

Clinical Trial Registration Audit Report

September 2015

Background

Since 30 September 2013, it has been a condition of the favourable ethical opinion for clinical trials (as defined by the first 4 categories on the IRAS form) to be registered on a publicly accessible database, no later than 6 weeks after recruitment of the first participant into the trial.

The HRA recognises that in certain circumstances, such as where details of the clinical trials could be considered commercially confidential, deferral of registration would be acceptable. A simple deferral mechanism was therefore put in place, as an option for all trials where the effect of current EU legislation does not provide public registration (the effect of EU legislation is that Clinical Trials of Medicines are registered. Although this legislation has specific exemption for Phase 1 trials involving healthy volunteers).

The HRA has therefore required research sponsors of new trials as a condition of the REC opinion since 30 September 2013 to register trials or to request, on a trial by trial basis, an agreed deferral to registration, with the expectation that assurance is given that the trial will be registered when no longer commercially confidential or immediately should the trial be terminated early for safety reasons.

The HRA introduced the specific REC condition to register clinical trials in September 2013, to set out the expectations to register for all clinical trials as a requirement of the REC favourable condition from that point. The purpose of creating this 'line in the sand' is to sharpen focus and awareness of the need to register and to enable, when we do look later at administrative measures and sanctions, to be able to apply them from that point to all clinical trials (not just those trials of medicines falling under current or new EU clinical trial legislation). There are no HRA sanctions in place at this time.

Where registration is a specific condition of the REC favourable opinion for that trial, a sponsor will be in "serious breach". Breaches are managed in accordance with REC standard operating procedures. The HRA is not actively pursuing this route at this time, the purpose of this audit is to scope the issue and to work with and support sponsors and others to promote research transparency and clinical trial registration in line with HRA statutory responsibilities.



Method

Compliance with the requirement to register as a condition of the favourable opinion is monitored by searching for clinical trials which have received a favourable opinion from a UK REC since 30 September 2013, and where an allowed deferral is not in place, on publicly accessible databases. CTIMPs, with the exception of Phase 1 trials involving healthy volunteers, are always registered on the EU clinical trials register via EudraCT and it can therefore be assumed that all CTIMPs have been registered and the monitoring therefore covers clinical trials other than CTIMPs, with the exception of Phase 1 trial involving healthy volunteers, which are monitored.

Publicly accessible databases (primarily clinicaltrials.gov and ISRCTN) were searched via google using the full study title and, if the trial could not be located using the title, the REC reference was searched. Where trials could not be located on a publicly accessible database, this does not necessarily mean that they have not been registered, nor does it necessarily mean therefore that the sponsor is in breach of the condition of the favourable opinion. The requirement to register is no later than 6 weeks after recruitment of the first participant and this time point may not have been reached at the time of searching. The audit period goes up to 30 June 2015 which allows 7 weeks from the end of the reporting period to the date of the audit and it is unlikely that studies will have commenced immediately after the favourable opinion has been issued; in which case there would be no expectation that these studies are registered at the point of audit. Further clarification will be sought from sponsors regarding the study status. Additionally, in some cases, not finding the trial may have been due to the search method rather than the trial not having been registered.

The proposed next phase will therefore involve writing to sponsors for the trials not located to request confirmation of whether the trial has been registered and if not, what is the reason for this and what is the expectation of the sponsor in terms of registering the trial. This extends an exercise undertaken earlier this year and presented to the HRA Phase 1 Advisory Group.

Audit findings

Phase 1 Clinical Trials

The HRA has been monitoring compliance with the condition for Phase 1 trials since the condition was introduced in 2013. The data for Phase 1 trials therefore covers the period 1 October 2013 to 30 June 2015.

Total number of Phase 1 trials with a FO during the reporting period	325	
Total number of Phase 1 trials found on a publicly accessible database	208	64%
Of the total number registered, those found on ISRCTN	(6)	(2%)
Of the total number registered, those found on clinicaltrials.gov	(198)	(61%)
The number of Phase 1 trials where a deferral was allowed	49	15%
The number of Phase 1 trials that could not be found	74	23%

Clinical trials of a medical device

The monitoring period for clinical trials of a medical device is 1 January 2015 to 30 June 2015.

Total number of medical device trials with a FO during the reporting period	169	
Total number of medical device trials found on a publicly accessible database	82	48%
Of the total number registered, those found on ISRCTN	14	(8%)
Of the total number registered, those found on clinicaltrials.gov	68	(40%)
Total number of medical device trials not registered but details of the trial could be found on the UKCRN site	19	11%
The number of medical device trials that could not be found	68	40%

Clinical Trials other than CTIMPs or Medical Device trials.

The monitoring period for 'other' clinical trials is 1 January 2015 to 30 June 2015.

Total number of other trials with a FO during the reporting period	300	
Total number of other trials found on a publicly accessible database	144	48%
Of the total number registered, those found on ISRCTN	75	(25%)
Of the total number registered, those found on clinicaltrials.gov	69	(23%)
Total number of other trials not registered but details of the trial could be found on the UKCRN site	36	12%
The number of other trials that could not be found	120	40%

Next steps

For clinical trials approved since 30 September 2013 we will e-mail each sponsor where the clinical trial could not be located on a public register and request details of registration or if not registered, details of why the trial is not registered and confirmation that the trial will be registered.

Additionally, since April 2015 the HRA has provided notice that it will extend this audit activity to check if registration of clinical trials which received a favourable opinion before 30 September 2013, which are in active recruitment have been registered, where registration is a best practice standard not a condition of the favourable REC opinion. Where clinical trials cannot be found the HRA will extend an enquiry to the research sponsor against these existing best practice standards.

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.