St George's University Hospitals NHS
NHS Foundation Trust

Standard Operating Procedure (SOP)

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They may print off this document for training and reference purposes.

Standard Operating Procedure (SOP)
Applying for NHS Ethics Approval

SOP Chronology		
SOP Version Number:	**Reason for Change:**	**Author:**
V1.0	Original Version	Nadia Azzouzi
V2.0	New Logo and Trust name. Allocation of studies to REC process changed to new process. Change of links from NRES to HRA,	Lucy H H Parker
V3.0	Updated with HRA process in England	Debs Rolfe

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1. Background

NHS Research Ethic Committees (RECs) will review most research conducted within the NHS. The service itself is called NRES (National Research Ethics Service). Such research could involve:

- Clinical Trials of Investigational Medicinal Products.
- NHS patients/service users (including potential participants recruited by their past or present treatment and NHS patients treated under contracts with private sector institutions).
- Potential participants identified because of their status as relatives/carers of patients and users of the NHS.
- Access to data (except anonymised data – see alternatives to NHS REC section below), organs or other bodily material of past and present NHS patients.
- Foetal material and IVF involving NHS patients.
- Recently dead in NHS premises.
- Use of/access to NHS premises or facilities.
- Healthy volunteers, where a drug or device is being tested within the NHS.

Key characteristics of NRES are that:

- All applications must be made by the Chief Investigator (CI) for the study.
- The CI must be professionally based in the UK.
- For international studies that will take place in the UK:
    - An application must be made to an ethics committee in the UK whether or not the study has a favourable ethical opinion outside the UK, and;
    - If there is a coordinating investigator outside the UK, a health professional based in the UK **must** be nominated as the UK CI and take responsibility for the conduct of the research in the UK.
- The REC must give an opinion on a project **within 60 days** of receiving a valid application, as required in law for CTIMPs and the Research Governance Framework, and for all other research in the NHS (unless it is a trial of a medicinal product for somatic cell therapy or the product contains a genetically modified organism, in which case the time limit is 90 days).

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- A single ethical opinion will be given for a project regardless of the number of sites at which it is to be conducted.
- The suitability of a research site and investigator taking part in the research will be assessed by the site (England only)/made by review of the site specific information form (SSI) (for all devolved nations) and forms part of the single ethical opinion.
- Each research site should have a PI responsible for the management and conduct of research at that site.
- If the CI is based at a site that will take part in the study, St George's policy is that they should also be named as the PI for that site.

2. Joint Research and Enterprise Office (JREO) Policy

All JREO SOPs will be produced and approved in accordance with the JREO SOP on SOPs and must be used in conjunction with local NHS Trust and St George's policies and procedures.

The JREO acts as the representative of both St George's University of London (SGUL) and St George's University Hospitals NHS Foundation Trust (SGHT). St George's will be the official name used on all SOPs to represent both institutions acting as Sponsor.

3. Scope

This SOP details how to apply for NHS REC approval for health-related research projects. It provides general information on the NHS REC system and outlines each step that should be completed in the application process.

Please note, the information within this SOP is only a summary. For more detailed guidance see the Standard Operating Procedures for RECs:

www.hra.nhs.uk/resources/research-legislation-and-governance/standard-operating-procedures

The application form for UK ethics review can be obtained via the Integrated Research Application System (IRAS) found at www.myresearchproject.org.uk which combines the ethics application with other regulatory forms such as Medicines and Healthcare Products Regulatory Agency (MHRA) applications and applications to the National Institute for Health Research (NIHR). All applicable UK studies must apply through this system.

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4. Definitions

Not applicable to this SOP.

5. Responsibilities

It is the Chief Investigator's responsibility to read and understand this SOP and to understand the process by which they apply to NRES for ethics approval for their proposed study to take place in the United Kingdom.

