG Research & Development
and University of Aberdeen Research & Innovation
University of Aberdeen – NHS Grampian Clinical Research Oversight Committees

- **UoA RESEARCH POLICY COMMITTEE**
- **UoA ADVISORY GROUP ON RESEARCH ETHICS & GOVERNANCE (AGREG)**
- **UoA COLLEGE OF LIFE SCIENCES AND MEDICINE RESEARCH COMMITTEE**
- **UoA IAHS RESEARCH GOVERNANCE AND QA COMMITTEE**
- **UoA MONITOR & AUDIT GROUP IAHS (MAGI)**

**CLINICAL RESEARCH OVERSIGHT COMMITTEES**

- **UNIVERSITY OF ABERDEEN – NHS GRAMPIAN: COMMITTEES & GROUPS WITH RESPONSIBILITIES FOR CLINICAL RESEARCH OVERSIGHT**
- **CLINICAL RESEARCH OPERATIONAL GROUP (CROG)**
- **CLINICAL STUDIES OVERSIGHT GROUP (CSOG)**
- **CLINICAL TRIAL FACILITATION GROUP (CTFG)**
- **LAB. CTIMP WORKING GROUP**
- **GRAMPIAN BIOREPOSITORY STEERING COMMITTEE**
- **GRAMPIAN DATA SAFE HAVEN (DASH) STEERING COMMITTEE**

**NHS GRAMPIAN CLINICAL GOVERNANCE COMMITTEE**

- Indicates joint NHSG – UoA committee or group
- Regular reporting
- Reporting as required
Clinical Research Steering Group (CRSG)

Remit

• Ensure appropriate facilities are in place to conduct high quality clinical research.
• Ensure clinical research on humans, their tissue and associated data is undertaken to required Research Governance standards and relevant statutory requirements.
• Maintain oversight of the preparation for, and management of, any regulatory inspections as well as oversight of any required responses to such inspections.
• Advise Co-Chairs who link to relevant management structures within their respective organisations. Prepare an annual governance report on the arrangements & management of clinical research undertaken in Grampian.
• Maintain a Risk Register.
Clinical Studies Oversight Group (CSOG)

Remit

• With a view to determining quality and rigour, the CSOG will review clinical research projects presented for sponsorship to UoA or NHS Grampian.

• CSOG will also undertake an overview of Pharmacovigilance events, serious breaches and summary monitoring or audit reports of red graded findings at the regular meetings.

• If NHS Grampian Research & Development consider it necessary, hosted studies may also be presented to the CSOG for input.
Clinical Research Operational Group (CROG)

Remit

• Advise and implement Clinical Studies Oversight Group (CSOG) actions.
• Identify, draft and review guidance documents / SOPs
• Oversee training in Sponsor SOPs
• Review trends from monitoring and audit reports and, where relevant, review Corrective Action Preventative Actions
• Oversee content and maintenance of Clinical Research Governance website
• Receive actions from MAGI and CTFG
Key staff: co-sponsored CTIMPs

Lead Nurse Manager
Carole Edwards

Training Facilitator
Karen Secombes

Training Facilitator
Anna Strachan

Research Governance Manager
Tricia Burns

Research Governance Assistant
Stacey Dawson
Key staff: co-sponsored CTIMPs

- QA Manager
  Richard Cowie

- Clinical Trial Pharmacist
  Pat Cooper

- Research Monitor
  Caroline Campbell

- Research Monitor
  Lynn Mckay

- Named Archivist
  Gary Cooper
Key staff: co-sponsored CTIMPs – funding and contracts

UoA Research and Innovation
Liz Rattray Deputy Director

Juliette Snow
BDO

Susan Ridge
NHS R&D
Sponsor Representatives

Depending on subject matter / issue:

**NHSG:**
Chief Exec., Med Dir., NHS R&D Dir., Clin. Governance etc

**UoA**
Principal, VP Res, Head of CLSM, HoS, HR, Deputy Dir. R&I etc
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Regulations, Qualifications & Training including SOPs
Karen Secombes, Training Facilitator
SOPs available at:

http://www.abdn.ac.uk/clinicalresearchgovernance
Clinical Research Governance & Quality Assurance

SOPs and Templates

Operating Procedures (SOPs) are detailed, written instructions to achieve uniformity of the performance of a specific function.

As sponsors and hosts of clinical research, the University of Aberdeen and NHS Grampian have legal responsibilities regarding the oversight and management of studies. On this page you will find a range of SOPs designed to guide investigators and researchers to ensure that studies are conducted and reported in compliance with GCP, regulatory requirements and research governance frameworks.

For information on training available please visit the NHS Grampian Research and Development webpage.

Please check this page regularly as new SOPs become available or updated versions may be added.

Study Set Up

<table>
<thead>
<tr>
<th>Reference</th>
<th>Version</th>
<th>Title</th>
<th>Associated Document(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UoA-NHSG-SOP-004</td>
<td>V2</td>
<td>Applying for Sponsorship for CTIMPs and high risk international studies V2</td>
<td>Externally Funded Studies: Sponsorship Registration Form&lt;br&gt;Internally Funded Studies: Sponsorship Registration Form</td>
</tr>
</tbody>
</table>
MHRA GCP Inspection 2015

Medicines and Healthcare products Regulatory Agency

UoA-NHSG-SOP-018-V2 Preparation and Participation in Inspection by the MHRA
Pre- MHRA Inspection

• MHRA give formal notification
  – Preparation of Dossier

• MHRA propose timetable
  – Detail departments to be inspected
  – Staff for interview

• Sponsor
  – Ensures all relevant staff prepared
  – Ensures requested documentation is available (may include archived documents)
During MHRA inspection

• CI & Staff must make themselves available during the inspection
• Inspectors must be accompanied at all times
• Interviewees should answer questions honestly and succinctly
• Interviewees can update or clarify information given during interview at any stage of inspection
• A scribe will attend all interviews
• Additional documents can be requested during inspection and must be delivered to the inspector
• A record must be kept of any documents given
After the Inspection

• Close out meeting
  – Verbal feedback on findings

• Written report from MHRA within 30 days
  – Document findings
  – List findings as critical, major or other

