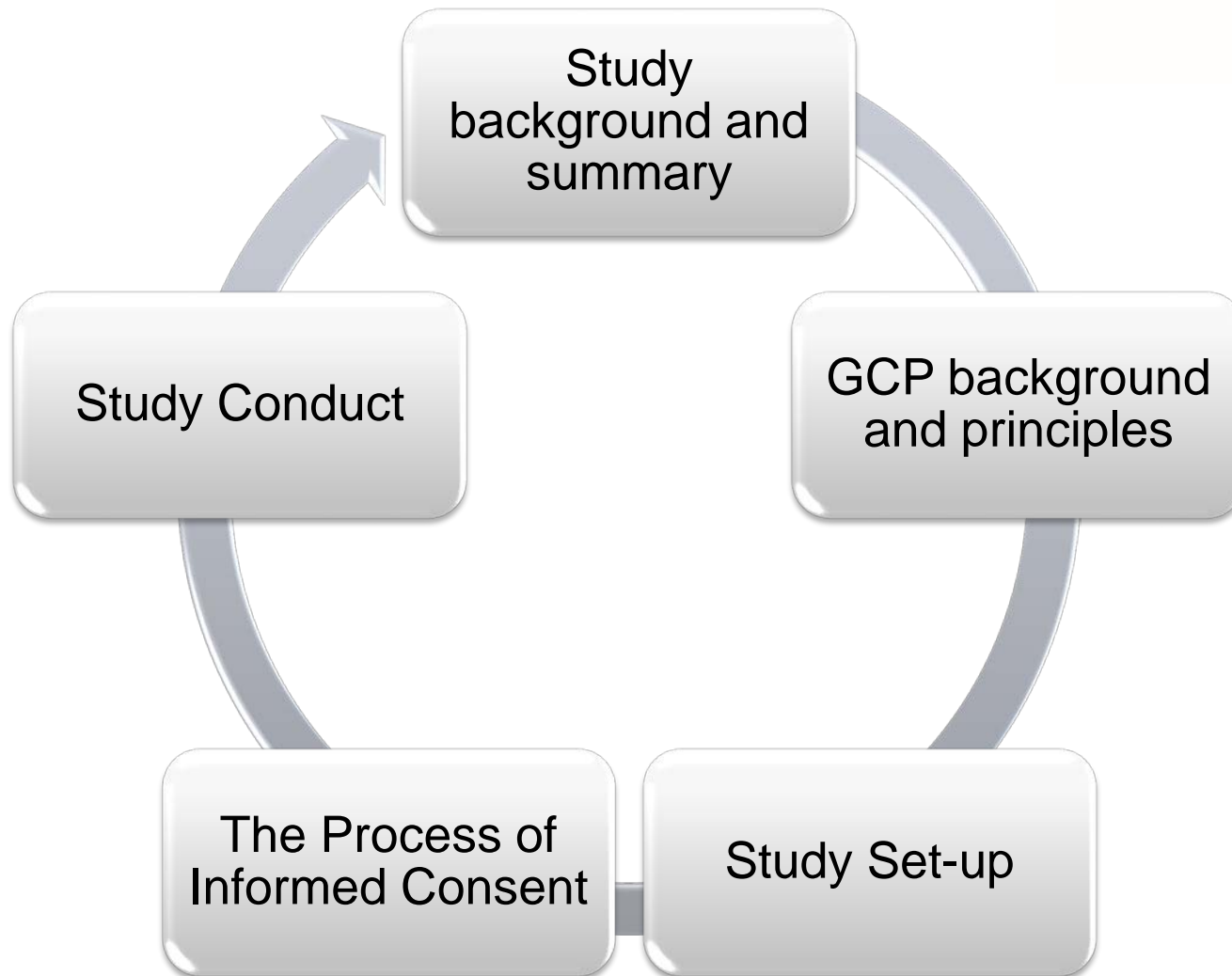


# Good Clinical Practice (GCP) and study specific training for the **GENVASC** Study

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



# Introduction



# Study Background

- 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

