NHS
Health Research Authority

HRA Clinical Trial Registration Deferral Policy and Procedure

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Owner:	HRA Director Guidance and Learning
Scope of Policy:	UK Wide

The HRA has reviewed this text to ensure greater consistency in the use of language in conveying standards that should be followed (ethical obligations or best practice) or must be followed (legal requirements) although readers are advised that the HRA holds both in high regard.
The HRA website material is a statement of the HRA understanding. Whilst the reader is encouraged to seek further clarification from the HRA in respect of any queries via the queries line, it will be for the reader to take their own legal advice as to what their legal duties are.

1. Background

The Heath Research Authority (HRA) expects all research to be registered and made registration of clinical trials on a publicly accessible register a condition of the favourable ethical opinion from 30 September 2013. This applies for those study categories outlined in 3.1. Research Ethic Committees (RECs) may make judgements on other study types and with a proposal to consult on an extension of the specific REC condition to other research in the future. To be compliant with the REC condition introduced in September 2013, registration must take place no later than 6 weeks after recruitment of the first participant into the study in the UK, although it is strongly recommended that all research is registered at the earliest possible opportunity and before participants are recruited. There is no requirement for registration to be prior to submission of an application to a REC.

The HRA recognises that research transparency is a global issue and that for some early phase trials there may be concerns that registration requirements may be perceived to make the UK a less attractive place for research. The HRA policy therefore provides for requests to defer registration to be made and the HRA will consider and accept these requests, where there is currently no requirement in legislation to register, and record them against the published REC opinion.

2. Purpose

The purpose of this document is to set out the HRA policy in regard to clinical trial registration deferral and to clearly define the procedure which should be followed.

3. Scope

3.1 The requirement to register on a publicly accessible register as a condition of the favourable ethical opinion extends to all studies which fall into the first four categories of question 2 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

3.2 It is considered good practice for all research to be registered on a publicly accessible register but it is only a condition of the favourable ethical opinion when the study falls into the categories set out in 3.1. The HRA recognises that for other study types, they may not fall within the remit of the available public registers and consideration is required.

3.3 This policy relates to all clinical trials being carried out in the UK.

4. Best practice standards and legal responsibilities

The HRA, along with many other bodies including the World Health Organization (WHO), recognises that ethical and moral obligations of researchers and researcher sponsors set out a best practice standard for all health research to be registered. In simple terms clinical trials of medicines are legally required to be registered under the current European Clinical Trials regulations, and UK Clinical Trial legislation, although this legislation has specific exemption for some early phase trials. The introduction of the specific REC condition from September 2013 provides a simple and consistent position for all clinical trials from that point. The policy allows for deferral only where there is not a legal responsibility in existing legislation to register clinical trials.

5. Reference Documents

- Research Governance Framework (RGF)
- Governance Arrangements for Research Ethics Committees (GAfREC)
- The Medicines for Human Use (Clinical Trials) Regulation (2004)
- EU Clinical Trials Regulation
- Research Ethics Service Standard Operating Procedures

6. Responsibilities

6.1 It is the responsibility of the sponsor to ensure that the conditions of a favourable ethical opinion are met prior to the study commencing and throughout the duration of the study.

6.2 It is the responsibility of the sponsor to ensure that the study is registered on a publicly accessible register or, where just cause can be clearly demonstrated and there is no legislative responsibility to register, that a deferral to register has been notified, in writing, to the HRA. An agreement to defer registration must be in place no later than 6 weeks after recruitment of the first participant. If the agreement is not in place within this timeframe, the HRA will consider this to be a breach of the conditions of the favourable ethical opinion.

6.3 The HRA is responsible for considering all requests to defer registration and confirming the outcome. Where requests to defer registration are not allowed, the HRA is responsible for providing a justification for this decision. This would usually be because there is a legislative obligation to register or an overriding matter of patient safety.

6.4 The HRA is responsible for maintaining a register of all requests to defer registration and informing the REC whether a request to defer has been allowed or not allowed.

6.5 The HRA monitors and reports on compliance with the REC conditions applied from September 2013, through audit and quality assurance. In April 2015 the HRA extended the audit approach to all trials in active recruitment in the UK. This is a simple enquiry on the status of studies approved before September 2013 that are still recruiting, and is an enquiry against expected best practice standards. Sponsors are reminded and prompted to register these studies through the sponsor declaration on IRAS, or they may opt to use this deferral procedure for older studies in order to demonstrate best practice.

7. Procedure

7.1 Submitting a notification to defer registration

7.1.1 All notifications to defer registration should be sent by e-mail to HRA.studyregistration@nhs.net. The title of the e-mail should be ‘Request to defer registration’.

7.1.2 The request should clearly state the justification to defer registration and include the following information (when available at the time of the request being made):

- Details of the clinical trial, including the full study title and IRAS ID.
- REC Information (Name of the REC and REC reference number)
- Contact information for the person making the request and their role in relation to the clinical trial

7.1.3 This information may be included in the body of the e-mail or it may be included in an attachment. It is acceptable to include the request to defer registration in a letter which is primarily for another purpose, such as a covering letter to the REC, and for this document to be attached to the e-mail request, in which case a separate letter would not be required. However, the request to defer registration must be made directly to the HRA and not via the REC.

7.1.4 All deferral requests will be given consideration. If further information is required to give the request full consideration, this will be requested.

7.1.5 A final response will be given in writing no later than 5 working days after the full information has been received by the HRA.

