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Good Clinical Practice (GCP) and study specific training for the GENVASC Study

GCP component, endorsed by the Clinical Research Network: East Midlands Training and Development Lead

16/11/2016

Delivering clinical research to make patients, and the NHS, better

Introduction

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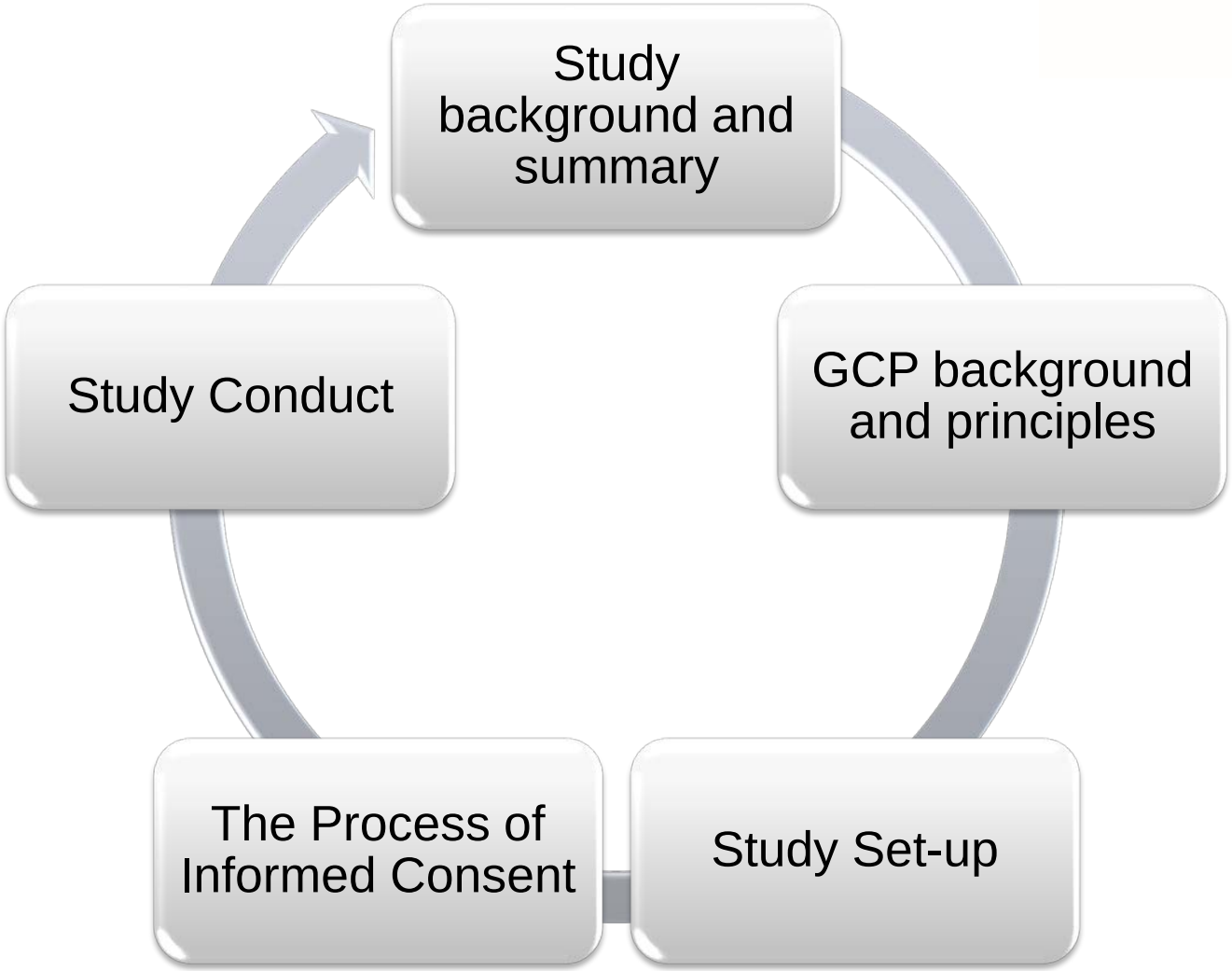

Study Background

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- Coronary artery disease (CAD) is one of the commonest cause of premature death and disability in the UK
- Lifestyle factors contribute to risk of CAD and risk scores are used to classify an individual's risk and target primary prevention measures
- Improving accuracy of risk categorisation is a high priority
- Inheritance plays an important role
- Significant progress has been made in identifying individual genetic variants that affect risk of CAD
- Framework for testing whether adding genetic information in the form of a genetic risk score (GRS) can improve current risk prediction of CAD
- The NHS Health Check Programme provides ideal opportunity to establish a large and representative cohort
- Adopted onto NIHR portfolio
- Led by Professor Nilesh Samani and run by Leicester Cardiovascular BRU

Study summary

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Objective

- To determine if the addition of genetic information can improve risk prediction of CAD

Target population

- All patients attending for the NHS Health Check

Inclusion criteria

- 40 to 74 years inclusive
- Able to give informed consent

Exclusion

- Known history of CVD
- Known history of blood transmissible infection (e.g. Hep B, HIV)

Duration of recruitment and sample size

- 10 years (end date 2022) with a target sample size > 30,000

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GCP BACKGROUND AND PRINCIPLES

At the end of this section you will have an understanding of:

The importance of GCP in relation to clinical research studies

An awareness of the main principles of GCP

Why do we have standards?

