Title: Applying for Research Ethics Committee opinion

1. Scope

1.1 This SOP applies to Chief Investigators (CI) planning studies sponsored or co-sponsored by the University of Aberdeen (UoA) and/or NHS Grampian (NHSG) which require NHS Research Ethics Committee (REC) approval.

1.2 NHS REC approval is required when NHS patients, tissues or data are used in a research project.

2. Responsibilities

Chief Investigator

Ensure sponsorship arrangements have been approved by Sponsor/co-Sponsor prior to submitting a study for ethical review. Ensure favourable ethical opinion, MHRA approval (if required), local NHS R&D permission (also known as Confirmation of Capacity and Capability in England and Wales) any other relevant approvals are in place, before recruitment begins.

Principal Investigator

Ensure local NHS R&D permission is in place before recruitment begins.

3. Procedure

Agreeing Sponsorship:

3.1 ▶ Before applying for an NHS REC ethical opinion, the sponsorship arrangements for the study must be confirmed. This shall be done in accordance with SOP-QA-4 - Applying for sponsorship.

Complete the Online IRAS Application System:

3.2 All applications are made using the Integrated Research Application System (IRAS) portal which can be accessed at https://www.myresearchproject.org.uk. Full instructions on how to complete the form are available through the ‘Help’ pages and via the online IRAS e-learning module.
3.3 Research projects which raise no material ethical issues may apply for NHS REC approval using the Proportionate Review Service (PRS). These applications are reviewed by a sub-committee rather than at a full REC meeting with an aim to notify the final decision to the applicant within 21 calendar days of receipt of a valid application. Potential applications for PRS shall be discussed with Sponsor before the application is completed and must still be submitted using the IRAS system. If the NHS REC deems the application unsuitable for PRS, REC will notify the applicant and explain the reasons. The application will then be booked to a full REC meeting, in discussion with the applicant.

Further information on PRS is available on the HRA website: http://www.hra.nhs.uk/resources/applying-to-recs/nhs-rec-proportionate-review-service/

3.4 When the application form is complete this must be electronically signed by the CI (and any other relevant signatories) before it is released to Sponsor for electronic authorisation.

3.5 If the application form is acceptable, the Sponsor shall assign an electronic signature to the form.

3.6 ⚠ Any changes made to the REC form after electronic signatures have been assigned shall invalidate all signatures on the form. If changes must be made, they shall be notified and approved by Sponsor prior to implementation; the form must be re-signed by all parties prior to submission.

**Submitting the application to the NHS REC for an Ethical Opinion:**

3.7 Once all required signatures have been obtained, the REC application shall be submitted to the REC electronically through IRAS. Step by step instructions can be found on the ‘E-submission’ tab within the REC form on IRAS. Each step of this process must be followed or the application to the NHS REC will not be valid. This includes the following steps:

- Check the form to ensure that all areas are complete.
- Upload the supporting documents to the IRAS checklist.
- Ensure that all electronic signatures are in place.
- Verify the application is ready to submit.
- Book the application via the Central Booking Service to arrange which committee shall review the application and the date of the meeting.
- Electronically submit the application.

3.8 Any incomplete applications will not be validated and shall be returned to the CI.

3.9 A validation letter, which acknowledges the submission and confirms that it is valid, shall normally be issued by the NHS REC after submission. The letter shall also invite the CI to attend, if they wish, the NHS REC meeting at a specific time.

**NHS Ethics Approval Process**

3.10 The NHS REC must notify its decision within 60 days of receiving the valid application submitted for full REC review, and within 21 days for applications submitted using the PRS. The NHS REC can reach the following decisions:

- Final decision – which could be favourable (with conditions) or unfavourable.
- Provisional decision with a request for further written information.
- No opinion.

3.11 The NHS REC may make a provisional decision about the research and ask for further information on specific aspects of the project. Such a request can only be made once. The 60 day
clock stops whilst the NHS REC await the response. Sponsor must be kept updated and copied in on any correspondence with the REC during the review period.

3.12 If the response is not deemed satisfactory, the NHS REC may request a second response to the same questions (no new issues can be raised) or can reject the application. The clock only re-starts when a complete response is received. A final decision should then be issued.

3.13 Once NHS REC approval has been granted, the research must not start at a site until all other relevant approvals have been granted (e.g., MHRA) and NHS R&D has given local R&D Management Permission, or Continued Capacity and Capability in England and Wales, for that site.

3.14 🟢 A copy of the NHS REC favourable opinion letter must be filed in the Trial Master File (TMF) alongside copies of the signed REC application, the supporting documents submitted for review and any correspondence relating to the review process. If the project involves multiple sites, a copy of the favourable opinion letter shall be sent to each PI for inclusion in each individual site file.

