Fundamentals of Clinical Research Delivery for Pharmacy (Secondary)
Welcome

- The importance of clinical research
- Pharmacy involvement in clinical research
- Practice standards
- Roles and responsibilities
- Documentation and data
The importance of clinical research
Why is clinical research important?

“Research is central to the NHS...

We need the evidence from research to deliver better care. Much of the care that we deliver at the moment is based on uncertainties or experience, but not on evidence.

We can only correct that with research.”

– excerpt from NIHR video
Enhancing Patient Care Through Research

Professor Dame Sally Davies, Chief Medical Officer for England, Director General of Research and Development and Chief Scientific Adviser for the Department of Health and NHS.
Research is a frontline service

The NHS is committed to “continuous improvement in the quality of services [patients] receive, identifying and sharing best practice in quality of care and treatments”.

An example of the importance of pharmacy in clinical research

The development of Herceptin®, the brand name of a medicine called trastuzumab

Research Idea

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

HER2 became a good target for drug development.
An example of the importance of pharmacy in clinical research

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**Research Idea**

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

*HER2* became a good target for drug development.

**Clinical Trials**

A monoclonal antibody drug was developed to block the receptor activity of *HER2*.

The monoclonal antibody drug eventually became known as trastuzumab (brand name Herceptin®), and was tested in clinical trials.
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HER2 became a good target for drug development.

Trastuzumab is now commonly used to treat pts who are HER2 +.

HER2 testing now routine in NHS practice.
Research is important to patients

How important is it to you that the NHS carries out clinical research?

- 94% Very/fairly important
- 4.7% Don't know
- 1.9% Not important
- 2.4% Not important
- 5% Don't know

How important is it to you to be offered new treatments by your healthcare professional?

- 93% Very/fairly important

Results are taken from a Countrywide consumer poll of 3,000 people in England, commissioned by NIHR CRN in September 2014.
Inspirational experiences from patients, their families and carers

We've gathered some fantastic stories from people across England, whose lives have been transformed by clinical research. All you need to do is click on the links below to access experiences relating to a wide range of conditions. You'll find short films and video-diaries to explore, plus audio and written accounts too.

If you want to tell us about your experiences, please email the team at cmcc.comms@nihr.ac.uk
You can also join the conversation on Twitter. Share your experiences with @nihrm using #cmcl.

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.

• Pharmacy 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.
Pharmacy can support clinical research in a variety of ways
Being aware of and promoting clinical research

You can support research by being positive about research and directing people to useful information.

The **UK Clinical Trials Gateway** provides easy to understand information about clinical research trials running in the UK. It is designed to enable patients and their clinicians to locate and contact trials. [http://www.ukctg.nihr.ac.uk](http://www.ukctg.nihr.ac.uk)

The ‘**Public**’ section on the Health and Care Research Wales website contains lots of useful information about how people can get involved in research. [https://www.healthandcareresearch.gov.wales/public/](https://www.healthandcareresearch.gov.wales/public/)

**HealthWise Wales** is an opportunity for everyone in Wales aged 16 or over to take part in research for better health, care and wellbeing. [https://www.healthwisewales.gov.wales](https://www.healthwisewales.gov.wales)
Encountering clinical trials medicines in normal practice

You may come into contact with clinical trials medicines in your everyday work:

- Medicines returns
- Medicines use reviews or reconciliation.
Medicines returns

• Clinical trials medicines could be returned to you along with other medicines

• Look for the study team’s details on the label

• Contact them to let them know the medicine has been returned to you and why (eg. the patient has died)

• They will tell you whether they need you to return or destroy it

• If they ask you to destroy it, check for any special instructions.
Medicines use reviews or reconciliation

• During a MUR you might identify that a patient is participating in a clinical trial.

• You may identify concerning issues such as:
  • their adherence to the trial instructions provided is poor
  • they express concerns about remaining on the study

• Establish as much information as practical

• Advise the patient to contact the study team and, if necessary, their GP

• If you feel it is appropriate to raise the issue with the study team yourself, ask for the patient’s permission to do so

• Record your actions in the Patient Medication Record (PMR).
Adverse events

• A patient might also tell you about an adverse event, such as a potential side effect or a minor injury they have suffered.

• An **Adverse Event (AE)** is any untoward medical occurrence which happens during a study.

• Adverse events **do not** have to appear to be related to the study medication or procedures.

• Sometimes it is only when data from a very large number of people is collated together that patterns emerge showing the medicine is resulting in unexpected reactions.

• If the patient is participating in a study your Health Board/Trust is involved in, **follow your local SOPs** for notifying the study team about adverse events.
Adverse events

• If the patient is involved in a study being conducted by another organisation, contact the study team to let them know about the side effect reported.

• They should not need any patient identifiable information, but they are likely to need the patient identification number, batch number and other information on the label.

• Advise the patient to tell the study team about the side effect themselves as well. They will have been provided with contact details for the Health Board/Trust that recruited them into the study.

• You might also suggest they let their GP know, depending on the specific circumstances and side effects.

• If you cannot contact the study team, report the side effects using the MHRA Yellow Card scheme.
Pharmacy can *contribute to* clinical research in a variety of ways
Identifying potential research participants

- Identifying the right people to participate in research is an important part of conducting effective studies.