## **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

# 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?

## Quality of Data

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

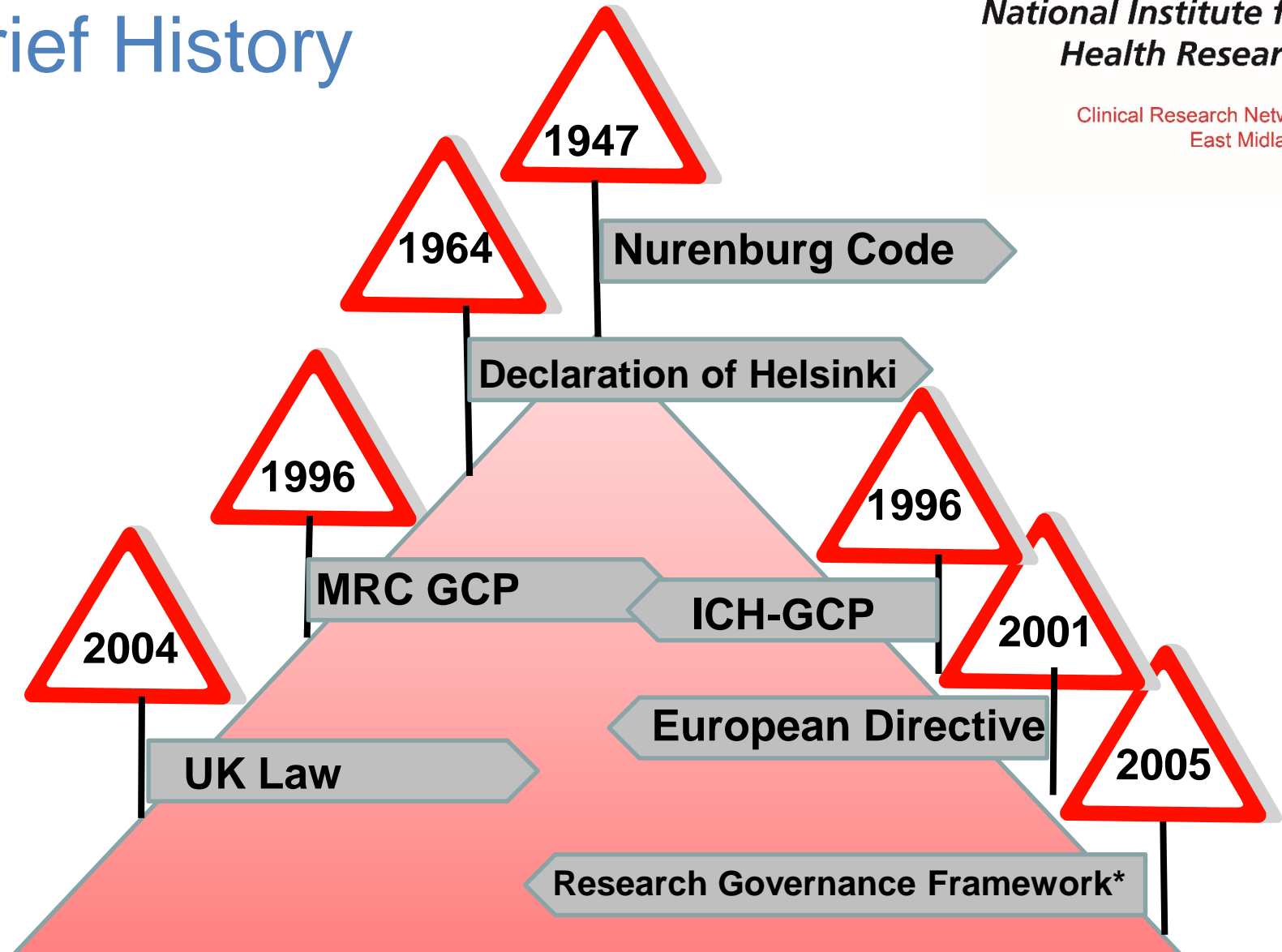
Give public assurance  
that the data is credible