3.15 Once all required approvals have been obtained, the final approved versions of the study documents shall be sent to Sponsor (researchgovernance@abdn.ac.uk) for the Sponsor file.

3.16 🟢 The research should start within 12 months of the date on which a favourable opinion from the NHS REC was given. A study is generally considered to have commenced when the first participant gives written informed consent to participate or, where this does not apply, when any procedures in the protocol are initiated.

3.17 ⚠️ Where research does not commence within 12 months, the CI should inform the NHS REC in writing in the Annual Progress Report (see SOP-QA-21 APRs and DSURs). If the research does not start within 24 months, the CI should inform the REC who may review the ethical opinion and decide that a new application is required, or they may grant a further 12 months of approval.

3.18 ⚠️ After approval, the NHS REC must be informed and an application submitted for approval of any substantial amendments to the protocol; this includes any changes to the end date specified in the application. All amendments must be approved by Sponsor in the first instance. This process is detailed in SOP-QA-19 - Amendments. Hard copies of any documentation requiring signatures, including covering letters, must be filed in the Trial Master File (TMF).

3.19 The CI also has the following responsibilities to the NHS REC:

- Provision of Annual Progress Reports (APRs) and Development Safety Update Report (DSUR) as detailed in SOP-QA-21 – APRs and DSURs.
- Notification of Suspected Unexpected Serious Adverse Reactions (SUSARs), as detailed in SOP-QA-22 - Adverse Events in CTIMPs, and relevant Serious Adverse Events (SAEs) for non-CTIMP studies.
- Inform the NHS REC who provided the favourable opinion when the project finishes, or terminates early, using the end of study declaration (see SOP-QA-31 Research project closure).

Regulatory and R&D Approvals
3.20 If MHRA Regulatory Authority approval is required (CTIMPs and Medical Device Clinical Investigations only), this must be in place before NHS R&D Management Permission is granted. It is the CI’s responsibility to apply for these approvals when they are required.

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Key to symbols 🟢 = Important point to note ⚠️ = Warning
NHS R&D Permission(s):

3.21  Local NHS R&D Management Permission/Confirmation of Capacity and Capability is required at each recruiting site if involving:

- NHS Staff
- NHS Patients
- Tissues
- Organs
- Data
- NHS Facilities
- NHS Equipment

The application process for R&D Permission is also completed using the IRAS system through the combined REC and R&D form, meaning only one electronic authorisation request is required by the CI and Sponsor for both REC and R&D approval, if applicable. Detailed guidance and instructions on completing and submitting R&D application forms can be found on the IRAS website. Once the application is complete it will be automatically and electronically submitted to NRSPCC through the IRAS system, as per the instructions on the E-Submission tab. The documents will then be sent electronically through IRAS to the relevant R&D office(s) for review.

If the project includes sites in England, Wales or Northern Ireland, the NRSPCC team will liaise with the coordinating centres for each nation and share the relevant documents to facilitate the setup of the study.

⚠️ If your project falls out with the remit of the NHS REC, but still requires local R&D approval, you must still phone the Central Booking System to book in your R&D application. E-submission to the relevant R&D office will not be enabled until this has been done.

4. Abbreviations and definitions

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<th>Abbreviation</th>
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<td>APR</td>
<td>Annual Progress Report</td>
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<td>CI</td>
<td>Chief Investigator</td>
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<td>CTIMP</td>
<td>Clinical Trials of Investigational Medicinal Products</td>
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<td>DSUR</td>
<td>Development Safety Update Report</td>
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<td>HRA</td>
<td>Health Research Authority</td>
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<td>IRAS</td>
<td>Integrated Research Application System</td>
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<td>MHRA</td>
<td>Medicines and Healthcare products Regulatory Agency</td>
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<td>NRSPCC</td>
<td>NHS Research Scotland Permissions Coordinating Centre</td>
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<td>PRS</td>
<td>Proportionate Review Service</td>
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<td>REC</td>
<td>Research Ethics Committee</td>
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<td>SUSAR</td>
<td>Suspected Unexpected Serious Adverse Reaction</td>
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<td>TMF</td>
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5. Related documentation and references

- SOP-QA-4 Applying for sponsorship
- SOP-QA-19 Amendments
- SOP-QA-21 APRs and DSURs
- SOP-QA-22 Adverse Events in CTIMPs
- SOP-QA-31 Research project closure
- TMP-QA-38 Patient Information Sheet guide

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