6. Procedures

The procedure for applying for NHS REC approval can be divided into the following steps:

Section 6.1 – NRES Research

1. Online Application Form via IRAS
2. Project filter questions
3. Applicant's Checklist
4. Decide Where to Apply/Book a Review Slot
5. Proportionate Review
6. Submit
7. Validation
8. **NHS Management permission**
9. Review/Notification of Decision
10. Request for Further Written Information
11. After Approval

Section 6.2 – Non NRES Research

1. Non-NHS resources/Overseas research
2. Studies needing R&D approval (host site) only
3. Participant Identification Centres

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Section 6.1 NRES Research

6.1.1 Online Application Form *(the information in this SOP is based on version 5.3 of the online form)*

All applications must be made using the IRAS online application form which can be accessed at www.myresearchproject.org.uk. If a first time user, you will need to register for an account online which is activated immediately. There is no requirement to complete the application form in one go – work can be saved and reloaded for further editing. The website also offers training on how to use and complete the form. It is recommended that all first time users of this form undergo this training.

The form is interactive. This means when you fill in certain answers, information will automatically populate in other relevant places. Your answers to certain questions, particularly the Project Filter Questions, will deactivate or activate other sections of the form. If you find you are answering questions that are not relevant to the research proposed, check the project filter questions and questions answered previously. You are never likely to complete every single page – the average is around 20 pages long. Every question that appears must be answered.

The application form is structured as in the table below. For a breakdown of each part, see Appendix 1.

Part	Details
Project Filter	Asks a limited number of key questions about the nature of your research. An application form specific to your project will be created from the answers you give. You need to select your answers carefully.
A	Asks for generic information relevant to all research proposals. Certain questions will be deactivated depending on your answers to the project filter.

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B	Is divided into several discrete sections, which refer to particular specialist topics. These appear (or disappear) in response to your answers to the project filter.
C	Asks for a list of sites that the study will be conducted at.
D	Section for the relevant signatories. Only members of the JREO are authorised to sign as the Sponsor Representative for St Georges Sponsored studies

More detailed information about using the form is available via the 'help' pages on the IRAS form website:

www.myresearchproject.org.uk/Help/HelpPage.aspx

6.1.2 Applicant's Checklist

You must also complete the ' Checklist' on the IRAS application form in IRAS and attach all your supporting documents to the Checklist electronically to ensure that all of the paperwork required to support your application is sent to the REC. You must complete the checklist online through the IRAS form system. A different version of the checklist must be completed depending on the type of research; there is one for CTIMPs and another for any other research in the NHS. The online system automatically generates the relevant checklist depending on your answers in the project filter questions. You must do this before the form is authorised. You must upload all of the documents for submission and complete the version and date fields correctly.

6.1.3 Decide Where to Apply/Book an Agenda Slot

When the application has been approved by the JREO, and they have agreed to Sponsor it in accordance with JREOSOP0003 (For CTIMPs) or JREOSOP0028 (for non-CTIMPs), the researcher needs to decide where to apply and book a slot at the next meeting of an appropriate REC. Instructions can be found on the E-Submission tab in IRAS.

The Central Booking Service (CBS) is the telephone booking service for NHS Research Ethics Committees.

Note: If the lines are busy, or if you call outside these hours, you will be directed to the voicemail. Please leave a message requesting a call back and the CBS team will call you back

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Some studies must go to a particular type of REC. There are RECs which have the expertise to look at certain types of studies. For example, a phase 1 drug study with healthy volunteers must go to a type 1 REC. The allocation system will ensure that the study is assigned to the correct type of REC.

6.1.4 Proportionate Review

For your application to be considered for proportionate review, it should fit one of the following categories:

- Research using data or tissue that is anonymous to the researcher.
- Research using existing tissue samples already taken with consent for research.
- Research using "extra tissue" (e.g. further blood taken at time of routine sampling or tissue taken at "clinically directed" operation).
- Questionnaire research or research interview/focus group that does not include highly sensitive areas or where accidental disclosure would not have serious consequences.
- Research surveying the safety or efficacy of established non-drug treatments, involving limited intervention and no change to the patients' treatment.
- Research involving children may also be considered for proportionate review where it meets the above criteria.

