

Phase 1 trials in healthy volunteers - Site-Specific Assessment (SSA)

Guidance for applicants

Summary

1. Under Regulation 15 of the Medicines for Human Use (Clinical Trials) Regulations 2004, the ethics committee is required to consider the suitability of each trial site and investigator in giving its opinion on a clinical trial. This process is referred to administratively as “site-specific assessment” (SSA).
2. Arrangements for site-specific assessment of Phase 1 trials in healthy volunteers have been established by the National Research Ethics Service (NRES) and agreed by the Phase 1 Advisory Group (February 2013).
3. In summary, these arrangements involve:
 - All applications for SSA will be submitted to the main NHS Research Ethics Committee (REC) carrying out the ethical review, using a common Site-Specific Information Form (SSIF).
 - Where the research site/unit holds Standard and Supplementary Accreditation from the MHRA (See 4 below), SSA will be carried out by the main REC in parallel with the ethical review of the full application. Where no such reassurance is available and where the main REC has any concerns about a particular study, they may approach the local REC and ask for their advice on the issue. The submission of a substantial amendment for the addition of subsequent sites will be undertaken by the main REC.

MHRA accreditation scheme for Phase 1 trial sites

4. The Medicines and Healthcare products Regulatory Agency (MHRA) operates a voluntary accreditation scheme for Phase 1 clinical trial units in the UK. For further details, see: <http://www.mhra.gov.uk/Howweregulate/Medicines/Inspectionandstandards/GoodClinicalPractice/Phase1AccreditationScheme/index.htm>
5. This ‘Accreditation’ is a separate process from site-specific assessment. The ethics committee has an obligation to consider the suitability of the site and investigator on a trial-specific basis as part of the ethical review.
6. However, an SSA will be based on many of the same criteria as the MHRA accreditation scheme and the REC will be informed regarding the accreditation status of the trial site. The GCP Inspectors will consult local committees when undertaking accreditation inspections, will provide the committee with a copy of the inspection report and accreditation certificate when issued, and will keep it informed of all subsequent developments. In this way, the aim is to minimise duplication of review between the licensing authority and the ethics committee.

SSA application procedures

7. All applications for SSA should be made using the Site-Specific Information Form (SSI Form) generated within IRAS. The version of the SSI Form applicable to non-NHS sites should be selected.
8. Application for SSA must be made in parallel with the main application, to the main REC using the Site-Specific Information Forms available in IRAS.

Information to be submitted with the SSI Form

9. The following information must be provided with the SSI Form for all SSA applications involving Phase 1 trials in healthy volunteers:
 - A current CV for the local Principal Investigator at this site
 - Evidence of the professional registration for the Principal Investigator

Procedures for SSA

10. The main ethics committee for the trial will undertake the SSA alongside the main review. If a favourable opinion is given, this will include approval for any sites assessed by the committee.

Issues addressed in SSA

11. The issues addressed in SSA are as follows:
 - The suitability of the PI, taking into account his/her professional qualifications, knowledge of the research field, expertise in the procedures involved, previous research experience, training in research methods (including informed consent, training in Good Clinical Practice (if applicable) and ability to take clinical responsibility for the local research team.
 - The adequacy of the local facilities.
 - The arrangements for notifying other health care professionals who may have an interest in the care of the participants about the research.
 - The availability of any extra support that might be required by research participants as a result of their participation.
 - The local arrangements for making legal representatives available to give informed consent on behalf of minors or adults unable to consent for the research.
 - The practical arrangements to be made at the site for providing information to potential participants who might not adequately understand verbal explanations or written information given in English, where it is planned to include such groups in the study as a whole. Where the Chief Investigator proposes that such groups are to be excluded

as a whole, this is an ethical issue for the main committee rather than the SSA committee.

- The following site-specific information should be included in the local version of the information sheet for the study or provided as additional standard information for local research participants but there is no longer a requirement to submit these to the main REC. :
 - The address and telephone number of the site
 - Contact details for local investigator(s) and if applicable, other staff such as research nurses
 - Emergency contact if appropriate
 - Contact information for complaints and, where appropriate, independent advisors.

- Where research is outside the NHS:
 - assurances may be sought that this will be made clear to participants in the informed consent process
 - evidence should be obtained of insurance or indemnity to cover the potential liabilities of the PI
 - evidence should be obtained that the PI has appropriate professional registration
 - additional documentation may be requested relating to the governance of the research site.

Where an individual study site does not hold MHRA Standard and Supplementary Accreditation and where the main REC has any concerns about a particular study, they may approach the identified local REC and ask for their advice on the issue. The addition of subsequent sites would also be undertaken by the main REC.

Visits to trial sites by SSA committees

12. The MHRA inspect Accredited sites on a two-yearly basis and previously RECs have visited sites on alternate years. The UK Research Ethics Operational Management Group has discussed this matter and agreed that RECs could make a decision if they wished to continue the visits to maintain contact with the sites, and this is recommended particularly where they are the main REC. Visits provide an opportunity for ethics committee members to talk to staff and volunteers. For example, it may be useful for staff to explain the unit's procedures, and for volunteers to describe their experience of participating in a trial and giving informed consent.

National Research Ethics Service
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Location of Site	MHRA Accreditation status of site	Submit SSIF to:
Site within area covered by main REC		Main REC
Site <u>NOT</u> within area covered by main REC	none	Main REC (may consult local REC)
Site <u>NOT</u> within area covered by main REC	Standard + Supplementary Accreditation	Main REC