## 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



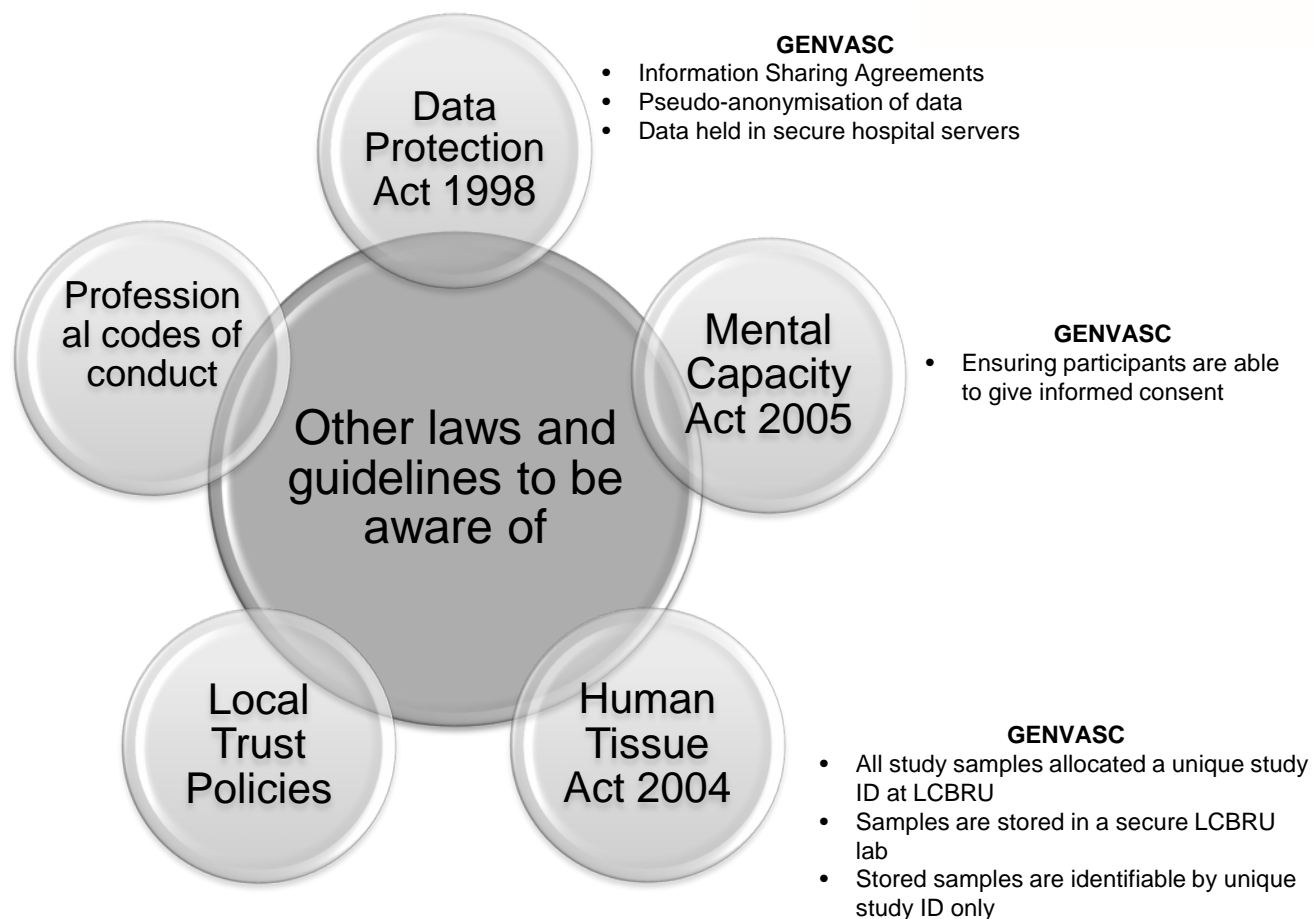
\*To be replaced by The Policy framework for health and Social Care Research. Currently in consultation

# 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



# 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

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

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

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

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

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

# INFORMED CONSENT

At the end of this section you will:

