Research Registration Deferrals Policy and Procedure

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Background

The Health Research Authority (HRA) has a duty to promote transparency and has committed to a range of activities to improve transparency in health and social care research. Two established methods to support the HRA's transparency agenda are:

- Registration of research onto a publicly accessible database
- Publication of research summaries onto the HRA website (see section 9)

Conditions of the UK Health Departments' Research Ethics Committee (REC) favourable opinion include that clinical trials and research tissue banks must be registered on a publicly accessible database.

The HRA recognises that for some early phase trials there may be concerns about registering the research on a publicly available database, for example for reasons of commercial sensitivity. The HRA considers requests to defer registration of clinical trials on a case-by-case basis and only where there is no legal requirement to register.

A public registry is defined as any register on the World Health Organisation (WHO) list of primary registries or the International Committee of Medical Journal Editors (ICMJE) list of registries.

Policy

Since 30 September 2013 it has been a condition of the favourable ethical opinion that clinical trials are registered on a publicly accessible database and since 24 February 2017 that research tissue banks are registered on the UK Clinical Research Collaboration (UKCRC) Tissue Directory.

It is recommended that all research is registered at the earliest possible opportunity and before participants are recruited, or for research tissue banks, before tissue is held with the intention to provide for research purposes. To be compliant with REC conditions, clinical trial registration must take place no later than six weeks after recruitment of the first participant into the study in the UK. Research tissue bank registration must take place no later than six weeks after the date of the ethical opinion letter or six weeks after the research tissue bank holds tissue with the intention to provide for research purposes. Failure to register within the specified timeframe is a breach of the favourable ethical opinion unless a request to defer clinical trial registration has been granted by the HRA and is still valid.

This policy allows for deferral only where there is not a legal responsibility in existing legislation to register clinical trials. The deferral of registration is valid for a maximum of 12 months. Before the deferral period ends, the sponsor needs to either register the study or request an extension to the deferral. There is an expectation that the trial will be registered when the reason for the deferral is no longer valid, for example, no longer commercially confidential, or immediately should the trial be terminated early for safety reasons.

The policy does not allow for deferral of the registration of research tissue banks. In cases where there are concerns about making the details of a research tissue bank public on the UKCRC Tissue Directory, registration can be completed with the minimum fields only.

In exceptional circumstances, where there is a greater need for the research community and wider public to see information about research (e.g. during a pandemic), there may be interim deviations to aspects of this policy and procedure. Where any aspects of this policy and procedure need to be changed, this will be communicated on the HRA website.

This policy and procedure has been developed with consideration to the HRA's six core values: Inspiring Leadership, Integrity, Trusted, Transparent, Collaborative and Empowering. Further information on our values is available on the HRA Website.

Procedure

1. Purpose

The purpose of this document is to define the HRA's policy and procedure regarding the registration of research, specifically:

- The requirements to register research
- The process of requesting to defer registration of clinical trials

2. Scope

2.2 The requirement to register on a publicly accessible register as a condition of the favourable ethical opinion extends to research tissue banks and clinical trials carried out in the UK reviewed by a UK Health Departments' Research Ethics Committee (REC).

2.3 Clinical trials are defined as all studies which fall into the first four categories of question two on the Integrated Research Approval System (IRAS) filter page:

- Clinical trial of an investigational medicinal product
- Clinical investigation or other study of a medical device
- Combined trial of an investigational medicinal product and an investigational medical device
- Other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice

3. Reference Documents

- UK Policy Framework for Health and Social Care Research
- Governance Arrangements for Research Ethics Committees (GAfREC)
- The Medicines for Human Use (Clinical Trials) Regulation
- Research Ethics Service Standard Operating Procedures
- WHO registry list https://www.who.int/ictrp/network/primary/en/

- ICMJE registry list http://www.icmje.org/about-icmje/faqs/clinical-trials-registration/

4. Responsibilities

4.1 For research tissue banks, 'Sponsor' refers to the Applicant.

4.2 'Deferrals Manager' refers to the individual at the HRA delegated to manage the deferrals mailbox (study.registration@hra.nha.uk) and procedures outlined in this document, it does not reflect a job title.