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Quality of Data

Ensure that the data about the drug/intervention is valid and reproducible

Give public assurance that the data is credible

Patient Protection

To ensure safety of patients participating in study is protected

To ensure that drugs/ interventions we develop are safe for patients in the future.

Brief History

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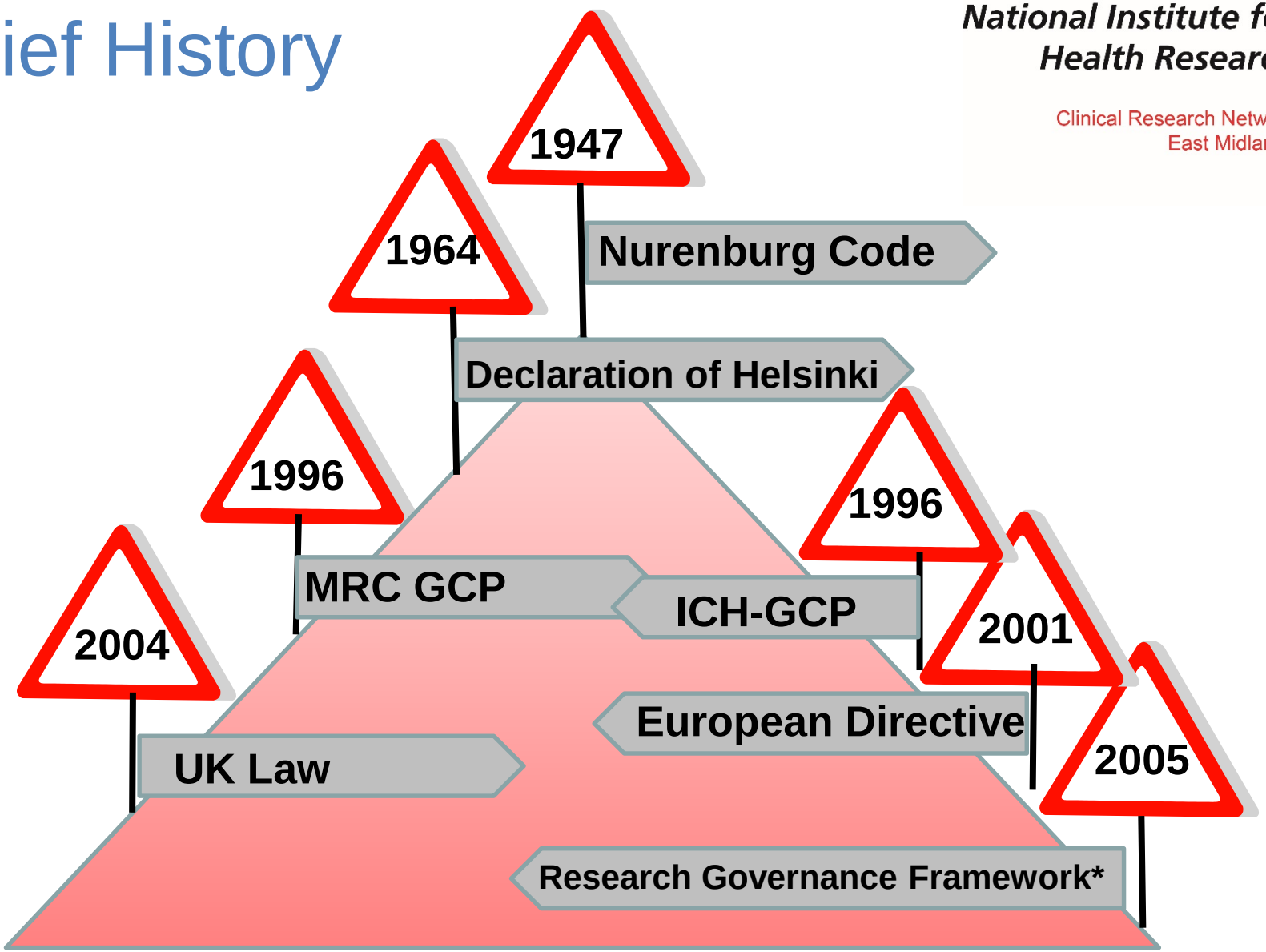

