Clinical trials – regulation and transparency

Position Statement from
The Institute of Cancer Research, London, and
The Royal Marsden NHS Foundation Trust

Summary

The Institute of Cancer Research (ICR) and The Royal Marsden believe the regulatory system for clinical trials puts an enormous administrative and financial burden on academic clinical trialists, and has damaged the ability of academic organisations to lead international studies. Since the introduction of the EU Clinical Trials Directive, the complexity, risk and cost associated with running trials has increased. We don't believe the apparently modest increase in the quality of trials data as a result justifies this increase in bureaucracy. We would like the regulation of trials to discriminate far better between the different levels of risk posed. We also believe regulations over safety reporting can be burdensome and excessive, and would like to see them refined, particularly for low risk trials, in order to avoid missing genuine safety concerns.

The ICR and The Royal Marsden support moves to ensure greater transparency in clinical trials and would recommend a legal requirement to make results publicly available within a reasonable timeframe in a form that is suitable for non-commercial sponsors. We support the use of data sharing plans, but stress that all data sharing needs to preserve patient confidentiality.

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Background information

Clinical trials of new treatments for diseases such as cancer are run by both commercial and academic organisations. Each trial will have a sponsor, which can be either a commercial or academic body, and is responsible for the initiation, managing and/or financing of the trial. Academic sponsors, such as the ICR and The Royal Marsden, are not normally responsible for the manufacture or development pipeline of drugs being studied.

Across the EU, clinical trials of drugs are governed by the EU Clinical Trials Directive. The main purpose of the Directive was to protect the health and safety of clinical trial participants and to simplify and harmonise administrative processes governing clinical trials across the EU. In practice, however, the Directive has been highly controversial, with many organisations warning that it has made the process of running trials more expensive and bureaucratic.

In July 2012, the EU Commission proposed to replace the Clinical Trials Directive with an updated Clinical Trials Regulation, to better standardise and streamline the process for authorising clinical trials. At the time of writing, MEPs are debating amendments to the proposed Regulation.

In the UK, the Directive was enacted into law through the Medicines for Human Use (Clinical Trials) Regulations 2004 with further amendments in 2006 and 2008. The UK authority for the regulation of medicines is the Medicines and Healthcare Products Regulatory Agency (MHRA). Researchers must apply to the MHRA for approval to perform a clinical trial, and the MHRA monitors safety and quality standards by inspecting good practice in clinical trials. For commercial trials, trial results are sent to the MHRA for assessment before an unlicensed drug is given marketing authorisation.

In recent years, there has been controversy around transparency in clinical trials reporting, leading to public campaigns including the All Trials campaign, and a select committee inquiry focusing on transparency in clinical trials was launched in 2012. In 2013 the Health Research Authority published plans to make trial registration a condition of ethical approval.

Clinical trials – regulation and transparency

Positions on clinical trials – regulation and transparency

- We support current moves to streamline clinical trial regulation. Since the introduction of the EU Clinical Trials Directive, the complexity, risk and cost associated with running trials has increased. We don't believe the apparently modest increase in the quality of trials data as a result justifies this increase in bureaucracy. Across Europe, member states interpret the Directive differently and have divergent approval processes and reporting requirements. As a result, we have been able to lead fewer international trials since the Directive came into force. We welcome the current moves to revise the Directive, but are concerned they may not go far enough.

- We recommend a more risk-adaptive approach to clinical trial regulation, to reduce unnecessary administrative and financial burdens on academic trials. The current 'one-size-fits-all' approach to the regulation of clinical trials does not distinguish sufficiently between the different levels of risk posed by trials, for example distinctions between those testing novel drugs with an unknown safety profile, and those testing licensed drugs in a new setting. The draft Regulation does introduce the concept of 'low interventional' trials where drugs are used within their licensed indication, but this does not go far enough, for example to cover the testing of well-established licensed drugs in a new setting.

- We believe safety reporting requirements for clinical trials need to be refined to become more risk adaptive. In the UK, the MHRA and academic community have already established a three-tiered system adapting trial conduct to the level of risk, and we recommend this approach is refined and adopted across the EU. We believe the level of safety reporting in trials needs to be proportional to the level of risk and we have concerns that excessive safety reporting, for example the reporting of known serious adverse reactions associated with licensed drugs, increases the risk of missing genuine safety concerns in a deluge of data.

- We feel that there is a great deal of subjectivity around inspection of clinical trials. Where inspections are considered necessary, they should focus on genuine risk to patients and non-compliance to legislation, rather than attempting to ensure that the level of documentation meets best practice levels more suitable for commercial trials.

Clinical trials – regulation and transparency

- We welcome the introduction of co-sponsorship models in the proposed Regulation. Co-sponsorship has been used by academic sponsors for many years in the UK but this approach has not been widely recognised or accepted across EU member states.

- The ICR and The Royal Marsden welcome moves to ensure greater transparency in clinical trials. We support moves to increase widespread registering of clinical trials and the use of trial registries such as clinical trials.gov to make the status of clinical trials publicly available. We would support a legal requirement to make the results of clinical trials publicly available within a reasonable timeframe in order to avoid deliberate or accidental publication bias. Results would need to be made available in a form that is suitable for academic as well as commercial sponsors. We support moves to make data sharing plans (which detail how and when data from clinical trials may be shared) a requirement for non-commercial trial sponsors to increase transparency. We feel it would be inappropriate to provide open access to raw trial data, and data sharing needs to be conducted in a controlled manner in order to protect patient confidentiality.