4.3 The Sponsor is responsible for:

- ensuring that conditions of the favourable ethical opinion are met prior to the research commencing and throughout the duration of the research study/research tissue bank
- ensuring that the research study/research tissue bank is registered on an appropriate register
- ensuring that where registration of a clinical trial has not been completed, that there is a valid deferral in place confirmed by the HRA

4.4 The HRA Deferrals Manager is responsible for:

- monitoring the study.registration@hra.nhs.uk mailbox
- managing requests to defer registration, ensuring that agreed deferrals are processed and recorded in accordance with this policy and procedure
- reviewing any agreed deferrals, where new information becomes available and/or where circumstances change that may affect the justification for deferral of registration
- managing requests to reconsider decisions in relation to requests for deferral or exemption that are refused by the HRA
- monitoring and reporting on compliance with the REC conditions, through audit and quality assurance

4.5 REC staff are responsible for:

- ensuring that systems are updated when registration details are provided by the sponsor
- sending any deferral requests or associated queries to study.registration@hra.nhs.uk

5. Breakdown of activities covered by the procedure

The activities described below refer to the HRA Assessment Review Portal (HARP) and the HRA Hub. HARP is a database used by RECs to record and track the progress of research applications submitted to the HRA and/or REC. Information held in HARP is held securely and confidentially and access is restricted to authorised users who manage, or review studies, submitted to the HRA and/or REC. The HRA Hub is a workspace for HRA staff and is used to record deferral requests. HARP and HRA Hub are not to be mistaken for publicly accessible databases for research registration.

5.1 Notification of registration details

5.1.1 Where registration occurs before submission to the REC, then the sponsor should include the registration details in the application form.

5.1.2 Where registration occurs after submission to the REC, the sponsor should provide the registration details (i.e. registry name and registration number) to the REC that reviewed the application, as soon as possible or within the next correspondence with the REC e.g. within the next amendment.

5.2 Requesting a deferral of registration

5.2.1 All requests should be made in writing to study.registration@hra.nhs.uk. If any requests are sent to the REC directly, REC staff should forward these requests to study.registration@hra.nhs.uk within two working days.

5.2.2 The sponsor should submit the deferral request as soon as possible after REC review. Any requests sent before REC review will not be actioned and the applicant will be asked to re-submit their request after the REC meeting.

5.2.3 If the study is not registered and a deferral agreement is not in place six weeks after

recruitment of the first participant, then the HRA will consider this to be a breach of the conditions of the favourable ethical opinion.

5.2.4 The deferral request must include:

- identification of the research that is the subject of the request (IRAS ID and REC reference as a minimum);
- clear justification for the request (whilst there is not a single reason for automatic deferral, the HRA does note the potential commercial confidentiality issues around research).
- the timeframe for the deferral (note 12 months is the maximum allowed time)

5.2.5 This information may be included in the body of the email or it may be included in an attachment.

5.2.6 The request to defer registration may also include a request to defer publication of the HRA Research Summary. The Research Summary Deferral Policy and Procedure (see section 9) sets out the process for requesting the deferral of Research Summary publication.

5.3 Reviewing a deferral request

5.3.1 The Deferrals Manager is responsible for reviewing requests sent to study.registration@hra.nhs.uk. The request will only be processed where all the required information (set out in section 5.2) is provided within the request. If any of the information is missing from the request, then the sponsor will be advised of this and asked to provide it before their request is considered.

5.3.2 The Deferrals Manager is responsible for replying to the request within five working days of receipt. Where a full request is sent (i.e. including all the required information set out in section 5.2) then the Deferrals Manager is responsible for processing the request within five working days.

5.3.3 The Deferrals Manager will consider all deferral requests on a case-by-case basis.

5.3.4 For requests to defer registration, apart from research tissue banks, these should be

accepted where all the requested information has been included in the request and a clear and reasonable justification is provided.

5.3.5 Where a deferral request is allowed, the Deferrals Manager should confirm this to the sponsor. The email reply will confirm the study identifiers, reason for deferral and deferral end date (maximum 12 months from receipt of valid request). The Deferrals Manager will ensure that the Chief Investigator and REC are copied into this email.

5.3.6 Where a request is not allowed, a reason for this will be explained to the sponsor. This would usually be because there is a legislative obligation to register or an overriding matter of patient safety.

5.3.7 Where a request to defer registration of a tissue bank is submitted, the HRA Deferrals Manager will explain to the sponsor that it is not possible to defer the registration and they should complete a minimum record in the UKCRC Tissue Directory.

