Health and Care Research Wales
Support and Delivery Centre

The Fundamentals of Clinical Research Delivery for Laboratory Staff
Welcome

- The importance of clinical research
- Practice standards
- Roles and responsibilities
- Laboratory considerations (approvals, sample receipt and processing, data management, quality systems)
Introduction: The importance of clinical research
Supporting and developing excellent research which has a positive impact on the health, wellbeing and prosperity of the people in Wales

Health and Care Research Wales will provide leadership for research professionals in Wales, develop and value individuals through training and mentoring, and work to improve the profile of Welsh health and social care research both within and outside Wales
Oral and Biomedical Sciences- Cardiff University

Themes

Our research is focused on the following themes:

**Oral and biomedical sciences**

- Our aim is to understand the cellular and molecular processes underpinning tissue responses to trauma and subsequent regeneration and reparative processes.

**Applied clinical research & public health**

- We aim to improve the effectiveness, efficiency and organisation of care including disease prevention and health promotion.

**Dental education, scholarship and innovation**

- We are committed to providing a high-quality, student-focused educational experience, and to improving the delivery and pedagogical understanding of dental education.
Research is a frontline service: the NHS and the university working together, in partnership
Why is laboratory analysis important in clinical research?

• Results help define whether individual patients are **eligible** for a study

• Results are monitored for signs of **safety or efficacy** issues

• Results are used as outcomes to **answer** a research question

• Results are monitored to see how a drug **moves through the body** (pharmacokinetics)
Why is laboratory analysis important in clinical research?

An example: Herceptin, the brand name of a medicine called trastuzumab

Pathophysiology

Research discovered that HER2 was amplified in some cancers and was associated with poorer outcome

HER2 testing developed in the laboratory

(Prognostic)
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HER2 testing defines eligibility for clinical trials

(Identification)
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HER2 testing defines eligibility for clinical trials
(Identification)

Treatment
Herceptin is now commonly used to treat pts who are HER2 +

HER2 testing now routine in NHS practice
(Stratified/Targeted)
Inspirational experiences from patients, their families and carers

Health and Care Research Wales

VISION

Our vision is for Wales to be internationally recognised for its excellent health and social care research that has a positive impact on the health, wellbeing and prosperity of the people in Wales.

Strategic Aims (part 1)

To achieve our vision we will:

• ensure public involvement and engagement is central to what we do and visible in all elements of it

• ensure our work is aligned to Welsh Government policy and has real impact;
Health and Care Research Wales

Strategic Aims (part 2)

To achieve our vision we will:

• fully integrate our infrastructure and programmes across health and social care;

• invest in areas in which Wales excels and is unique;

• increase capacity in health and social care research in Wales;

• develop systems that ensure excellent delivery and maximise the use of our resources.
Summary

• High quality research stops us making assumptions and ensures we have the evidence we need to deliver better care.

• Research is a frontline service, making a vital contribution to the improvement of the NHS and the treatments and services it delivers.

• Laboratory staff actively contribute to the research process, and are essential in ensuring the delivery of high quality clinical research.

• Health and Care Research Wales ensures that the delivery and support for research and development in the NHS and social care in Wales enables studies to happen as quickly and efficiently as possible.
Clinical research standards

We will now move on to look at the **practice standards** which must be met to ensure patients participating in clinical research are protected and research outcomes are reliable.
The significance of standards

• The outcomes of research inform clinical decisions and guidance.

• If the research process is flawed, the information becomes unreliable, undermining the day-to-day practice of healthcare.

• Quality standards for the conduct of clinical research are, therefore, essential to ensure we conduct safe and meaningful studies.

• The international standard for the conduct of clinical research is Good Clinical Practice (GCP).
The Principles of GCP

The Principles of Good Clinical Practice (GCP) are at the heart of the guidance and legislation which governs the conduct of any clinical research carried out in the NHS.

There are 14 principles of GCP including...

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.