• Response required within 30 days
  – CAPAs

• Documentation and record of outcomes kept by the Sponsor

• Overview of MHRA inspection disseminated to researchers
MHRA GCP Inspection
2015

Medicines and Healthcare products Regulatory Agency

Regulations, Qualifications & Training
Legislation

The main references used for the inspection will be:

- **EU Directives 2001/20/EC and 2005/28/EC** and supporting guidance documents as incorporated in UK National Legislation:

- **Statutory Instrument, Number 1031, the Medicines for Human Use (Clinical Trials) Regulations 2004** and subsequent amendments.
Medicines for Human Use (Clinical Trials) Regulations & Amendments

Relates to implementation of GCP in the conduct of CTIMPs in humans

2004: Medicines for Human Use (Clinical Trials) Regulations 2004 (SI: 1031)
1st May 2004

Lays down principles and detailed guidelines for Good Clinical Practice

2006: Amendment Regulations (S.I. No. 1928)
Responsibilities & Principles of Good Clinical Practice

2006: Amendment No 2 (S.I. No. 2984)
Emergency research incapacitated adults

2008: Blood, Safety and Quality (S.I. No. 941)
Emergency research in children

2009: Miscellaneous Amendments (S.I. No. 1164)
Urgent safety measures

2010: Advanced Therapy Medicinal Products (S.I. No. 1882)
Traceability; tissue engineered products.
Each individual involved in conducting a trial shall be qualified by education, training, and experience to perform his or her respective task(s).

Local SOP ‘UoA-NHSG-SOP-016 v2 Establishing & Maintaining a Training Record’ states:

‘All staff involved in establishing or undertaking research projects at the UoA and/or NHSG will be appropriately qualified by education, training and experience to carry out their respective tasks in accordance with the Scottish Executive Research Governance Framework (RGF) for Health and Community Care’
Medicines for Human Use (Clinical Trials) Regulations

2006: Amendment Regulations (S.I. No. 1928) Responsibilities & Principles of Good Clinical Practice

‘For Clinical Trials of Investigational Medicinal Products (CTIMPs) adherence to the principles of GCP is incorporated into UK legislation. The UK Clinical Trials Regulations (SI 2004/1031, as amended) state that no person shall conduct a clinical trial otherwise than in accordance with the conditions and principles of GCP (Regulation 28) .....................(Schedule 1, Part 2, 2)’
GCP Principles and Conditions in UK Legislation

1. The rights, safety and well-being of the trial subjects shall prevail over the interests of science and society.
2. Each individual involved in conducting a trial shall be qualified by education, training and experience to perform his tasks.
3. Clinical trials shall be scientifically sound and guided by ethical principles in all their aspects.
4. The necessary procedures to secure the quality of every aspect of the trial shall be complied with.
5. The available non-clinical and clinical information on an investigational medicinal product shall be adequate to support the proposed clinical trial.
6. Clinical trials shall be conducted in accordance with the principles of the Declaration of Helsinki.
7. The protocol shall provide for the definition of inclusion and exclusion of subjects participating in a clinical trial, monitoring and publication policy.
8. The investigator and sponsor shall consider all relevant guidance with respect to commencing and conducting a clinical trial.
9. All clinical information shall be recorded, handled and stored in such a way that it can be accurately reported, interpreted and verified, while the confidentiality of records of the trial subjects remains protected.
10. Before the trial is initiated, foreseeable risks and inconveniences have been weighed against the anticipated benefit for the individual trial subject and other present and future patients. A trial should be initiated and continued only if the anticipated benefits justify the risks.
11. The medical care given to, and medical decisions made on behalf of, subjects shall always be the responsibility of an appropriately qualified doctor or, when appropriate, of a qualified dentist.
12. A trial shall be initiated only if an ethics committee and the licensing authority comes to the conclusion that the anticipated therapeutic and public health benefits justify the risks and may be continued only if compliance with this requirement is permanently monitored.
13. The rights of each subject to physical and mental integrity, to privacy and to the protection of the data concerning him in accordance with the Data Protection Act 1998 are safeguarded.
14. Provision has been made for insurance or indemnity to cover the liability of the investigator and sponsor which may arise in relation to the clinical trial.
UoA-NHSG-SOP-51
GCP training Requirements
GCP training Requirements

‘GCP training is one component of the systems in place to ensure high quality research’

‘Researchers are required to maintain awareness of current standards through GCP training, reference to published guidance, relevant policies and legislation’
UoA-NHSG-SOP-51
GCP training Requirements

CTIMPs or classified High Risk Studies

NHSG and UoA require that evidence of attendance/certification at
a recognised GCP training* course for CTIMP research is available
every 2 years or after major changes in clinical trial legislation
(whichever is first).

‘It is the responsibility of the CI/PI to ensure that they and their
study team have relevant GCP training that is commensurate with
their role in the study. For CTIMPs and High Risk studies this must
be updated 2-yearly’

‘It is the responsibility of the CI/PI to ensure that they and their
study team are named on a Delegation Log and that evidence of
appropriate GCP training is available’
Sponsorship

For research involving CTIMPs or classified High Risk Studies and sponsored or co-sponsored by NHSG and/or UoA, evidence of valid GCP training for the CI and any local co-investigators will be checked on receipt of application for sponsorship offer appropriate training courses.
UoA- NHSG-SOP-016 v2
Establishing & Maintaining a Training Record
Establishing & Maintaining a Training Record

‘......will document evidence of education, training and experience by establishing and maintaining a training record’

— Applies to all staff conducting or supporting clinical research sponsored or co sponsored by UoA /NHSG

— Responsibility of the individual to create and update their own training record

— Responsibility of the individual to make their training record available for review during any internal/external audit or inspection
Establishing & Maintaining a Training Record

‘All staff should keep their training records either in hard copy and/or electronically in a secure but accessible area’

• Training Log: ‘... is an on-going cumulative list of all internal and external training’
• Training on SOPs

Contents should include:

• Current CV (should detail attendance at a GCP course)
• Current Job Description
• Certificates of all training attended – both general and study specific
  – Keep copies of handouts / agendas
• Professional qualifications

If a member of staff leaves – they may take original training record, but must leave a copy with the study file
## TRAINING LOG

**Name:** ...............................................................  **Job Title:** ...............................................................  