The aim of the system of proportionate review is for a project to be reviewed and a decision letter to be issued within 14 working days of receipt of a valid application. However, the project may be referred on to a full committee if necessary (which will then extend the timescale to the usual 60 days).

For further information, please refer to:

www.hra.nhs.uk/resources/applying-to-recs/nhs-rec-proportionate-review-service

6.1.5 Submission

Before phoning the allocation system, you must obtain all of the appropriate electronic authorisations for your application. "Sponsors representative" will be via the JREO Research Governance Officer (RGO) who will authorise the form, before proceeding to submission. Once you have booked an agenda slot with the REC, you should be sent confirmation of your booking by email, together with a unique REC reference number. You must ensure you add the REC reference number to your online application form at this

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point; it should be inserted in the header section of Page 1 (along with the name of the NHS REC and the submission date. Once the form has been electronically signed this will be the only permitted change. Any other changes will invalidate the form and re-authorisation will be required.

For all bookings through CBS, you will need to submit the application electronically to the allocated REC on the day of booking by pressing the "e-submission" button within IRAS.. .

The following documents must be submitted within IRAS in order for your submission to be valid.

- Application form with electronic signatures.
- Applicant's checklist
- All relevant supporting documents, as indicated on the Checklist.

6.1.6 Validation

If your application is valid and you have submitted it within the timeline, you will be issued with a validation letter **within 5 working days**, acknowledging your submission and confirming it is valid, or requesting changes or amendments from you before it can be validated. The letter will also provide details (time and venue) of the REC meeting and invite you to attend. It is recommended that you attend the meeting, in order to answer any questions that the REC may wish to address; however, attendance at the meeting is not mandatory.

If St George's is named as Sponsor for your research, the JREO will also receive a copy of this letter.

For proportionate REC review you will not be required to attend.

6.1.7 NHS Management permission

All CI and research teams are advised to visit the HRA website as there are different processes evolving for Host sites in England and Cross border studies in the UK.

http://www.hra.nhs.uk/research-community/applying-for-approvals/nhs-management-permission/.

Following a favourable ethical opinion, the PI should send the R&D office a copy of the REC letters (which may include requests for change), the response to requests for changes and all supporting documents approved by the REC. Each R&D department will notify the PI whether or not there is any objection to the research on site-specific grounds. If there are

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no objections, the Trust will issue the PI with either Confirmation of Capacity and Capability (England sites) or an R&D approval letter. The national target for this is 40 days.

Please note that any studies taking place on St George's University Hospitals NHS Foundation Trust (SHGT) premises or recruiting SGHT patients or staff must go through the SGHT Trust R&D process and obtain Confirmation of Capacity and Capability, in addition to ethical approval, before they start. Please see JREO SOP on Confirmation of Capacity and Capability (JREOSOP0017)

If studies are taking place at other sites, permission must be obtained from the R&D department at each site, before any research commences there. If research is initiated at a site without R&D permission, the study will be in breach of its ethics approval conditions.

6.1.8 Ethical Review/Notification of Decision

At the REC meeting, the Committee will review the ethics of your research in a completely independent way, free from bias or any conflicts of interest. They will consider such things as:

- Arrangements for the recruitment of subjects.
- How informed consent will be obtained, including the adequacy of written information for participants.
- Provision for compensation in the event of injury attributable to the research.
- Any insurance or indemnity to cover the liability of an investigator or Sponsor.

The Committee must notify you of their decision **within 60 days** of receiving your **valid application**. If you find this has not happened, you can complain to the REC's Centre Manager in the first instance. details can be found on:

www.hra.nhs.uk/contact-us/

You can also contact:

Complaints Manager
Health Research Authority
Skipton House
80 London Road
London, SE1 6LH
Tel: 020 797 22545

The REC can reach one of five decisions about your application:

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- Final decision – which could be favourable, favourable with conditions or unfavourable.
- Provisional decision – with a request for further written information.
- No opinion – a referee needs to be consulted.