4. The necessary procedures to secure the quality of every aspect of the trial shall be complied with.

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.
The Principles of GCP

The Principles of GCP are the foundation of high quality, ethical research practice. They developed from a real need, from real cases.
Clinical Trials of Investigational Medicinal Products (CTIMPs)

• Safety, quality and efficacy of medicines must be demonstrated before they are authorised for use.

— Medicines which are being investigated through a clinical trial are known as Investigational Medicinal Products (IMPs).

• Clinical Trials of Investigational Medicinal Products (CTIMPs) are conducted to gather the evidence for a licence (marketing authorisation) to be granted, or to find out more about medicines which already have a marketing authorisation.

• In the UK, Clinical Trials are governed by the UK Medicines for Human Use (Clinical Trials) Regulations 2004.
UK Policy Framework for Health and Social Care Research

- UK Policy Framework for Health and Social Care Research published in October, replaces the Research Governance Framework

- Sets out high-level principles and responsibilities, applicable to ALL health and social care research

- Aims to help make the UK an even better place to do research

- Updates and training will be made widely available to support implementation
Other standards

• **Overarching regulations**, for example
  – Data Protection Act and General Data Protection Regulations (2018)
  – Transport of dangerous good regulations

• Local NHS health board/trust/organisation **policies and procedures**

• **Professional standards**
  – Royal College of Pathologists
  – Institute of Biomedical Science (IBMS)
  – Health and Care Professions Council (HCPC)
  – United Kingdom Accreditation Service (UKAS)
The aim of GCP

… and all other standards which govern clinical research is to ensure:

• The rights, safety and well being of study participants are protected

• Research data are of a high quality
Summary

• Quality standards, including Good Clinical Practice (GCP), are essential to protect participants and ensure the integrity of research data.

• Guidelines and principles have been developed over time as a result of unethical and dangerous practice. In the UK these have culminated in the Medicines for Human Use (Clinical Trials) regulations.
Human Tissue Act training
Roles and responsibilities
There are three key roles in the research process that provide oversight and support study conduct:

- Sponsor
- Chief Investigator (CI)
- Principal Investigator (PI)

The person or people performing these roles can delegate the tasks associated with their role to others in the site team, but they always remain ultimately responsible for them.
Site team

• A wide range of people may make up the local Site team. These may include the clinical team, pharmacy, laboratories and others

• Laboratories provide sample processing and analysis that contribute to the safety of research subjects

• Laboratories also contribute to the main objectives of the study

• Research participants have given their consent to participate in research and for their samples to be processed as required as part of the study.
Your responsibilities

- You have a responsibility to follow the instructions provided.
- Sample processing and analysis will either be performed using existing procedures or a new procedure will be provided.
- You must be familiar with your role in sample processing and trained in the relevant procedures.
- You have a duty to report/escalate any deviation from the instructions you are given or any issues you feel may impact on the integrity of the data produced.
Research in your laboratory

• What research activity is your laboratory involved in?

• Who is your departmental nominated research lead/Champion?

• How is the information communicated to the wider team?
Summary

• The Sponsor, Chief Investigator (CI) and Principal Investigator (PI) are responsible for ensuring the study meets all the required standards.

• Laboratory staff are part of the PI’s site team and should understand their role in processing and analysing research samples.

• There should be a research champion in the laboratory with a more detailed understanding of clinical research and who can provide advice and be the point of contact to the research team and laboratory staff.
Documentation and data
Collection and use of research data

• Laboratory data forms part of the study data. It illustrates something needed to answer the research question and/or ensure participants are safe.

• Study data is recorded in various records such as patient notes or laboratory results. As this is the original record, it is known as Source data.

“All information in original records and certified copies of original record of clinical findings, observations or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents”

ICH GCP 1.51
Collection and use of research data

- Metadata is data that describe the attributes of other data, and provide context and meaning.

- Metadata describe the structure, data elements, interrelationships and other characteristics of data, and attribute the data to an individual.