Understand your responsibilities in the consent process



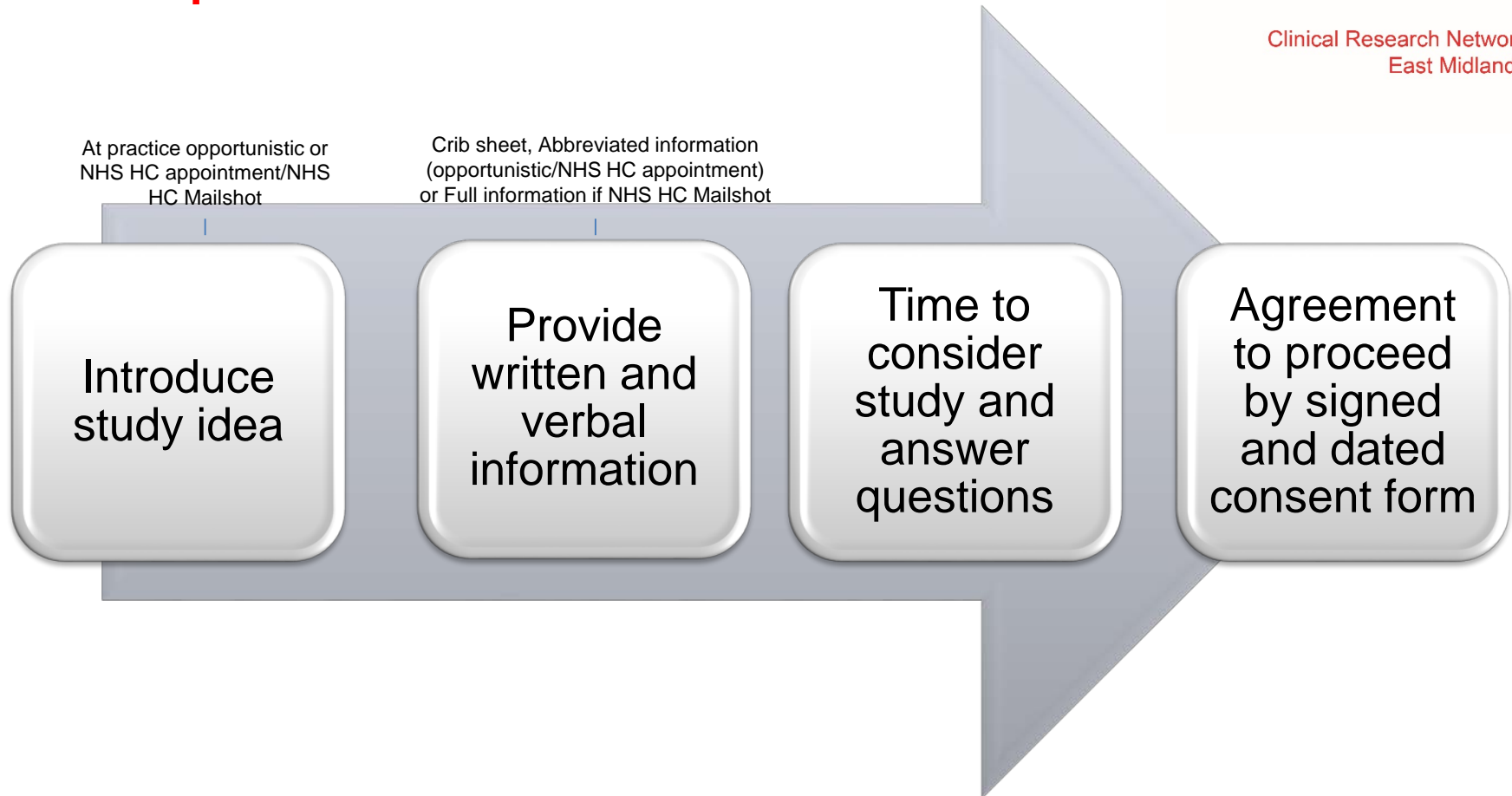
# What is informed consent?