<table>
<thead>
<tr>
<th>Date of Training</th>
<th>Subject</th>
<th>Training Provider / Type of Training (e.g. online course, lecture)</th>
<th>Duration</th>
<th>Topics Covered by Training</th>
<th>Counter Signature (If relevant)</th>
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Training Log and Records link to the Delegation Log

- The PI may delegate activities to appropriate members of the research team but MUST ensure they hold the appropriate qualification for that role.

- Signed and dated prior to any activity being undertaken by the individual.

- It is documented evidence of the appropriate delegation of the investigator’s responsibilities.
# SITE RESPONSIBILITIES / DELEGATION LOG

<table>
<thead>
<tr>
<th>Printed Staff Name</th>
<th>Signature</th>
<th>Initials</th>
<th>Role at Study Site (Co-Investigator, Study Nurse, etc)</th>
<th>Authorized functions (List all numbers that apply)</th>
<th>Start Date</th>
<th>Stop Date</th>
<th>CI Initials / Date</th>
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<td>Chief Investigator</td>
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## Authorized Functions:

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<td>Secure Approvals</td>
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<td>2</td>
<td>Obtaining Informed Consent</td>
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<td>3</td>
<td>Recruitment</td>
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<td>4</td>
<td>Randomizing subjects</td>
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<td>5</td>
<td>Completing &amp; Correcting CRFs</td>
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<td>6</td>
<td>Reviewing CRFs</td>
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<td>7</td>
<td>Dispensing Study Meds</td>
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<td>8</td>
<td>Drug accountability / storage</td>
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<tr>
<td>9</td>
<td>Assessing AEs / SAEs</td>
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<td>10</td>
<td>Reporting SAEs</td>
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<td>11</td>
<td>Study Admin.</td>
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<td>12</td>
<td>Other (Specify)</td>
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</tbody>
</table>
Possible Questions

Tell me about your qualifications

What type of GCP training have you had / who was the provider

Have you done any other research training

What is your clinical experience / experience on clinical trials

How do you assess that your team are competent to complete their delegated tasks – Is this documented
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Study Files & Documentation
Carole Edwards, Lead Research Nurse
“All Clinical Trial information should be recorded, handled and stored in a way that allows its accurate reporting, interpretation and verification”

“The confidentiality of records that could identity subjects shall be protected, respecting the privacy and confidentiality rules in accordance with the requirements of the Data Protection Act 1998 and the law relating to confidentiality”
Study Files and Documentation

• Trial Master Files (TMF)
  - Sponsor
  - Pharmacy
  - Investigator
• TMF Index
• Investigator Site File (ISF)
• Study Close Out
• Archiving
• Source Documentation
TMF & ISF Standard Operating Procedures (SOPs)

- Establishing and Maintaining a TMF for CTIMPs: UoA-NHSG-SOP-008
  - UoA-NHSG-TMP-003 – TMF Checklist
- Establishing and Maintaining an ISF for CTIMPs: UoA-NHSG-SOP-009
  - UoA-NHSG-TMP-002 – ISF Checklist
- Applies to all staff conducting or supporting CTIMPs sponsored or co-sponsored by UoA / NHS
Establishing and Maintaining a TMF for CTIMPs: UoA-NHSG-SOP-008

• Responsibility of the CI – can be delegated to research team – UoA-NHSG-TMP-034 Delegation Log
• Set up using a TMF checklist to create a file index - UoA-NHSG-TMP-003 – TMF Checklist
• Sponsor file and pharmacy file set up separately
• If document not applicable this should be noted in the TMF index
• Location of electronic documents must be noted in the TMF Index
Secure in a lockable cabinet or room with restricted access

Clearly state the location of all documents which are retained in different places

All approved amendments, essential correspondence with the MHRA and REC should be forwarded to Sponsor and pharmacy by the CI, or delegate.

Archived following UoA-NHSG-SOP-021 after reviewing all contents and adding closed minutes of the DMC where applicable
## Chief Investigator

**Trial Master File Checklist for CTIMP Studies**

### TABLE OF CONTENT

<table>
<thead>
<tr>
<th>CI TMF Index</th>
<th>Tick if present if not applicable enter N/A</th>
<th>Detail location if not held in the Paper TMF</th>
</tr>
</thead>
</table>

### 1.0 UCL SPONSORSHIP

- First Contact Questionnaire
- Sponsorship Letter(s) - In principle/Final
- Legal Representative Letter of Engagement (if applicable)
- Insurance Registration Form
- Insurance/Indemnity Letter
- Peer Review (if applicable)

### 2.0 FUNDING AND AGREEMENTS

#### IMP

- IMP Supply Agreement
- Technical Agreements (i.e. manufacturing/QP release, packaging, radiolabelling, IMP importation)
- Other

#### Central Services

- Central Laboratory Services Agreement/ Material Transfer Agreement if not with the CTSA (if applicable)
- CRO Agreement / Service Level Agreement (if applicable)
- Randomisation / Code break agreements (if applicable)
- Other

#### Funding

- Funding – Grant Application
- Funding – Grant Award
- Funding agreement
- Other

#### Responsibility Assignments (note CTSAs maintained in section 18)

- Sponsor-CI Agreement
- Legal Representative-Sponsor Agreement
- Other

#### Miscellaneous

- Confidentiality agreements
- Other

### 3.0 Research Ethics Committee (REC) and Medicines & Healthcare products Regulatory Agency (MHRA) (please file in chronological order and clearly label each submission separately)

- Initial signed application and supporting documentation to REC (including cover letter, REC validation letter, favourable/provisional/with conditions letter / response to conditions of approval)
- Initial signed application and supporting documentation to MHRA (including cover letter, validation letter, acceptance/with conditions/grounds for non-acceptance letter /response to conditions of approval/non acceptance)
- Substantial and Non Substantial Amendment(s) (including where applicable, Signed Annex 2, Supporting Documents, cover letter, favourable opinion letter /with conditions, response to conditions of approval)
- Log of Amendment(s) (non-substantial and substantial)
- Annual Progress Report to REC and acknowledgement
- Serious Breach notifications
- End of Trial Notification to REC and MHRA
- Final Report Notification and Supporting Documents