- For example: **data** (bold text) and *metadata* (italic text)
  
  **Joe Bloggs, Unit No. G35647, Na 142 mmol/l, 11/11/15**

- Metadata forms an integral part of the original record. Without metadata, the data has no meaning.
How we ensure the quality of the data

• All Sponsors must provide evidence of how they will maintain standards by monitoring and accounting for the study’s conduct.

• The UK Competent Authority, the Medicines and Healthcare products Regulatory Agency (MHRA), conducts GCP Inspections for CTIMPs, which may include the review of Laboratory data and systems.

• Good documentation serves to demonstrate the compliance with the standards of GCP and with all applicable regulatory requirements, and therefore the quality of the research.
Summary

• Laboratory data, including metadata, forms part of the study data, helping to answer the research question and/or maintain patient safety

• The Sponsor will monitor the quality of study data, including laboratory data

• The MHRA may also inspect the laboratory data if the study is a CTIMP.
Laboratory considerations
The clinical research delivery pathway

**Research ideas**
- Attracting studies
- Feasibility
- Study capacity and capability assessment
  - Protocol and Laboratory manual review
  - Laboratory agreement
- Study set up
  - Site initiation visits
  - Documentation
  - Working arrangements, SOPs

**Study development & planning**

**Study Set-up**

**Study recruitment & follow up**
- Study sample processing
  - Request
  - Receipt
  - Identification
  - Processing
  - Analysis
  - Reporting/recording
  - Storage
  - Shipping
  - Destruction

**Study close**
- Laboratories should be informed when the study is closed
- Archiving material

Laboratory involvement

- Study may be closed to recruitment but participants may still need follow up requiring study activity
The study protocol

- Sets out how the research question will be answered through the conduct of the study
- States how scientific integrity and data quality are to be achieved in the study, including laboratory processes
- Helps to ensure the rights, safety and wellbeing of participants are protected
The laboratory manual

- The sponsor may also provide a laboratory manual detailing laboratory specific requirements for the study including:
  - Analytical method
  - Validation
  - CE marked kits
  - Storage, shipping and chain of custody

- The details of what is required vary from study to study and may be different from your standard practice.
Laboratory SOPs

Your laboratory’s research lead will:

• ensure there are local Standard Operating Procedures (SOPs) in place which provide instructions on identifying and processing research samples

• consider how the protocol and laboratory manual will be implemented for each study

• ensure there are study specific SOPs in place if any changes to standard practice are needed

• ensure appropriate training is provided.
Knowing your responsibilities

• You have a responsibility to follow the instructions provided through documentation and training on:
  
  • Local SOPs
  • Study specific SOPs
  • Study specific laboratory manual

• If you are unsure about anything in these documents, or have a question/issue that is not covered, escalate it to your laboratory research lead.
Laboratory research sample processes
Patient consent to study (includes specified use of patient samples)

Patient consent to samples being taken

Sample sent away by research team

Sample arrival in Laboratory

Analysis

External quality assurance

Reporting arrangements
- Safety reporting
- Maintaining blinding
- Reference ranges

Any specific requirements?

Storage | Recording/Reporting

Destruction

Anonymisation

Sample transport and shipping regulations
Things to consider

Consent will have been received and documented by the study team. A process should be in place to inform the lab if the patient withdraws consent or is withdrawn from the study.
Patient consent to study (includes specified use of patient samples)

Patient consent to samples being taken

Sample sent away by research team

Sample arrival in Laboratory

Sample processing arrangements
- Recognised as a research sample
- Unique patient identifier
- Timelines for analysis etc.

Things to Consider

Timing: Will the sample be analysed in a timely manner?

Labelling: Is it a study sample?
Labelling: Does the sample have a unique patient identifier?

Sample integrity

Data quality - Audit/Tracking

Any specific requirements?

Destruction

Transport

Anonymisation
Sample transport and shipping regulations

External quality assurance

Reporting arrangements
- Safety reporting
- Maintaining blinding
- Reference ranges

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Patient consent to study (includes specified use of patient samples)

Patient consent to samples being taken

Sample sent away by research team

Sample processing arrangements - Recognised as a research sample - Unique patient identifier - Timelines for analysis etc.

