National Institute for Health Research

Public consultation on the revision of "Risk proportionate approaches in clinical trials"

Response on behalf of the NIHR Clinical Research Network

NIHR Clinical Research Network
Date 31 August 2016

Delivering research to
make patients, and the NHS, better

Stakeholder details

This response is submitted on behalf of the National Institute for Health Research (NIHR) Clinical Research Network.

Our national network makes people and the NHS better by enabling and embedding high quality clinical research as an integral part of healthcare. As part of the NIHR, we improve the health and wealth of the nation through health research.

The NIHR Clinical Research Network aims to:

- Increase the opportunities for ALL people across England to participate in and contribute to research
- Provide researchers with the practical support they need to make clinical research studies happen in the NHS
- Work as a single network to improve the efficient and effective delivery of high quality clinical research
- Increase national and international clinical research investment to support the country's growth
- Provide a coordinated and innovative approach to national research priorities.

General comments

The NIHR CRN welcomes this opportunity to comment on the draft guideline for risk proportionate approaches in clinical trials. This is a welcome document which recognises that each clinical trial has its own risks which should be assessed during protocol development and reviewed throughout the lifetime of the clinical trial. The guideline encourages proportionate measures and a move away from a 'one size fits all' approach to risk management, which is a positive step.

We would note that access to early, non-binding feedback on the classification of the trial and potential for inclusion of risk adapted elements in the design and delivery, may support more sponsors to apply risk-based proportionate approaches.

We have the following specific comments on the proposed text.

Line number(s)	Comments and proposed changes
55-57	We are fully supportive of a proportionate approach to the design and conduct of clinical trials.
95-98; 107-108	We welcome the notion that risk adaptations may be appropriate for any type of clinical trial and not just those designated as low intervention clinical trials. We suggest adding a stronger statement that trials of neutraceuticals/food supplements/functional foods (with the appropriate GMP certification, etc) should be considered low risk if there is evidence of safety from widespread use in trials and general consumption, and that there should be a 'fast track' mechanism for Investigators to confirm the status of the IMP as 'low' or 'normal' at an early stage.

Line number(s)	Comments and proposed changes
112-131	We welcome the potential for IMPs used off-licence to be categorised as low intervention trials, where their use is evidence based and the additional research procedures are comparable to the risk and burden profile of normal clinical practice. It is unclear though what 'quantity' of supporting evidence is required e.g. would one published RCT be sufficient? For example, there have been decades of experience of Aspirin but it has not been treated as low intervention when used in cancer prevention trials to date.
158-242	Section 4.1: Risk based quality management: We suggest adding wording around risks associated with compliance at individual sites. While the guidance is clear about assessing, and taking a proportionate approach to the risks associated with the research itself, the potential for risks to increase if sites do not comply with the risk management plan is not included. We suggest this is threaded through each of the steps presented. We note that within the Regulation, the list of elements to be included in the dossier does not include a copy of the risk management plan for the trial, rather several areas of the guidance make reference to elements of the risk management plan that need to be described in the protocol so that these can be reviewed by regulatory authorities as part of the trial dossier. We think it would be helpful to include a clearer statement at the outset regarding the expectations of what should be submitted as part of the dossier. It should also be clear whether a risk proportionate approach is mandatory or optional. For example, will it be acceptable for a trial which fits the description of a low intervention trial to be conducted without a risk adapted approach plan should the sponsor not know about or wish to take a more proportionate approach? Guidance for applicants needs to be made more explicit. Based on our experience of risk proportionate approaches already in use, many activities traditionally associated with sponsor-led monitoring are becoming routinely expected of sites. This is an inappropriate use of site resources, and raises the potential situation of sites demonstrating their own compliance without appropriate oversight. It would be useful if the guidance highlighted the need for inappropriate 'scope creep' around site responsibilities to be avoided.