*To be replaced by The Policy framework for health and Social Care Research. Currently in consultation

Research Governance Framework

- Introduced to ensure a common quality standard applied to **all** research in the NHS
- Not law but must be adhered to for all studies conducted within the NHS in England
- Outlines the standards and principles of good governance that apply to all research involving patients, includes clinical and non-clinical research

UK Regulations

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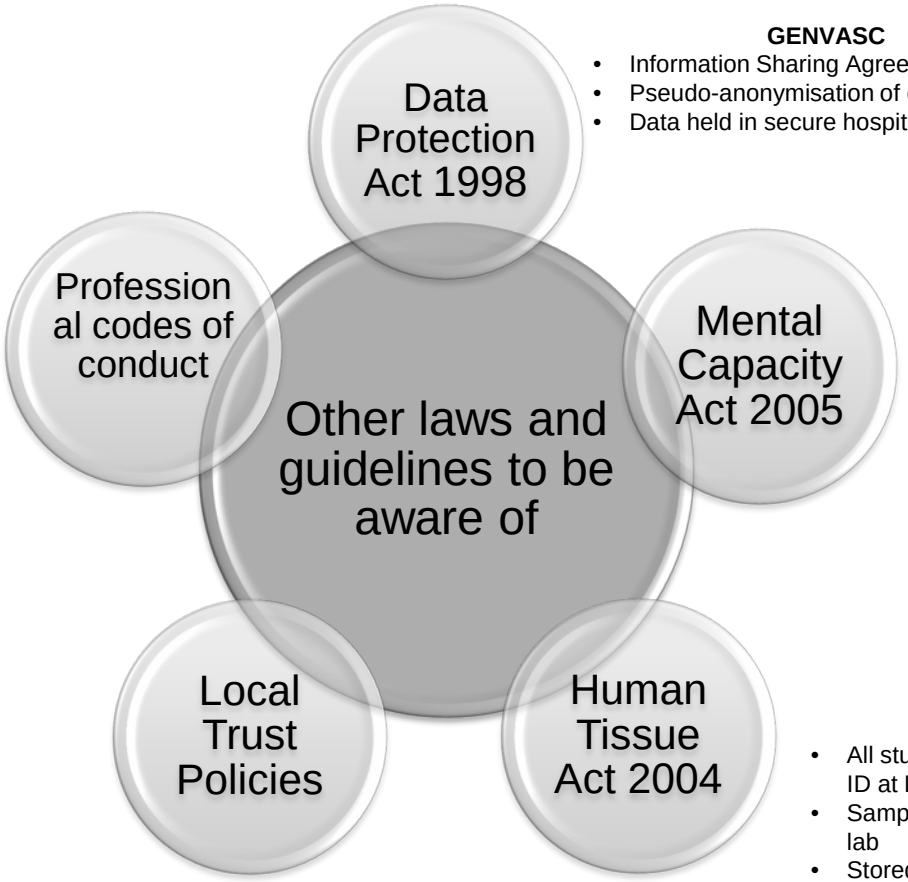

GENVASC

- Information Sharing Agreements
- Pseudo-anonymisation of data
- Data held in secure hospital servers

GENVASC

- Ensuring participants are able to give informed consent

GENVASC

- All study samples allocated a unique study ID at LCBRU
- Samples are stored in a secure LCBRU lab
- Stored samples are identifiable by unique study ID only

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STUDY SET-UP

At the end of this section you will have an understanding of:

The regulatory approvals that need to be in place before a clinical trial can be started in the UK
The responsibilities and/or duties of different members of the research team
Be able to identify a range of essential documents
The purpose of setting up and maintaining a site file

Responsibilities

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The Sponsor, Chief Investigator (CI) and Principal Investigator (PI) have defined responsibilities

Your responsibilities

- Study site collaborating agreement
- Abide by RGF, HTA and DPA
- Maintain site file
- Follow procedures outlined in protocol
- Only use approved information documentation
- Personnel appropriately trained and supervised
- Permit supply of clinical data to NIHR Leicester Cardiovascular Biomedical Research Unit
- Permit monitoring at site
- Ensure the safety and well-being of participants
- Report any concerns about study conduct

Approvals

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A study can only start when you have

- A favourable opinion from a Research Ethics Committee
- Approval from the HRA
- Approval from local Trust/Organisation
- Plus any other relevant approval: i.e. MHRA in case of a drug study and/or Sponsor green light

Essential documents

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These are documents which permit the evaluation of the conduct of a trial and quality of data produced

Demonstrate compliance with GCP and regulatory requirements e.g.