- 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



**Before any trial related procedure take place**

# Witnessed consent process

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

## 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

## 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.)

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

## 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


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

  
**National Institute for  
Health Research**

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 (12<sup>TH</sup> 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 12 <sup>th</sup> September 2013 and been given the Participant Information Leaflet version 4.0 dated 12 <sup>th</sup> 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 <u>initial</u> 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)      Person Taking Consent: \_\_\_\_\_ (Print Name)  
Position: \_\_\_\_\_ (eg. GP, Practice Nurse)  
Signature: \_\_\_\_\_      Signature: \_\_\_\_\_  
Date: \_\_\_\_\_ (dd/mm/yyyy)      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](mailto:genvasc@le.ac.uk)  
PISICF version 4.2, 12<sup>th</sup> September 2013

Page 1 of 1

# 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

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

			
		<b>National Institute for Health Research</b>	
<b>The GENVASC Study</b>			
<b>GENETICS AND THE VASCULAR HEALTH CHECK PROGRAMME</b>			
<b>UN-WITNESSED CONSENT SHEET FOR PARTICIPANTS V 1.1 12/09/2013</b>			
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 <u>tick</u> the statements to indicate you agree			
		Yes	No
1.	I have read and understood the Participant Information Leaflet version 4.0 dated 12 <sup>th</sup> September 2013	<input type="checkbox"/>	<input type="checkbox"/>
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.	<input type="checkbox"/>	<input type="checkbox"/>
3.	I agree to my blood samples being stored for future cardiovascular research.	<input type="checkbox"/>	<input type="checkbox"/>
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.	<input type="checkbox"/>	<input type="checkbox"/>
5.	I understand the Research Sponsor and UK Authorities may access my records to audit the conduct of the research	<input type="checkbox"/>	<input type="checkbox"/>
6.	I agree that future details of my medical situation may be obtained from database searches using my NHS number.	<input type="checkbox"/>	<input type="checkbox"/>
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:	<input type="checkbox"/>	<input type="checkbox"/>
<b>THE FIELDS BELOW (except signature) MUST BE HAND WRITTEN IN BLOCK CAPITALS</b>			
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: <a href="mailto:lcbru@le.ac.uk">lcbru@le.ac.uk</a>			
UWICF version 1.1, 12/09/2013			

# Withdrawal

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

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 text 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

# 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

## 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

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

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

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:

- 3 x EDTA 2.7ml (red top) then 1 x Serum Gel 4.9mls (brown top)
- Label tubes with patient demographics and date
- Tick GENVASC participant on sunquest ICE, if taking alongside clinical samples
- Send study samples to UHL pathology using routine pathology service

# Sample packaging

**NHS**  
**National Institute for  
Health Research**

The GENVASC Study  
GENETICS AND THE VASCULAR HEALTH CHECK PROGRAMME

CONSENT SHEET FOR PARTICIPANTS  
4.2 (12<sup>TH</sup> 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 12 <sup>th</sup> September 2013 and been given the Participant Information Leaflet version 6.0 dated 12 <sup>th</sup> 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 sample.	
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)      Person Taking Consent: \_\_\_\_\_ (Print Name)  
 Signature: \_\_\_\_\_ (dd/mm/yyyy)      Position: \_\_\_\_\_ (e.g. GP, Practice Nurse)  
 Date: \_\_\_\_\_ (dd/mm/yyyy)      Signature: \_\_\_\_\_ (dd/mm/yyyy)

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

Inquiries 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 5QP, UK  
 Telephone Number: 0116 2543395/2502425 // email: [genvasc@lhc.ac.uk](mailto:genvasc@lhc.ac.uk)  
 PIDG version 4.2, 12<sup>th</sup> September 2013

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**GENVASC**  
GP Practice:  
• With consent, please draw 3 x EDTA Tubes 2.7ml (red) & 1 x Serum Gel Separator 4.9ml (brown)  
• Send to Pathology separate to clinical samples  
• Attach the GENVASC consent form to the bag

**UHL Pathology:**  
Please forward to GGH Pathology where the samples will be collected by a member of the research team

**GENVASC**  
GP Practice:  
• With consent, please draw 3 x EDTA Tubes 2.7ml (red) & 1 x Serum Gel Separator 4.9ml (brown)  
• Send to Pathology separate to clinical samples  
• Attach the GENVASC consent form to the bag

**UHL Pathology:**  
Please forward to GGH Pathology where the samples will be collected by a member of the research team

UNIVERSITY HOSPITALS OF LEICESTER NHS TRUST

ASADISEAL SPECIMEN FORM PATENT NO. 2221208 B  
HAVE YOU LABELLED THE SPECIMEN CORRECTLY?