7.1.6 All requests to defer registration will be recorded on a register which is managed by the HRA External Assurance Lead. The register maintains a record of all requests to defer registration and includes the details of the study, the sponsor and the REC who reviewed the study, the reason for the request, whether the request was allowed and when the study will be registered. The register also includes a field to complete once registration has been confirmed.

7.2 **After a request has been allowed**

7.2.1 When a request to defer registration is allowed by the HRA, a point at which the study will be registered on a publicly accessible register must be agreed, or where that is not possible a time limited point at which to review the deferral. This will be the point at which the reason for the deferral is no longer of direct relevance. For example, when registration of a phase 1 study in healthy volunteers for reasons of commercial confidentiality is deferred, the requirement is that the study will be registered once the study reaches phase 2 (in line with EU Clinical Trials Directive). Studies which are terminated early for safety reasons should be registered with immediate effect.

7.2.2 Once a study is registered on a publicly accessible register, this should be confirmed by e-mail to the REC who gave ethical approval and HRA.studyregistration@nhs.net so that the records can be updated.

8. Confidentiality

8.1 The HRA registration deferral register (and trends on requests), will be reviewed annually by the HRA Board at its public meeting. The Board will note the organisation requesting deferral in the confidential part B of proceedings only, to maintain confidentiality. However, this information may be subject to requests under the Freedom of Information Act and consideration given to being released under the requirements of that Act.

8.2 The HRA anticipates at a future juncture in time, for the full deferral register to be made public.

9. Monitoring of activities covered by the process

9.1 The HRA will monitor compliance of sponsors with this policy and procedure. A list of all clinical trials given a favourable ethical opinion will be maintained by the HRA and compared against the clinical trials on the HRA registration deferral register and clinical trials on publicly accessible registers. This will be undertaken on a monthly basis by the HRA External Assurance Lead.

9.2 When a clinical trial is identified, which is not on the HRA registration deferral register and cannot be found on a publicly accessible register 8 weeks after ethical approval was granted; the sponsor will be contacted and asked to confirm the current stage of recruitment.

9.3 Where non-compliance with registration (within 6 weeks of recruitment of the first participant) as a condition of the favourable ethical opinion is identified, (when no request to defer registration has been received by the HRA) this will be managed as a breach of the terms of the favourable ethical opinion, in accordance with Research Ethics Service Standard Operating Procedures.

9.4 The HRA Board will review annually the audit reports on registration and compliance with this deferral policy. The Board will note any organisation failing to comply (where a specific REC condition has been set) or failing to demonstrate best practice (where the finding is from the

enquiry against best practice) in the confidential part B of proceedings only, to maintain confidentiality. However, this information may be subject to requests under the Freedom of Information Act and consideration given to being released under the requirements of that Act.

9.5 This policy and procedure will be subject to internal and external audits (including the Health Group Internal Audits) in line with ISO 9001:2015 requirements.

10. How lessons are learnt and incorporated into the process

10.1 All feedback regarding the process for requesting registration deferral is welcomed by the HRA. Comments or feedback should be sent to HRA.studyregistration@nhs.net.

10.2 This policy and procedure will be reviewed annually or more frequently in the event of changes in research regulations, policy or governance frameworks.

11. Management of Documents and Records.

11.1 The HRA registration deferral register and all related correspondence will be kept in a restricted access electronic folder maintained by the HRA.

11.2 Copies of the HRA registration deferral registers will be retained for three years after the year to which they relate.

11.3 All correspondence regarding requests for registration deferral will be destroyed three months after confirmation is received at HRA.studyregistration@nhs.net that the clinical trial has been registered on a publicly accessible database.

12. Supporting paperwork/forms

12.1 HRA Registration Deferral Register.

13. Dissemination and Publication

This document will be available on the HRA website.

<table>
<tr><td colspan="4">EQUALITY AND PRIVACY SCREENING QUESTIONS</td></tr>
<tr><td colspan="2">FOR EVERY HRA POLICY (defined by the Equality and Human Rights Commission (EHRC) as a function, strategy, procedure, practice, project, or decision) PLEASE ANSWER THE QUESTIONS BELOW TO DETERMINE WHETHER FURTHER ANALYSIS IS REQUIRED.</td><td>YES / NO</td><td rowspan="3">If yes, please copy and complete as required either the HRA Initial Equality Analysis and / or Initial Privacy Impact Assessment Template below. This one document can be found on the Intranet.</td></tr>
<tr><td>Equality</td><td>With due regard to our Equality Duty, could this policy have the potential to have a detrimental impact on anyone with a protected characteristic?</td><td>No</td></tr>
<tr><td>Privacy</td><td>With due regard to the Data Protection Act, does this policy involve the use of Personal Information?</td><td>No</td></tr>
</table>

Document Control

Change Record

Version Status	Date of Change	Reason for Change
V1.1	08.04.14	Submitted for comment
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
V1.7	25/08/16	Annual Review

Reviewers

Name	Position	Version Reviewed
Joan Kirkbride	HRA Director of Operations	1.1 & 1.2
Tom Smith	HRA Director of Quality Standards	1.2
UK Research Ethics Development Group		1.3
HRA Executive Management Team		1.4
Quality Assurance Team		1.4
Sue Bourne	HRA Guidance and Advice	1.4
Janet Wisely	HRA Chief Executive	1.5
Janet Wisely	HRA Chief Executive	1.6
Tom Smith	HRA Director of Guidance and Learning	1.7
Carla Denneny	External Assurance Lead	1.7

Distribution of Approved Versions

Where distributed	Version released	Date
HRA Staff Intranet	V1.5	Sent 10.12.14
HRA Website	V1.5	Sent 10.12.14
Staff Intranet	V1.6	Sent 20.08.15
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