- Protocol
- Approval documentation
- Information sheet/consent form
- Relevant correspondence
- CV's of personnel involved in study

Section 8 of E6 document provides full details (ICH Guidelines for GCP)

Site file

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All essential documents are stored in designated file

Kept in designated place and maintained by designated person

- Secure area
- Limit access
- Protect from damp, fire etc.
- Provided at start of trial and maintained throughout
- File chronologically with most recent uppermost
- Label superseded documents but do not destroy them

Archive

- Minimum 5 years
- Stored securely, adequately protected, controlled access

Protocol amendments

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Substantial amendments require a favourable opinion from the REC, HRA and local Trust/Organisation before they can be implemented

Except where urgent safety measures need to be taken

Amendments may result in changes to other essential documents (e.g. PIS/ICF)

- New versions must not be used until appropriate approvals are obtained

Version control

- All study documents must be version controlled

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INFORMED CONSENT

At the end of this section you will:

Understand your responsibilities in the consent process

What is informed consent?

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- ICH-GCP E6 Document 1.28 (1996)

- A process by which a subject **voluntarily confirms** his/her willingness to participate in a trial, after having been **informed of all aspects of the trial** that are relevant to the subjects decision to participate. Informed consent is **documented** by means of a **written, signed and dated Informed Consent Form.**

In order to be valid consent should be
- Voluntary
- Informed
- Competent

The process of informed consent

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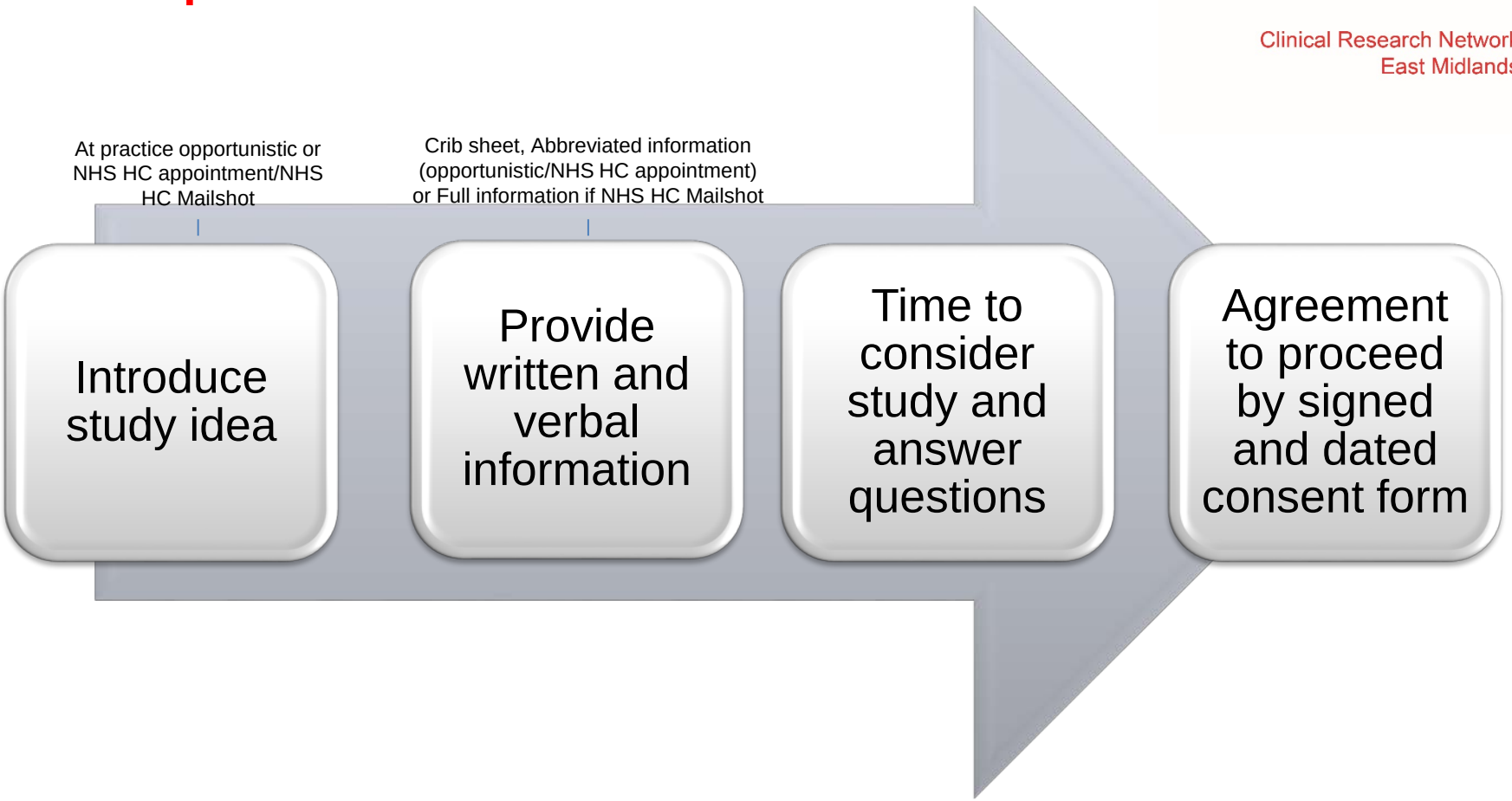

