Phase I Accreditation Scheme Update

Proposal for Small Stakeholder Approval

Summary:

There have been a number of enquiries to the MHRA GCP Inspectorate expressing a need to expand the voluntary Phase I accreditation scheme to allow non-commercial facilities to gain acceptance.

Currently:

Currently 14 phase I units are accredited (12 commercial and 2 non-commercial). None have standard accreditation only.

The first NIHR non-commercial facility (Edinburgh Wellcome Trust facility) inspection was conducted in November 2010 and they were accredited in July 2011. The outcome was very positive, however 2 issues were identified that need to be re-considered in order to truly open the accreditation scheme up to non-commercial facilities:

- ILS training for all clinical staff – this may be an issue where a unit allows the investigator's own research team to conduct the trials in the unit (i.e. to "rent" the space) as they may not all be ILS trained.
- Potential investigators meeting qualifications for those who wish to be authorised to act as Principal Investigators on FIH trials; specifically in relation to the post graduate qualification.

In addition, there has been feedback via the ABPI survey:

- Consensus that the accreditation scheme was supported, seen as a "kite mark" and should remain voluntary.
- Two types of accreditation (i.e. standard and supplementary) is unnecessary and confusing, especially as the gap between the two types is seen as minimal. Moving to a single accreditation would also help increase sponsor awareness.
- One standard assures high quality and safety procedure at all accredited sites.
- Same scheme/standards should also apply to academic units, including requirements for recruitment of volunteers, patient volunteers and, patients.

Proposals:

Based on all the feedback, the following aspects were considered to be the most relevant to any updates to the accreditation scheme:

1. ILS Requirements:

Review current requirements or clarity of who requires to be at a minimum ILS trained. Jerry Nolan our stakeholder form the Resuscitation Council has advised that BLS/AED training is not equivalent to ILS. There are BLS/AED courses (either as a combined course or as separate courses) that are provided by various training organisations throughout the UK. These courses will not include airway management beyond the basic level and will not include how to participate in a resuscitation team. Therefore, should ILS training be all clinical staff regardless, or only the facilities clinical staff? What would the expectation be for a "research team"?

a. Proposal that ALL accredited units' "clinical" staff are, at a minimum, ILS trained.
b. Where the unit provides support to the "research team" then only the accredited unit's staff require to be ILS trained. The research team can then be considered non-clinical and have a minimum of BLS plus AED or alternative suggestion?

c. If no support by the accredited unit then ALL research team "clinical" staff must have a minimum of ILS.

This would require a change to the current wording of the accreditation scheme **OR** have to be clearly identified as to meaning in the FAQs.

2. Reduce to a Single Type Scheme:

It would appear that all are agreed that a single accreditation would be sensible. As there are now no units which have standard accreditation only, it is proposed that we move to a single type scheme and remove the standard option.

This would require a change to the current wording of the accreditation scheme.

3. Principal Investigator Qualifications for first in human (FIH) trials

It is clear that for non-commercial facilities these units may have the ability to fully manage a trial on behalf of a researcher or that the researcher can utilise the unit's facilities and bring in their own team. This could create the potential for a "double standard" in terms of the qualification of the PI, which is unacceptable within the current accreditation requirements. This proposal intends to ensure that there is no opportunity for a double standard, but, give consideration as to how to manage these occurrences, which do not occur in commercial units.

The proposal by Edinburgh Wellcome Trust CRF is to establish a Phase I Safety Review Committee (PISRC). This committee would to all intents and purposes be equivalent to the qualified for FIH Principal Investigator. It would:

- Have a minimum quorum of members that include a toxicologist, a pharmacologist and a physician who is experienced in phase I clinical trials. It should also have a member who would meet the requirement to act as a PI for FIH trials in their own right (if one of the aforementioned members does not already meet this requirement) and ensure they invite any experts/specialists if they do not have the relevant experience themselves in a particular area. [However, clear conflict of interest policy should be considered if the requesting physician is a member of the committee.]
- Peer review any proposed FIH trials and provide a risk assessment report (as we expect from the PI in commercial organisations currently). For example: it would include (but not be limited to) review of PI and co-investigators, minimum staffing requirements, safety and antidotes in respect of the IMP/patient population etc., confirmation of starting dose, CT EAG assessment, statistics, dose escalation, amendments and ongoing safety updates etc.
- They would review the requesting PIs qualifications and experience. If the requesting PI meets the current requirements they can then approve the investigator per se. However, should the requesting PI not meet the minimum standard as detailed in the accreditation scheme, the committee can specify an oversight and mentoring programme within the risk assessment report. As such this committee would be providing the necessary qualifications and experience required by the accreditation scheme. In these cases the committee would be actively involved in key aspects of the trial, for example, dose escalation decisions and ongoing safety review etc.

  However, it should be specified that this mechanism is not used as an alternative for physicians gaining an approved post graduate qualification, especially where the requesting physician is intent on conducting subsequent or numerous FIH trials.

The above points would require a change to the current wording of the accreditation scheme.

4. Over-volunteering

The accreditation scheme currently does not provide any clarity around what checks are expected in relation to "over-volunteering" or how this may differ for healthy volunteers, patient volunteers or patients. Also there have been clear examples where the use of databases has identified that healthy volunteers are prepared to travel the country and be registered at multiple units.

Proposal to discuss with stakeholders what should be incorporated into either the scheme or the FAQs surrounding expectations and requirements.

5. Risk Management

There are various opinions on how risk should be assessed and mitigated in relation to phase I trials and how this is expected to be achieved.

Proposal to discuss whether the scheme needs to be updated to be consistent with the terminology and expectations identified in the FAQs. Also how the components of the risk assessment will be pulled into a single place and built into the quality system of units which wish to be part of the accreditation scheme.

6. Miscellaneous items

The following items also need some minor discussion:

- Medical emergencies: does there need to be more information in the FAQs regarding the expectations of how these should be conducted and documented for the accreditation scheme?
- Clinical staff: does this need further definition in the FAQs?
- PI qualifications and experience: there has been an update to the ABPI guidelines for phase I clinical trials (2012) that has removed the detail surrounding the minimum requirements for PIs, which is not covered in detail in the accreditation scheme. Does this need to be addressed via the scheme or FAQs?
- Any other topics from stakeholders.

Stakeholder buy-in:

Propose a small stakeholder group consisting of:
2x AHPPI, 2x ABPI, 2x CCRA, 2 x Wellcome Trust CRF representatives (Edinburgh plus 1 other), 2x RLBUH CTU representatives, William Rosenberg (Wellcome), John Posner (FPM), Jerry Nolan (Resuscitation Council) and 2x independent non-commercial phase I facilities.

Invite Simone Bayes (DH), David Neal (NRES) and Martyn Ward (MHRA CTU), welcome to attend, but not required.
Circulate to all stakeholders, Simone Bayes, David Neal, Martyn Ward and updated Phase I accreditation stakeholder group.

Plan:

1. Convene first meeting to discuss this proposal (week commencing 22 Oct 12) - (face-to-face or telecon).
2. Convene second meeting to finalise any changes to the accreditation scheme wording & FAQs.
3. In between meetings:
   Circulate a questionnaire to each accredited unit to gauge their opinions and concerns.
   Draft and circulate new proposed working for accreditation scheme and FAQs.