- Pharmacy may be asked to:
  - display a poster about a specific study
  - give leaflets about a study to patients who meet certain criteria
  - search patient databases to identify and contact patients who meet certain criteria

- All study activities, including those to identify potential participants must be approved by a Research Ethics Committee, which the researcher will arrange.

- It is important your Health Board/Trust clinical research lead agrees the activity is appropriate before agreeing to anything.
Identifying potential research participants

• You must carry out any activities in line with the instructions provided by the researchers. Do not change any language or images in the letters, leaflets or posters provided.

• The researchers will notify you when the study has begun and you can carry out the activities required, it is important not to begin the study before all the checks and approvals are complete.

• The documents can be changed several times before they are approved by the Research Ethics Committee. New versions can also be provided once the study has begun. Ensure you are always using the correct version.
Pharmacy can also *contribute to* clinical research by...

- Providing a **study intervention** such as weight loss or smoking cessation support
- Ensuring study medicines are **stored** appropriately and the right participant receives the **right medicine** at the **right dose**
- **Recruiting participants** into studies and **gathering data** to answer the research question
Find out more

• If you’re thinking about engaging in research activity, talk to your organisation/company/Health Board/Trust clinical research lead or research and development department

• Health and Care Research Wales provides an innovative infrastructure to support and increase capacity in research and development. https://www.healthandcarereresearch.gov.wales/research-infrastructure/

• Health and Care Research Wales also provides training to help you deliver research activities effectively. https://www.healthandcarereresearch.gov.wales/training-and-development/
Clinical research in your pharmacy

- What clinical research activity is your pharmacy involved in?
- What clinical research are you being asked to support?
- Who is your clinical research lead?
- How is information communicated to the wider team?
Standards for clinical research delivery
The significance of standards

- The outcomes of research inform clinical decisions and guidance, and may contribute to the licensing of new treatments.

- 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
  - General Data Protection Regulations (2018)
  - Human Medicines Regulations (2012)
  - Transport of dangerous good regulations

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

- **Professional standards**
  - Royal Pharmaceutical Society (RPS)
  - Health and Care Professions Council (HCPC)
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.
Roles and responsibilities
Key roles
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.

• Providing clinical trial medicines management is one of the key roles for pharmacy staff.

• Pharmacy may also support the identification and signposting of potential participants to clinical research studies.

• Research participants have given their consent to participate in research and to take the medicines prescribed in clinical trials.
Your responsibilities

- You have a responsibility to follow the instructions provided for the task you are performing.
- You must be familiar with your role and trained in the relevant procedures.
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 pharmacy processes

- Helps to ensure the rights, safety and wellbeing of participants are protected
The pharmacy manual

- The sponsor may also provide a pharmacy manual detailing pharmacy specific requirements for the study including:
  - Ordering and receipt of clinical trial medicines
  - Storage
  - Temperature monitoring
  - Dispensing
  - Drug accountability
  - Processing returned clinical trial medicines
  - Key contact points for the sponsor

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

Your pharmacy’s clinical research lead will:

- ensure there are local Standard Operating Procedures (SOPs) in place which provide instructions on dispensing and supply of the medicinal product and other activities relevant to your involvement in research
- consider how the protocol and pharmacy manual will be implemented for each study
- ensure there are study specific instructions 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 instructions
  • Study specific pharmacy manual

• If you are unsure about anything in these documents, or have a question/issue that is not covered, escalate it to your clinical research lead.

• You should also escalate any issues you feel may impact on the integrity of the data produced or the safety of participants.
Summary

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

- Pharmacy staff are part of the PI’s site team and should understand their roles, which may include clinical trial medicine management, identification of participants, signposting to clinical research studies or others.

- There should be a research champion in the pharmacy with a more detailed understanding of clinical research and who can provide advice and be the point of contact to the research team and pharmacy staff. This is likely to be your clinical trials lead.
Documentation and data
Collection and use of research data

- Pharmacy 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 dispensing records. 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
Collecting high quality data

- All data, whether handwritten or electronic, should be:
  - Accurate
  - Complete - Always provide all the data required. Blanks fields mean the data is incomplete, and the sponsor will require an explanation from the research lead as to the reason
  - Legible - It is usual to write in black ink as completed documents may be photocopied or scanned
  - Attributable - It should be clear who has completed the data
  - Timely - the data should be recorded at the time it is collected, or as close to this as possible.
Collecting high quality data: metadata

• 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)

  *enalapril, batch 1234, 2.5mg. J Smith 01/07/14*

• Metadata forms an integral part of the original record. It is important the records are fully complete - without the metadata, the data has no meaning.
Collecting high quality data: participant initials and ID

- Participant initials and identification number must always be provided where required
- This ensures the data is associated with the right participant throughout the study
- Check local or study specific conventions for completion
Collecting high quality data: dates and numbers

• All dates and numbers should be provided where required

• Complete all the fields so it is clear all data has been provided

• Check local or study specific conventions for completion
Collecting high quality data: making changes

- If you make a mistake place a single line through the entry, and make the amendment clear.

- Initial and date any alteration, even if completing blank fields retrospectively

- Never occlude the original entry

- Never, ever use Tippex or Post-it notes

- Always document the reason for the change.
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 pharmacy 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

• Pharmacy 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 pharmacy data

• The MHRA may also inspect the pharmacy data if the study is a CTIMP.
Session complete!

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