Before any trial related procedure take place

Witnessed consent process

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The witnessed process can be used opportunistically when patients attend for a clinical visit and have a NHS Health Check

or when they attend specifically for a NHS Health Check

- Discuss concept of study
- If interested provide verbal information

Provide information

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Verbal information

Key points to relay to participant

- Purpose
- Voluntary/right to withdraw/will not effect their care
- What will they have to do: consent, blood sample (DNA), permit use of data
- Storage of samples and data
- Confidentiality
- Contact/further information
- Crib sheet available: section 1 of site file

Witnessed consent process - Providing further information

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Written information

- Provide the participant with the abbreviated participant information sheet (version 3 12/09/13) to read prior to consent
- Provide detailed participant information leaflet (version 4 12/09/13) to take home and read later
- Only use Information sheet and consent form approved by REC
- Must not be changed except by formal amendment
- Multiple languages available

Information (cont.)

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Establish level of understanding

Mental capacity act (2005)

A person is able to make a decision for themselves if they are able to
Understand information relevant to decision

- Retain the information
- Use or weigh the information
- Communicate their decision (by any means)

Answer questions
Provide time to consider participation

Samples not analysed for 30 days to allow more time to consider participation

Agreement to proceed

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Informed Witnessed Consent Sheet
Produced from electronic patient record: Version 4.2 (12/09/13)

- Relay each point verbally
- Participant to initial boxes (not tick)
- Participant to print name, sign and personally date
- Researcher to print name, position, sign and date

Consent form filed with Information Sheet

- Original in site file
- Copy in primary care records
- Copy to participant
- Copy with sample

Optional consent

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Optional consent field number 7: to be contacted in the future for potential participation in additional studies

- Lack of consent for this aspects does not preclude participation into study

Participant to **initial box** to consent or **cross box** if they do not consent to this optional element

Witnessed ICF template

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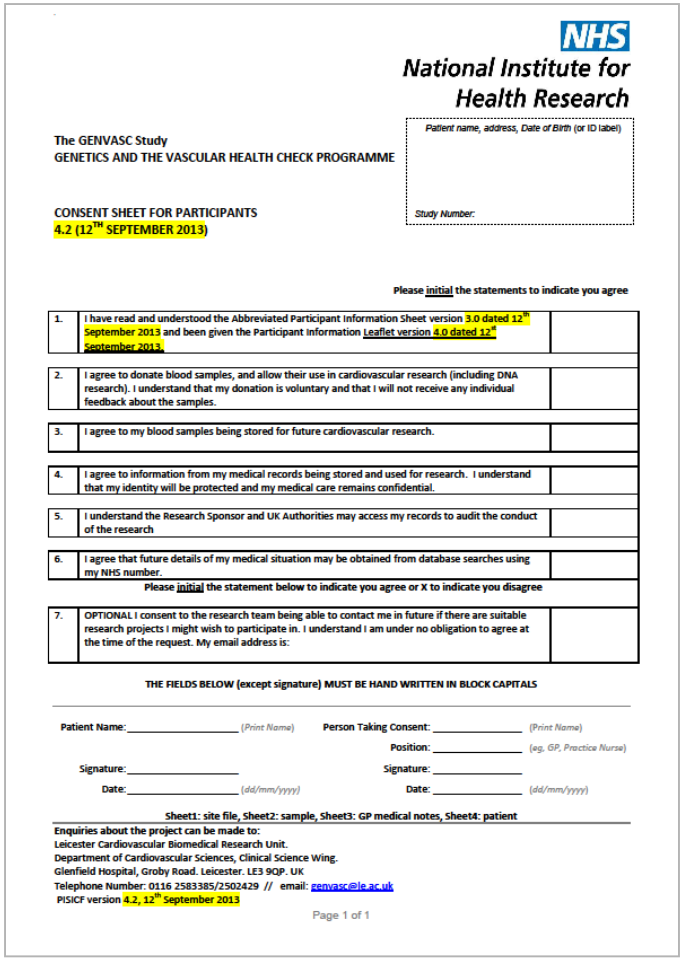

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The GENVASC Study
GENETICS AND THE VASCULAR HEALTH CHECK PROGRAMME

Patient name, address, Date of Birth (or ID label)