Sample arrival in Laboratory

Analysis

External quality assurance

Things to consider

Quality - Sample integrity
Quality - QA, QC
Data integrity and quality
Standardisation and Reproducibility

Any specific requirements

Anonymisation
Sample transport and shipping regulations

Recording/Reporting

Reporting arrangements - Safety reporting - Maintaining blinding - Reference ranges

Destruction

Transport
Patient consent to study (includes specified use of patient samples)

Patient consent to samples being taken

Sample sent away by research team

Transport

Storage

Recording/Reporting

Destruction

Anonymisation

Sample transport and shipping regulations

Things to consider
Will the result be reported in the required time frame?
Expedited reporting
Any study blinding requirements, including reporting?
Reference ranges and units
Exclusion or withdrawal from study participation
Interpretation errors
Analytical errors

External quality assurance

Reporting arrangements
- Safety reporting
- Maintaining blinding
- Reference ranges

Any specific requirements?
Patient consent to study (includes specified use of patient samples)

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Analysis

External quality assurance

Reporting arrangements
- Safety reporting
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- Reference ranges

Any specific requirements?

Anonymisation

Sample transport and shipping regulations

Things to consider

Environmental conditions

Equipment: space, calibration, maintenance, back up

Records: Sample inventories, servicing, temperature monitoring
Patient consent to study (includes specified use of patient samples)

Patient consent to samples being taken

Sample sent away by research team

Sample arrival in Laboratory

Sample processing arrangements
- Recognised as a research sample
- Unique patient identifier
- Timelines for analysis etc.

Analysis

External quality assurance

Things to consider
Shipping regulations
Anonymisation
Shipping conditions
Method of transfer
Destination UK/Europe?

Any specific requirements?

Transport

Anonymisation
Sample transport and shipping regulations

Reporting arrangements
- Safety reporting
- Maintaining blinding
- Reference ranges

Destruction
Deviations from SOPs

• Deviations sometimes happen which are beyond our control, for example equipment failure

• While you should avoid errors wherever possible, human factors also lead to deviations

• Ensure you tell your research lead about all deviations from the SOPs immediately

• If you are not able to carry out the study requirements in line with the SOPs escalate this to your research lead immediately and before taking any action.
Summary

• Laboratories play an essential role throughout the clinical research delivery pathway

• Each study will have specific requirements for every stage of the sample handling process

• What you do impacts on the integrity of data for each participant and the study as a whole, and you should escalate any mistakes and deviations immediately

• Your local SOPs, study specific SOPs and laboratory manuals, and your laboratory research lead are important sources of information about these requirements.
Laboratories impact on the patient pathway

Although laboratory teams may not interact directly with the patient, their contribution to the research process has a direct impact on the patient’s safety and wellbeing.
Laboratories impact on the patient pathway

1. **Patient** identified, approached & has given their **consent**

2. **Patient Screening**
   - Samples taken & sent to lab
     - Samples inadequately processed or delayed analysis or reporting
       - Results not available for review - **Patient** not eligible to continue
     - Samples processed according to protocol within specified timeline
       - Results reviewed against inclusion criteria
         - **Patient** randomised into study
         - **Patient** referred back to standard of care pathway

3. **Patient** attends study visits
   - Safety and efficacy bloods taken for analysis
     - Samples not analysed in line with study protocol
       - Delay in study timelines protocol deviation
       - Next medication cannot be dispensed
     - Samples analysed in line with protocol
       - **Patient** at (potential) risk
       - **Patient** continues on study
       - **Patient** withdrawn and referred back to standard of care pathway

4. **Patient** referred back to standard of care pathway
Session complete!

• The importance of clinical research
• Practice standards
• Roles and responsibilities
• Laboratory considerations (approvals, sample receipt and processing, data management, quality systems)

thank you!