### 4.0 PROTOCOL

- Current Approved Protocol & Signature Page
- Superseded versions and Signature Pages
- Protocol Development Documentation
Establishing and Maintaining an ISF for CTIMPs: UoA-NHSG-SOP-009

- Responsibility of the PI – can be delegated to research team – UoA-NHSG-TMP-034 Delegation Log
- Set up using an ISF checklist to create a file index - UoA-NHSG-TMP-002 – ISF Checklist
- Hosted studies may use the ISF checklist if not provided with one by external sponsor
- Kept secure in a lockable cabinet or room with restricted access
- Clearly state the location of all documents which are retained in different places
- The site agreement will determine if the ISF is archived on site or at the sponsors archive facilities
# Investigator Site File Checklist for CTIMP Studies

## TABLE OF CONTENT

<table>
<thead>
<tr>
<th>Section</th>
<th>Tick if present</th>
<th>If not applicable enter N/A</th>
<th>Detail location if not held in the Paper TMF</th>
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</thead>
<tbody>
<tr>
<td>ISF Index</td>
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<tr>
<td>Key Clinical Trial Contacts</td>
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<tr>
<td><strong>1. SPONSORSHIP AND INSURANCE</strong></td>
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<td>Sponsorship Letter</td>
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<td>Insurance/Indemnity Letter</td>
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<td>Open to Recruitment Letter</td>
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<td>Site Closedown Letter</td>
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<td>Related Correspondence</td>
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<td><strong>2. FUNDING AND AGREEMENTS</strong></td>
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<td>Clinical Trial Site Agreement</td>
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<td>Laboratory Services Agreement</td>
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<td>Funding Arrangements/Agreements</td>
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<td>Other Agreements (if applicable)</td>
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<td><strong>3. REGULATORY</strong></td>
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<tr>
<td>Research Ethics Committee/GTAC Favourable Opinion Letter (including composition of REC/GTAC committee)</td>
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<tr>
<td>MHRA Notice of Acceptance Letter (CTA)</td>
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<tr>
<td>Substantial and Non Substantial Amendment documentation (including where applicable, Signed Annex 2, cover letter)</td>
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<tr>
<td>Amendment REC/GTAC/MHRA Approval Letter(s)</td>
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<tr>
<td>Log of Amendments</td>
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<tr>
<td>Annual Progress Reports (REC/GTAC)</td>
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<tr>
<td>End of Trial Notification</td>
<td></td>
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<tr>
<td>Related Correspondence</td>
<td></td>
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<tr>
<td><strong>4. SITE SPECIFIC APPROVALS</strong></td>
<td></td>
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<tr>
<td>IRAS R&amp;D Form</td>
<td></td>
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<tr>
<td>IRAS Site Specific Information (SSI) Form (signed)</td>
<td></td>
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<tr>
<td>Trust R&amp;D NHS permission letter / Site approval (NHS R&amp;D Management Approval letter for Research)</td>
<td></td>
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<tr>
<td>Trust R&amp;D NHS permission letter / acknowledgement for Trial Amendments</td>
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<tr>
<td>Trust R&amp;D notification of end of trial</td>
<td></td>
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<tr>
<td>ARSAC Licence</td>
<td></td>
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<tr>
<td>Genetic Modification Safety Committee Approval (for Gene Therapy Trials only)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Other Site Specific Approvals</td>
<td></td>
<td></td>
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<tr>
<td>Correspondence</td>
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<tr>
<td><strong>5. PROTOCOL</strong></td>
<td></td>
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<tr>
<td>Current Approved Protocol (signed by PI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superseded Protocol Versions (signed by PI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Correspondence</td>
<td></td>
<td></td>
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<tr>
<td><strong>6. PATIENT INFORMATION AND CONSENT</strong></td>
<td></td>
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</tr>
<tr>
<td>Current Patient/ Information Sheet and Consent Form (PIS)/ICF (on Trust headed paper)</td>
<td></td>
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<tr>
<td>Current GP Letter (on Trust headed paper)</td>
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<tr>
<td>Superseded versions of Patient/ Information Sheet and Consent Form (PIS)/ICF, GP letter</td>
<td></td>
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<tr>
<td>Patient Contact/Alert Card</td>
<td></td>
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<tr>
<td>Original Signed Informed Consent Forms (per patient/donor)</td>
<td></td>
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<tr>
<td>Other</td>
<td></td>
<td></td>
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<tr>
<td><strong>7. INVESTIGATIONAL MEDICINAL PRODUCT (IMP)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>* Note maybe located in separate pharmacy/IMP file (if so file note location)</td>
<td></td>
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</tr>
</tbody>
</table>

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*Tick if present* | *If not applicable enter N/A* | *Detail location if not held in the Paper TMF*
Possible Questions

Who is managing your TMF / ISF

Who has access to your files

Do you keep electronic versions of documents

How do you ensure the security of your records

MHRA Inspector
**Research Project Closure**

UoA-NHSG-SOP-20

- Including procedure for project suspension and early termination
- Responsibility of the CI to ensure that the ‘end of study/trial’ is clearly defined in the protocol - any change to this is a substantial amendment
- Contact R&D so that locally sponsored studies can have trial close out monitoring visit
- Declaration of End of Trial form must be sent to Sponsor, MHRA and REC within **90 days** of the trial ending (copy to R&D)
- Check for completeness of TMF & Data Collection
- Final reports & dissemination of results - UoA-NHSG-SOP-039 Research Project Publications and Dissemination for all CTIMPs
Archiving Data from Interventional Research Projects Involving Human Participants
UoA-NHSG-SOP-021
Archiving Data from Interventional Research Projects Involving Human Participants: UoA-NHSG-SOP-021

• Applies to all research – sponsored and/or co-sponsored by UoA and NHSG and hosted studies
• Sponsor and CI must ensure essential documents are retained for an appropriate period of time - and made available for monitoring and audit
• 25 years minimum (unless 3rd party obligations differ)
• Defined on REC application
• Multicentre studies- CI must determine where the ISF and other associated essential data will be archived.
Essential Documents / Source Documents