You should receive notification of the decision **within 10 working days of the review meeting**. If St George's is named as Sponsor for your research, the JREO will also be notified of the ethical decision.

6.1.9 Request for Further Written Information

The REC may make a provisional decision about your research and ask for further information about specific aspects of the project. Such a request can only be made once the 60 day clock stops whilst the REC awaits your response.

If the request for change included any adjustments to the study related documents you will be required to re-upload each of the amended documents with updated version numbers and date reference within IRAS against the checklist.

If St George's is Sponsor of your study, you must send the RGO a copy of your response to the request for information and any changed documents.

You should not amend the IRAS form (which would invalidate any authorisations) unless you are specifically instructed to do so within your REC decision letter.

You may need to contact the REC manager to re-activate the E-Submissions tab to submit your amended documents. You will be given a deadline that you will need to have addressed any comments/corrections made within your resubmission.

If your response is not deemed satisfactory, the committee may ask you to respond again to the same questions or reject your application. They cannot raise new issues. The clock only starts again when a complete response is received. A final decision should then be issued.

6.1.10 After Approval

Once you have received NHS REC approval, you still must not start your research until you have all the relevant regulatory approvals e.g. MHRA, NIGB, HRA <u>and</u> Confirmation of Capacity and capability from the relevant NHS Trust(s). Please see JREOSOP0017 Confirmation of Capacity and capability (formerly Trust) approval.

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Your research must start **within 12 months** of the date on which a favourable ethical opinion was given. A study is generally considered to have commenced when the first subject gives written informed consent to participate or, where this does not apply, when any procedures in the protocol are initiated. If your research does not commence within 12 months, you must notify the REC (and if it does not start within 24 months, you may have to re-apply).

After approval, you will also need to:

- Apply to the REC for approval of any substantial amendments to the protocol. For any St George's Sponsored study, you will need permission from the JREO before submitting any amendment. You must also apply to the HRA and request each Trust for R&D approval of any amendment before it is implemented at that site (please see the JREO SOP on Amendments JREOSOP0011).
- Submit safety reports when appropriate (please see JREOSOP0008 on development update safety reporting for CTIMP studies and JREOSOP0033 for non CTIMP safety reporting.).
- Provide an annual progress report to the REC each year of the project's duration (see JREOSOP0043).
- Inform the REC, the JREO and any sites when the project finishes using the end of study declaration form.

Please note that if St George's is sponsoring your study then you must also copy development update safety update reports (DSUR), annual progress reports (APR) and end of study reports to the JREO.

Section 6.2 – Alternatives to NRES

6.2 .1 Non-NHS resources/Overseas research

St George's has set up an ethics review board to deal with studies that fall outside the remit of the NHS ethics committees. - SGREC.

Meeting schedule and deadlines, application process and forms can be found located on the SGUL portal https://portal.sgul.ac.uk/research/research-ethics-committee

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6.2.2 Studies needing R&D (host site) only approval

A harmonised UK-wide edition of GAfREC (Governance Arrangements for Research Ethics Committees) was published by the UK Health Departments in May 2011 and came into effect on 1 September 2011. This means the following projects need management permission (host site approval) from host care organisations, but are excluded from REC review:

- Studies involving retrospectively collected anonymised data or tissue samples.
- Research involving acellular material extracted from tissue previously collected in the course of normal care.
- Research involving health or social care services staff recruited by virtue of their professional role (no patient involvement).
- Healthcare market research.
- Research involving the premises or facilities of care organisations.

Researchers undertaking the above studies should contact the R&D Trust where they wish to conduct their study. The documents that will need to be submitted for this type of project are:

- IRAS form available at www.myresearchproject.org
  (Complete the filter questions as normal and only tick NHS/HSC Research and Development offices to Q4. This will create a shortened version of the application form for completion).