Study Number:

CONSENT SHEET FOR PARTICIPANTS
4.2 (12TH SEPTEMBER 2013)

Please initial the statements to indicate you agree

1.	I have read and understood the Abbreviated Participant Information Sheet version 3.0 dated 12th September 2013 and been given the Participant Information Leaflet version 4.0 dated 12th September 2013.	
2.	I agree to donate blood samples, and allow their use in cardiovascular research (including DNA research). I understand that my donation is voluntary and that I will not receive any individual feedback about the samples.	
3.	I agree to my blood samples being stored for future cardiovascular research.	
4.	I agree to information from my medical records being stored and used for research. I understand that my identity will be protected and my medical care remains confidential.	
5.	I understand the Research Sponsor and UK Authorities may access my records to audit the conduct of the research	
6.	I agree that future details of my medical situation may be obtained from database searches using my NHS number.	
	Please initial the statement below to indicate you agree or X to indicate you disagree	
7.	OPTIONAL I consent to the research team being able to contact me in future if there are suitable research projects I might wish to participate in. I understand I am under no obligation to agree at the time of the request. My email address is:	

THE FIELDS BELOW (except signature) MUST BE HAND WRITTEN IN BLOCK CAPITALS

Patient Name:_____ (Print Name)
Signature:_____
Date:_____ (dd/mm/yyyy)

Person Taking Consent:_____ (Print Name)
Position:_____ (eg, GP, Practice Nurse)
Signature:_____
Date:_____ (dd/mm/yyyy)

Sheet1: site file, Sheet2: sample, Sheet3: GP medical notes, Sheet4: patient

Enquiries about the project can be made to:
Leicester Cardiovascular Biomedical Research Unit.
Department of Cardiovascular Sciences, Clinical Science Wing.
Glenfield Hospital, Groby Road. Leicester. LE3 9QP. UK
Telephone Number: 0116 2583385/2502429 // email: genvasc@le.ac.uk
PISICF version 4.2, 12th September 2013

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Unwitnessed consent process

To be used in conjunction with postal invite for the NHS Health Check or provided prior to attending NHS Health Check. Patient must have time prior to their appointment to read the detailed participant information sheet

In case of invite via NHS Health Check mail out:

- GP study specific invitation letter can be used (version 1 28/04/14) or the approved paragraph about GENVASC incorporated into the NHS Health Check invitation letter (version 1 21/04/2016)
- Detailed participant information leaflet (version 4 12/09/13) included
- Unwitnessed consent form (version 1.1 12/09/13) included

Agreement to proceed - Unwitnessed consent process

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Patients wishing to take part in the study return completed unwitnessed consent form to healthcare provider (GP, Nurse, HCA or Phlebotomist) when attending for their clinical Health Check appointment

Consent form must be checked for completeness:

- If patient ticks ‘no’ in any boxes (other than last optional element), the consent form is **not valid**
- Check level of understanding and answer any questions
- Copies of consent form required as per witnessed consent process

Unwitnessed ICF template

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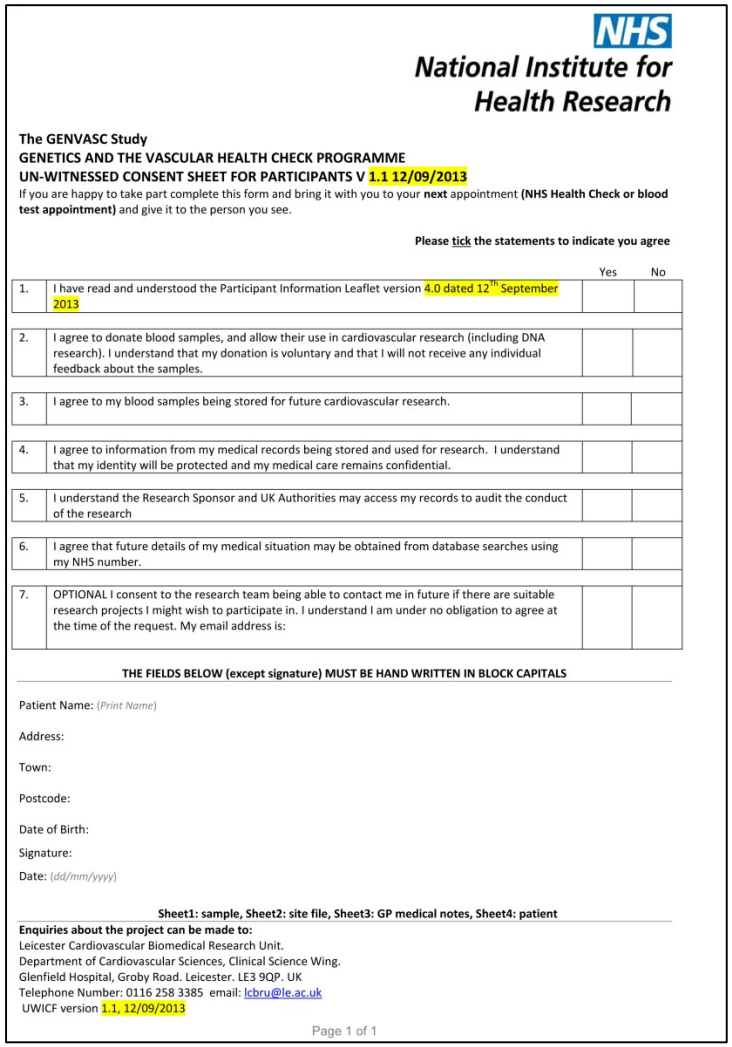