- TMF / ISF
- Data
- Hospital Records
- Clinical and office charts
- Lab notes
- Memoranda
- Subjects diaries
- Case Report Forms
- Evaluation checklists
- Recorded data from automated instruments
- Copies of transcriptions
- Records kept at pharmacy / Labs
- X-Rays / reports
- Photographs / microfilm
- Other – if appropriate
Hospital Health Records:

Health records and source data therein should be retained throughout the archiving period:

• NHSG policy – destroy after 6 years inactivity or 3 years after death
• Scanned onto C-Cube – sometimes poor quality
• Adhere sticker to front of ‘pink cover sheet’ or inside of medical records documenting:
  – Short Trial Title
  – Trial ID no – R&D/ Ethics/ EudraCT
  – Name of local CI or PI
  – Department name / contact number
  – Retention Date
• New SOP – Procedure for Retention of Health Records
  – to include PMS entry to back up retention sticker
• Archiving Process Summary
• For hosted studies - sponsor is responsible for archiving. PI – check contract to establish if archiving has been delegated from the sponsor to PI
• Electronic data files:
  - held on a UoA or NHSG secure networked server.
  - ‘locked’ in a read only format,
  - documented in the TMF
• Access to archive
• Destruction of Archive

• Do not destroy early or take with you if you leave – must be retained within the Sponsors locality
Possible Questions

What happens with the archiving at other sites

What will be forwarded to the TMF for archiving

What happens to the study material and patient medical notes at the end (archiving arrangements, who, where, how long)
MHRA GCP Inspection
2015

Medicines and Healthcare products Regulatory Agency

Pharmacovigilance
Patricia Burns, Research Governance Manager
WHAT IS PHARMACOVIGILANCE?

THE SCIENCE AND ACTIVITIES RELATING TO THE DETECTION
Definition of Adverse Events

• Any untoward medical occurrence or the deterioration of a pre-existing medical condition in a subject in a clinical trial

• An AE does not necessarily have to have a causal relationship with the study treatment / procedure

• An AE can therefore be any unfavourable and unintended sign (eg. tachycardia) including laboratory findings which are clinically significant, symptom (eg. nausea, chest pain) or a disease

• The term AE is used to include both serious and non-serious AEs

• Elective hospitalisations for pre-treatment conditions are not AEs
AR - Adverse Reaction

- An adverse reaction (AR) is where it is suspected that an AE has been caused by a reaction to a trial drug

SUSAR – Suspected Unexpected Serious Adverse Reaction
- An AR which is not described in Investigator’s Brochure (IB) or Summary of Product Characteristics (SmPC)
Purpose of recording Adverse Events ??

Legal requirement - The Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 1031)

• Regulatory authorities want to see if a drug trial follows reported side effect profiles as reported in the Investigators Brochure and Summary of Product Characteristics

• Safeguards the interests of trial participants
• Informs Data Monitoring Committee
• Assess the safety and efficacy of the interventions during the trial

• Companies must keep track of the side effect profile of their drugs
• New drugs have to build up this profile in clinical trials
Recording, Managing and Reporting Adverse Events, Serious Adverse Events and Suspected Unexpected Serious Adverse Reactions in Clinical Trials of an Investigational Medicinal Product

- Adverse Event / Adverse Reaction
  - Serious?*
    - Not Related to IMP?
      - Serious Adverse Event (SAE)
        - Unexpected?
          - Inform Sponsor and the Chief Investigator within 24 hours of learning of the event
        - Expected?
          - Suspected Unexpected Serious Adverse Reaction (SUSAR)
            - Sponsor must inform the MHRA within 7 days (life threatening) or 15 days (non-life threatening) of learning of the SUSAR
    - Related to IMP?
      - Serious Adverse Reaction (SAR)
  - Not Serious?
    - Related to IMP?
      - Adverse Reaction (AR)
        - Record and report as per protocol
    - Not Related to IMP?
      - Adverse Event (AE)

* Recurrence in Death
  - Life threatening
  - Hospitalisation / prolongation of hospitalisation
  - Persistent / significant disability
  - Congenital anomaly / birth defect
# Adverse Event Log

## Adverse Event Form

< STUDY TITLE>

Has the participant had any Adverse Events during this study?  
☐ Yes  ☐ No  *(If yes, please list all Adverse Events below)*

<table>
<thead>
<tr>
<th>Severity</th>
<th>Study Intervention Relationship</th>
<th>Action Taken Regarding Study Intervention</th>
<th>Outcome of AE</th>
<th>Expected</th>
<th>Serious</th>
</tr>
</thead>
</table>
| 1 = Mild | 1 = Definitely related  
          2 = Possibly related  
          3 = Not related | 1 = None  
          2 = Discontinued permanently  
          3 = Discontinued temporarily  
          4 = Reduced Dose  
          5 = Increased Dose  
          6 = Delayed Dose | 1 = Resolved, No Sequelae  
          2 = AE still present - no treatment  
          3 = AE still present - being treated  
          4 = Residual effects present - not treated  
          5 = Residual effects present treated  
          6 = Death  
          7 = Unknown | 1 = Yes  
          2 = No | 1 = Yes  
          2 = No *(If yes, complete SAE form)* |

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Start Date</th>
<th>Stop Date</th>
<th>Severity</th>
<th>Relationship to Study Treatment</th>
<th>Action Taken</th>
<th>Outcome of AE</th>
<th>Expected?</th>
<th>Serious Adverse Event?</th>
<th>Initials</th>
</tr>
</thead>
<tbody>
<tr>
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</tbody>
</table>
Generating Quality AE Data

Avoid:

Ambiguous information
Congestion (nasal, liver, sinus, pulmonary?)
Cramp (muscle, menstrual, abdominal?)
Pain (where?)