- Protocol.
- Participant Information Sheet.
- Consent Form.
- Any other supporting documents you intend to use.

The JREO will then assess the study and register it on the ReDA database. You must not commence your research until you have confirmation from the JREO that the study has been registered and you are in receipt of the Trust approval letter.

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6.2.3 Participant Identification Centres

If research participants are being identified at another organisation this organisation may be classed as a Participant Identification Centre (PIC). A PIC is an NHS Trust where participants are identified and given information on a research project but no research activity, e.g. consent, medical screening, blood tests, is taking place. If research activity is taking place at an NHS Trust it must be identified as a research site and the full site specific assessment process must be completed, as described in section 6.1.7 of this SOP. Otherwise, the PIC should be listed in Part C of the application form as a PIC.

7 References

Standard Operating Procedures for Research Ethics Committees (version 5.1), March 2012
http://www.hra.nhs.uk/resources/research-legislation-and-governance/standard-operating-procedures/
Medicines for Human Use (Clinical Trials) Regulations 2004

http://www.hra.nhs.uk/research-community/applying-for-approvals/nhs-management-permission/
IRAS form website – www.myresearchproject.org.uk

8. Appendices

8.1 IRAS Form layout

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Appendix 8.1 – IRAS form layout

PART A - Core study information

1. Administrative details

IRAS question number	*Reference in NRES application form or other source*	*Subject*
A1	A1	Title of research
A2-1	A70	Student project details
A2-2	None	CI for student project
A3	A2	Chief Investigator details
A4	None	Central study co-ordinator details
A5-1	A65	Research reference numbers
A5-2	None	Other linked studies or applications

2. Overview

IRAS question number	*Reference in NRES application form or other source*	*Subject*
A6-1	None	Lay summary
A6-2	A68	Overview of study purpose and design

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3. Purpose and design

IRAS question number	*Reference in NRES application form or other source*	*Subject*
A7	None	Methodology description
A8	A5	Type of CTIMP
A9	A5a	Phase of CTIMP
A10	A7	Principal research question/ objective
A11	A8	Secondary research question/objective
A12	A9	Scientific justification
A13	A10-1	Summary of design and methodology
A14-1	A10-1	Patient/public involvement
A14-2	NIGB form	Consulting patients/public on use of data without consent

4. Risks and ethical issues

Research participants

IRAS question number	*Reference in NRES application form or other source*	*Subject*
A15	None	Sample group or cohort
A16	A5c	First time in humans?
A17	A22/A23	Inclusion/ exclusion criteria

Research procedures, risks and benefits

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IRAS question number	*Reference in NRES application form or other source*	*Subject*
A18	A13	Details of non-clinical interventions or procedures
A19	A12	Details of clinical interventions or procedures
A20	A11	Withholding of clinical interventions or procedures
A22	A16/A17	Potential risks and burdens
A23	A14	Potential for distress in interviews, questionnaires, or group discussions
A24	A18	Potential benefits
A25	A67	Arrangements for continued provision of intervention after research finished
A26	A19	Potential risks for researchers

Research procedures, risks and benefits

IRAS question number	*Reference in NRES application form or other source*	*Subject*
A27-1	A20 (part)	Identification of potential participants
A27-2	None	Screening personal data
A27-3	None	Methods/resources
A27-4	None	Access to personal data outside the care team
A27-5	None	Consent to access identifiable data

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A28	A21	Details of recruitment through posters or adverts
A29	A20 (part)	How and by whom potential participants will be approached
A30-1	A26	Informed consent
A30-2	A27	Recording consent
A30-3	NIGB form	Use of data without consent
A31	A28	Time to decide on participation
A32	A25	Participants involvement in other research
A33-1	A29	Participants with inadequate English language skills or special communication needs
A33-2	None	Welsh language
A34	A30	Providing information to participants during the research
A35	A30-1	Loss of capacity to consent during the study