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The GENVASC Study
GENETICS AND THE VASCULAR HEALTH CHECK PROGRAMME
UN-WITNESSED CONSENT SHEET FOR PARTICIPANTS V 1.1 12/09/2013

If you are happy to take part complete this form and bring it with you to your **next** appointment **(NHS Health Check or blood test appointment)** and give it to the person you see.

Please tick the statements to indicate you agree

		Yes	No
1.	I have read and understood the Participant Information Leaflet version 4.0 dated 12th September 2013		
2.	I agree to donate blood samples, and allow their use in cardiovascular research (including DNA research). I understand that my donation is voluntary and that I will not receive any individual feedback about the samples.		
3.	I agree to my blood samples being stored for future cardiovascular research.		
4.	I agree to information from my medical records being stored and used for research. I understand that my identity will be protected and my medical care remains confidential.		
5.	I understand the Research Sponsor and UK Authorities may access my records to audit the conduct of the research		
6.	I agree that future details of my medical situation may be obtained from database searches using my NHS number.		
7.	OPTIONAL I consent to the research team being able to contact me in future if there are suitable research projects I might wish to participate in. I understand I am under no obligation to agree at the time of the request. My email address is:		

THE FIELDS BELOW (except signature) MUST BE HAND WRITTEN IN BLOCK CAPITALS

Patient Name: *(Print Name)*

Address:

Town:

Postcode:

Date of Birth:

Signature:

Date: *(dd/mm/yyyy)*

Sheet1: sample, Sheet2: site file, Sheet3: GP medical notes, Sheet4: patient

Enquiries about the project can be made to:
Leicester Cardiovascular Biomedical Research Unit.
Department of Cardiovascular Sciences, Clinical Science Wing.
Glenfield Hospital, Groby Road. Leicester. LE3 9QP. UK
Telephone Number: 0116 258 3385 email: lcbru@le.ac.uk
UWICF version 1.1, 12/09/2013

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Withdrawal

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All participants must be provided with a copy of withdrawal form (V1 27/04/12)

Participants can withdraw at any time and do not have to provide a reason

Participant that do wish to withdraw complete withdrawal form and return directly to study team

- Freepost number is included on withdrawal form
- They can indicate whether samples/data already collected can be used or destroyed

Document in patient notes if you are made aware of a withdrawal

Document the process

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It is a GCP requirement to document the recruitment process

- Any research activity must be recorded in the participant notes, i.e. recruited, declined or withdrawn consent
- There are generic research read codes for SystMone & EMIS, but free test must be used to reflect that this activity relates to GENVASC
- For example: Participant identified as suitable for the GENVASC study, inclusion/exclusion criteria verified. Information sheet/s and withdrawal form (include version numbers) provided. Study discussed and participant happy to proceed, consent obtained, samples taken.
- Entry will be date and time stamped according to login details

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STUDY CONDUCT

At the end of this section you will:

Understand how to record study data
Know how to record and report a protocol deviation
Understand how to process study samples

Recording data

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Sample bottles & consent forms

- Records must be accurate, legible and complete
- All fields must be completed
- Any change should be initialled and dated
- Strike through original entry with single line (should not obscure original entry)
- Always use black pen
- No abbreviations

If its not documented it did not happen

Protocol deviations

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The Protocol must be followed at all times. However, occasionally deviations to the approved protocol may occur. If this happens:

- Record in the patient notes
- Complete the deviation log
- **Report to study team**

Data and anonymisation

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There is a secure GENVASC database, which holds:

- Participant demographics
- Cardiovascular risk factors/scores
- Relevant health information extracted from GP practice databases and hospital systems
- Over time this database is populated with additional relevant participant health information

All participants are allocated a unique study identification number to pseudo-anonymise data

- Data is gathered using participant NHS and System numbers
- Data Sharing Agreements are in place between data controllers and data processors

Sample collection/processing

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Ensure informed consent is obtained **prior** to taking any study samples