Ambiguous abbreviations
MI (myocardial infarction or mitral incompetence?)
GU pain (gastric ulcer pain or genito-urinary pain?)
Decreased BS (breath sounds, bowel sounds or blood sugar?)
Source data

- All AEs reported by the patient should be documented in the patient’s medical notes.
- If any action has been taken by the study team this should be recorded.
- GP should be informed if it is felt necessary, ask the patient’s permission.
- Medical notes can be used as source data for AEs.
Requirements for Pharmacovigilance

Report SAEs to the sponsor immediately (in practice 24 – 48 hours) pharmaco@abdn.ac.uk

Report SUSARs to the MHRA within 7 days if fatal/life threatening otherwise within 15 days

Urgent safety measures implemented, notify MHRA within 3 days.
Internal sponsor reference: Centre (if multicentre trial): UoA-NHSG
R&D reference: Participant Number:
EudraCT number: 
Study Title: 

Is this a possible SUSAR? Yes [ ] No [ ]

Date of report: D D M M Y Y Y Y Y
Initial Report [ ] Follow Up Report [ ]

<table>
<thead>
<tr>
<th>Subject Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initials</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Serious Adverse Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Seriousness criteria (Check all that apply):</td>
</tr>
<tr>
<td>Resulted in death [ ] Life-threatening [ ] Hospitalisation/Prolongation of hospitalisation [ ]</td>
</tr>
<tr>
<td>Persistent/Significant Disability/Incapacity [ ] Congenital anomaly/Birth defect [ ] Other medically important condition [ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>If Resulted in Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of Death: D D M M Y Y Y</td>
</tr>
<tr>
<td>Cause of Death:</td>
</tr>
<tr>
<td>Cause of Death determined by Autopsy: Yes [ ] No [ ]</td>
</tr>
</tbody>
</table>

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<thead>
<tr>
<th>Action taken:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug withdrawn [ ] Dose reduced [ ] Dose increased [ ]</td>
</tr>
<tr>
<td>Dose not changed [ ] Unknown [ ] Not applicable [ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Expectedness:</th>
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</thead>
<tbody>
<tr>
<td>Expected [ ] Unexpected [ ] Onset Date: D D M M Y Y Y</td>
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<tr>
<th>Diagnosis:</th>
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</table>

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<thead>
<tr>
<th>Relationship to Study Drug:</th>
</tr>
</thead>
<tbody>
<tr>
<td>None [ ] Possible [ ] Probable [ ] Definite [ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Severity:</th>
</tr>
</thead>
<tbody>
<tr>
<td>MILD [ ] Moderate [ ] Severe [ ]</td>
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</table>

<table>
<thead>
<tr>
<th>Outcomes:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recovered [ ] Recovered with sequelae [ ] Recovering [ ] Not recovered [ ] Unknown [ ] Fatal [ ]</td>
</tr>
<tr>
<td>Date of recovery: D D M M Y Y Y</td>
</tr>
</tbody>
</table>

DO NOT SEND IDENTIFIABLE DATA OR SOURCE DOCUMENTS WITH THIS REPORT
Contact Details
pharmaco@abdn.ac.uk

- Initial report may be by telephone (Ext: 51123)
- Detailed written report by email within 24 hours

CI to forward copy of eSUSAR report to RGM

https://esusar.mhra.gov.uk
Possible questions

Would CI report to MHRA if a SUSAR?

Who assesses SUSARs?

(How) Does the protocol permit for any non-escalated SAES?

What is the process for reporting SAEs?

Where do you send the annual safety report?

What is the process for reporting SUSARs?

MHRA Inspector
MHRA GCP Inspection
2015

Medicines and Healthcare products Regulatory Agency

Serious Breaches
Richard Cowie
Quality Assurance Manager
(1) The sponsor of a clinical trial shall notify the licensing authority in writing of any serious breach of:

(a) the conditions and principles of GCP in connection with that trial; or

(b) the protocol relating to that trial, as amended from time to time in accordance with regulations 22 to 25, within 7 days of becoming aware of that breach.

(2) For the purposes of this regulation, a ‘serious breach’ is a breach which is likely to affect to a significant degree –

(a) the safety or physical or mental integrity of the subjects of the trial; or

(b) the scientific value of the trial”.
Condition which applies to all clinical trials:

Rights, safety, and well being of trial participants are the most important considerations and shall prevail over interests of science and society.
Management of Deviations, Breaches and Urgent Safety Measures
UoA-NHSG-SOP-045 (replaces SOP 015)

Describes the procedure for identifying and managing Deviations, Breaches (Serious and Non-Serious) and Urgent Safety Measures, identified as a non-conformance with an approved research protocol, research project documentation, SOPs and/or the principles of Good Clinical Practice (GCP).
Definitions

**Deviation** is a minor deviation from an SOP, or a planned event.

**Non-Serious Breach:** may be considered a ‘minor non-conformance’ or ‘violation’ and has no impact on a participants’ safety or wellbeing, and/or the scientific integrity of the research. No substantial amendment is required to the approved protocol, trial documentation or trial SOPs.
Definitions (cont)

Serious Breach: a breach which is likely to affect, or have the potential to affect, to a significant degree:
- the safety, physical or mental integrity of the research participants; and/or
- the scientific value of the research.

Urgent Safety Measure: when a research participant is identified as being at risk of harm in relation to their involvement in a research project and urgent action, which deviates from the approved protocol, is required to manage the event and protect the participant(s).
The relationship between a Deviation, Non-Serious Breach and a Serious Breach
Examples of a Deviation include:
• An SOP being used beyond its review date.
• An audit or monitoring visit taking place outside of schedule.

Examples of a Non-Serious Breach include:
• A study visit out with a defined schedule.
• Boxes on the consent form ticked rather than initialled.
• Misplaced consent form (completed but mis-filed).
Examples of Serious Breaches

The premature destruction of investigator site files

No statement of patient eligibility signed by medically qualified individual
Examples of Serious Breaches

Patient identifiable data on laptop stolen from investigator’s car

IMP temperature excursions reported
Current Procedure for Serious Breaches

• CI to report all breaches to the Research Governance Team pharmaco@abdn.ac.uk within 24 hours.

• Complete Log of Deviations, Breaches and Urgent Safety Measures (appendix).