Confidentiality

IRAS question number	*Reference in NRES application form or other source*	*Subject*
A36	A39	Checklist of data processing activities
A37	NIGB form	Physical security of data storage
A38	A40	Confidentiality of data
A39	NIGB form	Separation/encryption of identifiers
A40	A43	Access to identifiable data during the study
A41	A41	Analysis of data and location

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A42	A42	Data custodian
A43	NIGB form	Retention of identifiable data at end of study
A44	A44	Period of data storage
A45	NIGB form	Long term arrangements for data storage

Incentives and payments

IRAS question number	*Reference in NRES application form or other source*	*Subject*
A46	A33/A34	Financial payments/incentives (participants)
A47	A61/A62	Financial payments/incentives (researchers)
A48	A64	Conflicts of interest

Notifying other health professionals

IRAS question number	*Reference in NRES application form or other source*	*Subject*
A49-1	A32a	Notifying GP or health professional
A49-2	A32b	Permission to notify

Publication and dissemination

IRAS question number	*Reference in NRES application form or other source*	*Subject*

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A50	None	Trial registration
A51	A37	Dissemination of study results
A52	NIGB form	Ensuring the anonymity of published data
A53	A38	Informing participants of the study results

5. Science

IRAS question number	*Reference in NRES application form or other source*	*Subject*
A54	A45-1	Scientific critique
A55	None	Assessment by Expert Advisory Group and Commission on Human Medicine
A56	A45-2	Statistical critique
A57	A48	Primary outcome measure
A58	A49	Secondary outcome measures
A59	A50	Sample size
A60	A51	Sample size determination
A61	A52	Randomisation
A62	A53	Methods of analysis

6. Management of the research

IRAS question number	*Reference in NRES application form or other source*	*Subject*
A63	A66	Key collaborators

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A64-1	A59	Lead Sponsor
A64-2	A59	Sponsor's contact point
A64-4	A59	Legal representative in EEA
A65	A58	External funding
A66	A60	Subcontractors
A67	A55	Previous rejection by a REC
A68	None	Lead R&D contact
A69	A3	Duration of study
A70	None	Definition of the end of the study
A72	A56	Overview of host organisations
A73-1	None	Identification of participants by other organisations
A73-2	None	NHS participant identification centres (PICs)
A73-3	None	Resources for PICs
A74	A57	Monitoring and auditing the conduct of the research
A75	A57a	DMC and stopping rules
A76-1	A35-1	Insurance/indemnity - management of study
A76-2	A35-2	Insurance/indemnity - design of study
A76-3	A35-3	Insurance/indemnity - conduct of study
A77	A36	No fault compensation
A78	A10-3	Intellectual property
A79	None	Level of commercial participation

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PART B - Additional information for specific applications

IRAS question number	*Reference in NRES application form or other source*	*Subject*
B1	EudraCT form	Investigational medicinal products
B2	B2	Medical devices (populates MHRA Devices forms)
B3	B3	Exposure to ionising radiation (populates ARSAC forms)
B4	B4	Use of existing human tissue samples
B5	B5	Use of new human tissue samples
B6	B7	Adults unable to consent for themselves
B7	None	Children
B8	NIGB/HES Forms	Additional information for NIGB (populates NIGB form)
B9	NIGB security form	Information security measures (populates NIGB form)
B10	MoJ forms	Additional information for Ministry of Justice (populates MoJ form)

PART C - List of research sites

IRAS question number	*Reference in NRES application form or other source*	*Subject*
C1	B1	List of research sites NHS participant identification centres (for R&D offices only)

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PART D - Declarations

IRAS question number	*Reference in NRES application form or other source*	*Subject*
D1	B7	Chief Investigator
D2	B7	Sponsor's representative
D3	A71	Academic supervisor
D4	NIGB Form	Information Guardian (NIGB only)

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