08/06/2016 V3

**ASADISEAL SPECIMEN FORM PATENT NO. 2221208 B**  
**HAVE YOU LABELLED THE SPECIMEN CORRECTLY?**

08/06/2016 V3

**GENVASC**

GP Practice:  
• With consent, please draw 3 x EDTA Tubes 2.7ml (red) & 1 x Serum Gel Separator 4.9ml (brown)  
• Send to Pathology separate to clinical samples  
• Attach the GENVASC consent form to the bag

**UHL Pathology:**  
Please forward to GGH Pathology where the samples will be collected by a member of the research team

# Sunquest Ice desktop

Sunquest Ice Desktop - Windows Internet Explorer

sunquest  
ICE Desktop  
Test

Patient Name: ADULT MALE EDITESTPATIENT Hospital Number: S0029257 Sex: Male  
Date of Birth: 01 January 1975 NHS Number: No NHS Number  
Address: LEICESTER ROYAL INFI, LEICESTER ROYAL INFI, INFIRMARY SQUARE, LEI... Telephone No: View Details User: PSr

Common Requests Chemistry Haematology Micro/Virology Immunology Cell Path Sexual Health Testing DO NOT USE

GP Multi Disc GP Path Profile ED Multi Disc ED Path Profile Search Set as Default Panel

Following clinical samples please take these additional bottles. EDTA (Red Top) x2, Serum (Brown Top) x2

Chemical Pathology	Haematology	Microbiology	Immunology
<input type="checkbox"/> Urea & electrolytes	<input type="checkbox"/> Gamma GT	<input type="checkbox"/> Urine for Microscopy and Culture	<input type="checkbox"/> Rheumatoid Factor
<input type="checkbox"/> Liver Function Test	<input type="checkbox"/> Vitamin B12	<input type="checkbox"/> High Vaginal Swab	<input type="checkbox"/> Liver, Kidney, Parietal Ab Screen
<input type="checkbox"/> Bone Profile	<input type="checkbox"/> Folate	<input type="checkbox"/> Lower Vaginal Swab	<input type="checkbox"/> Coeliac Disease Screen
<input type="checkbox"/> C reactive protein	<input type="checkbox"/> Ferritin	<input type="checkbox"/> Endocervical Swab	<input type="checkbox"/> Thyroid peroxidase antibody
<input type="checkbox"/> Vitamin D	<input type="checkbox"/> Iron	<input type="checkbox"/> Chlamydia detection (Swab)	<input type="checkbox"/> ANA (includes Centromere Antibody)
<input type="checkbox"/> Lipids	<input type="checkbox"/> Thyroid Function Test	<input type="checkbox"/> Rubella immunity	
<input type="checkbox"/> Lipids + HDL	<input type="checkbox"/> GTT	<input type="checkbox"/> Faeces	
<input type="checkbox"/> Glucose (Plasma)	<input type="checkbox"/> Creatine Kinase		
<input type="checkbox"/> HbA1c	<input type="checkbox"/> Full Blood Count		
<input type="checkbox"/> Albumin (random urine)	<input type="checkbox"/> Reticulocytes		
<input type="checkbox"/> Protein/creatinine ratio (Random)	<input type="checkbox"/> INR		
<input type="checkbox"/> Protein/creat (24 hr urine)	<input type="checkbox"/> D-dimers		
<input type="checkbox"/> Prostate Specific Antigen	<input type="checkbox"/> Glandular fever test		
<input checked="" type="checkbox"/> GENVASC Participant			

Live Admin  
Manuals  
Reporting  
ED Requesting

New Request  
Specimen Reception  
View Pending Requests  
View Requests By Patient  
View Requests By Location

**ANY QUESTIONS?**