• Complete a Breach Report form (UoA-NHSG-TMP-067):
  - An overview of the incident and its cause.
  - Detail of Corrective and Preventive Action (CAPA).
  - An assessment of the likelihood of a recurrence.
  - An impact assessment on any work performed prior to the event, which may be compromised.
  - Outline of any changes which may be required to the protocol.
  - Likely timeline for CAPA and amendment approval (if applicable).
Current Procedure for Serious Breaches

- Initial assessment serious/non-serious made by CI.
- Review by Research Governance Manager (RGM) and QA Manager, who make a final assessment on seriousness.
- Breach Assessment Team may be called:
  - Confirm whether the Breach comprises a Serious Breach or not.
  - Identify which section of GCP or the approved protocol has been breached.
  - Identify how the Breach impacts on trial participants and/or the scientific integrity of the research.
  - May implement urgent safety measures.
  - Will work with the CI to identify CAPA.
  - Agree who needs to be notified and any follow-up action.
## Serious Breach Reporting

<table>
<thead>
<tr>
<th></th>
<th>CTIMP *</th>
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</thead>
<tbody>
<tr>
<td><strong>Sponsor</strong></td>
<td>Breach Report Form &amp; Breach Report Log - emailed to <a href="mailto:pharmaco@abdn.ac.uk">pharmaco@abdn.ac.uk</a> within 24h by CI</td>
</tr>
<tr>
<td><strong>MHRA</strong></td>
<td>YES - Within 7 days by Sponsor</td>
</tr>
<tr>
<td><strong>REC</strong></td>
<td>YES - Within 7 days by CI</td>
</tr>
<tr>
<td><strong>R&amp;D</strong></td>
<td>YES - Within 7 days by CI</td>
</tr>
<tr>
<td><strong>CSOG</strong></td>
<td>YES - At next meeting by Sponsor</td>
</tr>
<tr>
<td>Clinical Studies Oversight Group</td>
<td></td>
</tr>
<tr>
<td><strong>PMG</strong></td>
<td>YES by CI</td>
</tr>
<tr>
<td>Project Management Group</td>
<td></td>
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<tr>
<td><strong>TSC</strong></td>
<td>YES by CI</td>
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<tr>
<td>Trial Steering Committee</td>
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<tr>
<td><strong>DMC</strong></td>
<td>YES by CI</td>
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<tr>
<td>Data Monitoring Committee</td>
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</table>

* May involve follow up reporting
Have there been any deviations from the protocol?

What do you class as a deviation?

Have there been any breaches of GCP?

Have there been any persistent deviations of GCP or the protocol?
MHRA GCP Inspection
2015

Medicines and Healthcare products Regulatory Agency

Informed Consent
Anna Strachan, Training Facilitator
Preparation for MHRA Inspection

Informed Consent

1.
Informed consent in regulations and guidelines
Declaration of Helsinki

‘Subjects must be volunteers and informed participants in the research project’

Research Governance Framework

“Informed consent is at the heart of ethical research. Most studies involving individuals must have appropriate arrangements for obtaining consent and the NHS ethics review process pays particular attention to those arrangements”.
For the purposes of this Schedule, a person gives informed consent to take part, or that a subject is to take part, in a clinical trial only if his decision:

(a) is given freely after that person is informed of the nature, significance, implications and risks of the trial; and

(b) either

(i) is evidenced in writing, dated and signed, or otherwise marked, by that person so as to indicate his consent; or

(ii) if the person is unable to sign or to mark a document so as to indicate his consent, is given orally in the presence of at least one witness and recorded in writing.
Preparation for MHRA Inspection
Informed Consent

2.
Informed consent monitored before, during and at the end of the trial
Aspects and objectives of monitoring a clinical trial before, during and at the end of the trial.
Monitoring checks before

• Approved versions of documents available for use
• Appropriate procedures are in place
• Local arrangements with consent processes are in accordance with favourable REC opinion
Monitoring checks during

✓ Correct versions of documentation are being used
✓ Check any re-consent has been conducted (where appropriate)

Consent:
✓ appropriately undertaken
✓ taken by an authorised delegated person
✓ taken prior to participation/trial assessments
✓ personally signed and dated by subject
✓ signed by an appropriate witness or legal representative (as required)
✓ assented to (if required)
Monitoring checks after

✓ Ensure all consents are present and complete and filed
Preparation for MHRA Inspection

Informed Consent

3.

Documenting informed consent process
Informed Consent: Documentation in Medical Notes

- Date PIS given
- Patient meets eligibility criteria (medic signed)
- Opportunity for questions to be asked/answered
- Who took consent, date
- Version number and date of PIS and consent form used
- GP informed if appropriate
You: “Are you happy to continue taking part in the study?”

Participant: “Yes” ...or “No”

✓ Write down in health records “Happy to continue”

or

✓ Tick a box on the Case Report Form
Preparation for MHRA Inspection
Informed Consent

4.
Local SOPs on Informed Consent
(incl. new SOP training)
Old & New Informed Consent SOPs

Obtaining Informed Consent from Competent Adults for Research Studies

“Old” – UoA-NHSH-SOP-010 version 1.02
14th March 2012 until 14th March 2014

“New” – UoA-NHSG-SOP-010 version 2
from 15th April 2015
• Written informed consent
• Definition
• Applies to all studies unless study specific SOP
• Applies to NHSG and UoA staff & collaborators involved in obtaining informed consent
• Applies to competent adults only
Responsibilities

• PI – ensure ethical approval for informed consent form & other information for participants
• PI can delegate taking informed consent (delegation log)
• PI – fully inform the subject
• Delegated staff appropriately trained
• PI – informed consent is obtained before any research procedures begin
Patient Information Sheet

- Full information about the research
- Encourage participant to ask questions
- Give time for deliberation and consulting family/GP etc. if necessary
- Template PIS
Informed Consent Form (ICF)

- Local headed paper
- Version number and date
- Unit & department conducting research
- Identifiable with the study
- Study title
- If CTIMP, EudraCT number
- Currently approved, most recent version
- Template Informed Consent Form
Procedure: Obtaining Informed Consent (1)

- Only staff named on delegation log. Those named on the delegation log cannot be consented into the study.
- No pressure on potential participant
- If doubt as to understanding, do not recruit
- No obligation to participate, free withdrawal & future treatment not affected
- Obtain consent before any study procedures
Procedure: Obtaining Informed Consent (2)

- Check name, DoB, study title and documentation
- Participant should read ICF statements, initial the boxes, write name, sign and date
- The person taking consent must countersign & date
- Non-CTIMPs: consent as approved by REC
- If not written, create study specific procedure
Procedure: Obtaining Informed Consent (3)