Obtain clinical samples in their normal order first, followed by the study samples

Study samples may be drawn separately from a second needle if necessary. The GENVASC study samples are:

- 2 x EDTA 4.0ml tubes
- Label tubes with patient demographics and date
- Bag samples separate to study samples, affix a bag label and attach a copy of the consent form
- Send study samples to NGH pathology using routine pathology service
- If no research sample are obtained, just send the participant consent form in a labelled sample bag

Portal Registration & Sample Tracking

- When the samples arrive at LCBRC they will be registered on the GENVASC portal
- The Portal will allow for accrual, quarterly reimbursement reporting and document management i.e. recording of study Delegation Log
- https://genvasc.uhl-tr.nhs.uk
- Each member of staff working on the study will be provided with their own Portal login

Portal

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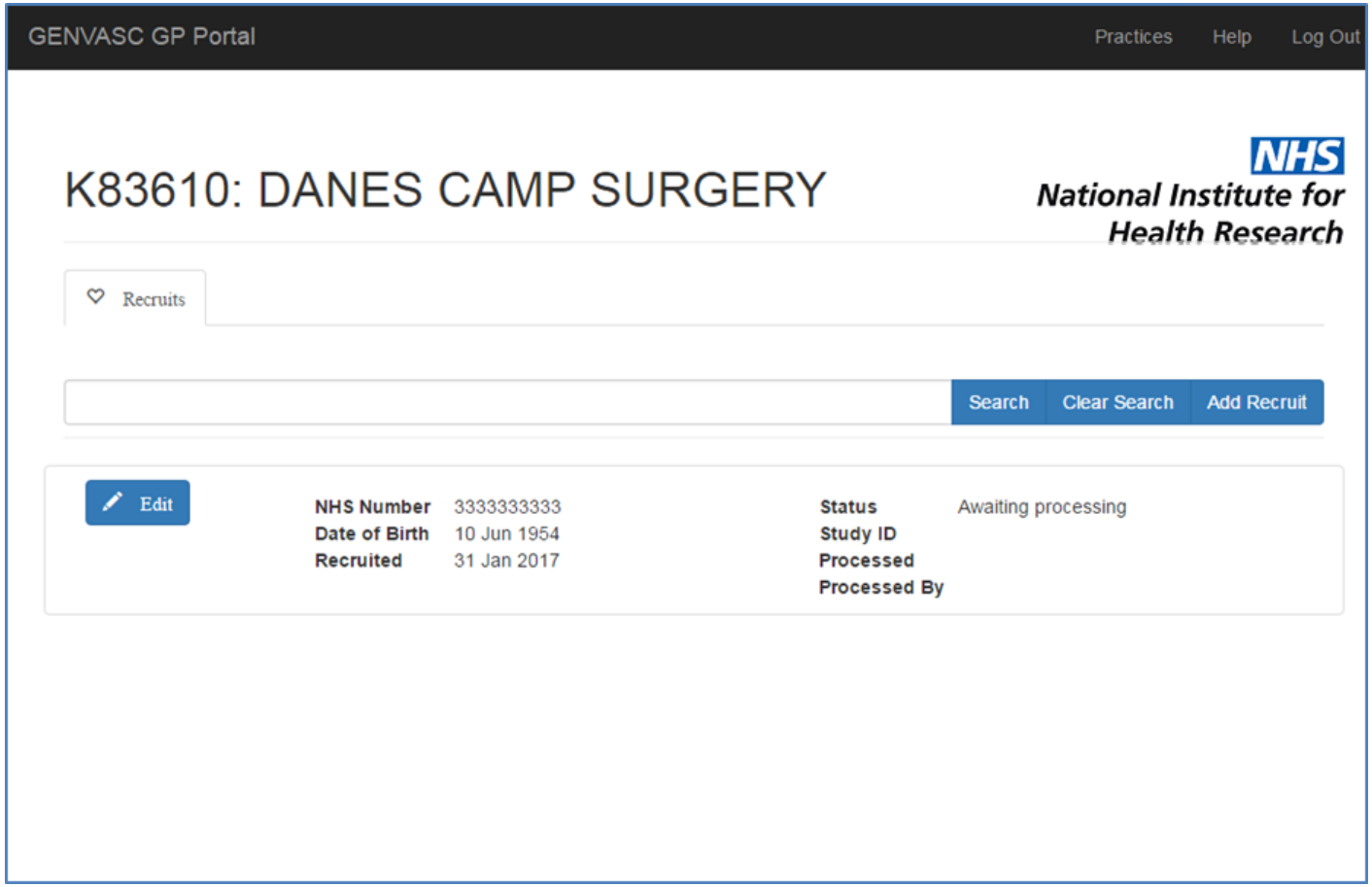

ANY QUESTIONS?