5.3.8 If the sponsor is dissatisfied with the outcome they may query this decision in writing to study.registration@hra.nhs.uk who will provide a written acknowledgement within five working days. If required, the Deferrals Manager should seek further advice from the HRA Head of Guidance and Advice.

5.4 End of a deferral period

5.4.1 At the end of the deferral period the sponsor is responsible for completing registration or requesting an extension of the deferral by following the steps in 5.5.

5.4.2 Once a study is registered on a publicly accessible register, this should be confirmed by email to the REC which gave ethical approval and study.registration@hra.nhs.uk so that records can be updated. The sponsor should provide the registry name and registration number.

5.5 Requesting an extension to a deferral

5.5.1 Should the sponsor require an extension of a deferral, they should request this by emailing the HRA (study.registration@hra.nhs.uk), at least 10 working days before the end of the deferral period.

5.5.2 Deferrals can only be extended for a maximum of 12 months at one time.

5.5.3 The Deferrals Manager is responsible for confirming to the sponsor, via email, whether the extension is allowed. A justification for the outcome should be provided, and if the request is allowed, the new deferral period end date specified in the response to the sponsor.

5.6 Recording requests

5.6.1 The Deferrals Manager should ensure that all correspondence relating to registration is uploaded onto HARP. The Deferrals Manager will also add a comment to the HARP publication tab with up to date information on registration including the deferral end date.

5.6.2 All requests to defer registration will be recorded on the Clinical Trial Registration and Research Summaries Deferral Log which is managed by the HRA and is located in the HRA Hub. The log is updated with all new requests, any subsequent requests relating to the same record (e.g. extension to deferral date) and when the sponsor advises that the study is registered.

6. Monitoring of activities covered by the procedure

6.1 The Deferrals Manager will regularly monitor compliance of sponsors with this policy and procedure. This will include conducting regular audits, the reports of which will be published on the HRA website.

6.2 During monitoring and audits, where a clinical trial is identified which has not been registered in accordance with the REC conditions, and does not have a valid deferral in place, the Deferrals Manager will contact the sponsor.

6.3 Where no compliance has been identified, this may be managed as a breach of the terms of the favourable ethical opinion, in accordance with the Research Ethics Service Standard Operating Procedures.

7. How lessons are learnt and incorporated into the procedure

7.1 The HRA monitors feedback from stakeholders, not least through a formal complaints process and user feedback. Any specific feedback regarding the registration of research and/or the request to defer registration, is welcome via study.registration@hra.nhs.uk.

7.2 This policy and procedure will be reviewed annually or more frequently in the event of changes in regulations or policy.

8. Management of Documents and Records

8.1 Periodic review of the document and associated forms will be managed through the HRA Hub. Records associated with the process will be retained and destroyed in line with the HRA Records Retention Schedule.

9. Supporting paperwork/forms

- Clinical Trial Registration and Research Summaries Deferral Log (located in HRA Hub)
- Deferrals Standard Responses (located in HRA Hub)
- Research Summaries and Deferrals Policy and Procedure (located on HRA website and HRA Hub)

10. Dissemination and publication of the document

This document will be available via the HRA website and on the HRA Hub.

Screening Questions - HRA Equality Analysis and Privacy Impact Assessment

Equality and privacy screening questions

Instructions: For every HRA policy, defined by the Equality and Human Rights Commissions (EHRC) as a function, strategy, procedure, practice, project, or decision, please answer the questions below to determine whether further analysis is required. If the answer is yes, please complete as required either the HRA Initial Equality Analysis and / or Initial Privacy Impact Assessment Template and copy and paste the completed assessment (s) below. This one document can be found on the Intranet.

Category	Question	Answer yes or no
Equality	With due regard to our Equality Duty, could this policy have the potential to have a detrimental impact on anyone with a protected characteristic?	No
Privacy	With due regard to the Data Protection Act, does this policy involve the use of Personal Information?	No

Document Control

Change Record

Version Number & Status	Date of Change	Reason for Change
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V1.2	17.04.14	JK changes made
V1.3	23.04.14	JW & TS comments
V1.4	07.05.14	UKREDG comments
V1.5	11.11.14	Internal Audit
V1.6	19.08.15	6 Month review
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Reviewers

Name (name of reviewer and/or management group reviewing)	Version Reviewed
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