CTIMPs only

- telephone or verbal consent not allowed
- PI or delegate to document in the clinical notes:
  - Date when PIS given
  - Meeting inclusion/exclusion criteria and eligibility
  - Date & time the person consented to be participant (may also apply to other studies)
• Original ICF placed in the investigator site file
• One copy for the subject and one for the clinical notes or GP (if required)
• Do not store with CRFs!
• If changes to study protocol / PIS / CRF, discuss the need to re-consent with the REC
• Deviations to the approved consent process must be reported in writing to REC
Vulnerable Participants

1. Difficulty reading/writing
   - Impartial witness
   - Read PIS to participant
   - signature of witness

2. Minor – child under 16
   - consent of parent required

3. Adult – unable to give informed consent due to physical or mental incapacity
   - Adults with Incapacity (Scotland) Act 2000
   - consent by a legal representative
Preparation for MHRA Inspection
Informed Consent

5.
Common MHRA findings and questions
Common MHRA findings

They will check source data from medical notes!

- No record of study visit in medical notes
- No records of consent being taken – medical notes or ISF
- Poor version control
- Inconsistencies with protocol/amendments
- Missing elements e.g. signature
- Unclear process
Talk me through the consent procedure

How do you approach patients?

Who tells participants about the trial

Where do you store PIS & Consent form

Can all participants consent on their own?

How have other clinicians been told about the trial?
MHRA GCP Inspection
2015

MHRA

Medicines and Healthcare products Regulatory Agency

Communication
Karen Secombes, Training Facilitator
Communication is everyone’s responsibility and not just the role of one team.

All medical research subjects should be given the option of being informed about the general outcome and results of the study.

The physician must fully inform the patient which aspects of their care are related to the research. The refusal of a patient to participate in a study or the patient’s decision to withdraw from the study must never adversely affect the patient-physician relationship.

Communication is everyone’s responsibility and not just the role of one team.
Communication – with Who?

- Research team
- Clinical team (e.g. ward nurses/HCSW/doctors/AHPs)
- Pharmacy
- Labs – internal & external
- Sponsor
- Ethics/R&D/MHRA
- Monitors, Inspectors, Auditors
- Project Management Groups, TSC/DMC
Communication – What?

- Research proposal/Submissions/Amendments/Approvals
- Protocol/SOPs
- Lab manuals
- PIS/IC
- CRFs
  - UoA – NHSG - 012 Data Management for Clinical Trials
  - UoA - NHSG - 026 Case Report Forms
- Pharmacovigilence
- GCP
Communication – Study Set Up

- UoA-NHSG-004 V2 Applying for Sponsorship for CTIMPs and High Risk Interventional Studies
- UoA-NHSG-006 V3 Study Start Up
- UoA-NHSG-024 V2 Applying for REC Ethical Opinion
- UoA-NHSG-025 V3 Submitting a CTA or a Notification for a Trial to MHRA
- UoA-NHSG-051 V1 GCP Training requirements
Communication – Who & How?

Internally: Research Team

- Regular meetings – dates, agenda, minutes
- Training sessions – detailed in training log (signed off if required)
- Email updates
- Written correspondence
Written correspondence

– Record file notes if there is any deviation from the protocol
– Record all informal meetings and their outcomes. Use confirmation email to document verbal discussions.
– Evidence of documentation of eligibility of patient in medical records by the investigator (qualified physician or dentist)
– Letters to GPs re medical decisions
– Documentation of reason for withdrawal from study (if known)
– Always maintain a paper trail
‘Correspondence which is necessary to construct key activities and decisions must be retained. Key E-mail correspondence must be saved individually and not as conversations, and filed appropriately’
Communication – Who?

Externally: Clinical team

- Ward staff: presentations/posters
- New staff/rotational staff – documented procedure of how they are informed of study
- External clinicians – e.g. labels on notes
Communication – How?

Externally: Pharmacy, Sponsor, Ethics, R&D, MHRA, PMG, TSC, DMC

• Email updates
• Written correspondence
• Amendments – inform correct people

• Annual Progress Reports to NHS REC
• Notify MHRA & REC at End of Trial
• Development Safety Update Report to MHRA & REC

Preparation & Submission of APRs for all Research Projects & DSURs  UoA-NHSG-SOP-013 v2
Research Project Closure (Including Procedure for project suspension or Early Termination)  UoA-NHSG-SOP-020 v3
SOPs

UoA-NHSG

- 006 V3 - Study set up
- 016 V2 - Training record
- 051 V1 - GCP Training
- 002 V1 - Creation of PMG, TSC and DMC
- 010 V2 - Informed Consent
- 026 V3 - CRFs
- 047 V1 - Good Documentation Practice
- 014 V3 - Recording, Managing & Reporting AEs, SAEs & SUSARs in CTIMPs
Communication

Keep a record of everything & file appropriately in the TMF/ISF

Inspectors will look for evidence that a study team communicates well

“if it isn’t written down, it didn’t happen”
Possible questions

- How do clinicians know this patient is part of a study?
- How is communication maintained?
- What do you cover in these meetings – are they minuted?
- How do staff on call (not part of core team) know what to do?
- How do clinicians know this patient is part of a study?
- How have other clinicians been told about the trial?
Summary

Medicines for Human Use (Clinical Trials) Regulations 2004 (SI: 1031)

- Review your trial documentation and training files of staff
- Have evidence of training (GCP certificate, CV) - keep your training log up to date
- Ensure delegation log reflects the research team roles
  - Who is responsible for which task?
- Know your roles and responsibilities in trial
- Know the protocol / PIS / Patient Journey
- Revisit SAE/ SUSARs

Familiarise yourself with SOPs – knowing where to find them is key
• Record file notes if there is any deviation from the protocol
• Always maintain a paper trail
• Record all informal meetings and their outcomes. Use confirmation email to document verbal discussions.
• **Document it - if it isn’t written down, it didn’t happen**

• Be confident of your trial and processes
• Review the typical questions and answers provided
• Always be prepared – would your study stand up to inspection NOW?

*Remember that you know your trial better than anyone else!*
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