

Clinical Trial Transparency – Principles and Facts

Information for clinical researchers on transparency of clinical research reporting



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This document has been produced by leading UK healthcare organisations including the medical Royal Colleges and senior representatives of the pharmaceutical industry in order to support best practice in transparency and publication of data arising from clinical research studies.

The document contains a set of best practice principles¹, supported by information about the legal and voluntary accountabilities that exist to ensure clinical research activity is transparent, based on:

- A robust regulatory framework governing disclosure of clinical trial information
- The many benefits of transparency for all stakeholders. Reporting of clinical research has a potential interest for healthcare providers, healthcare professionals and their patients, as well as any commercial sponsor and other researchers
- The fact it is impossible to get new medicines approved or data published in the top medical journals without prospective disclosure of clinical trial information on approved registries

1. The principles are based on the work of the RCP Medicines Forum – Clinical Trial Transparency Subgroup and aligned to the Faculty of Pharmaceutical Medicines best practice guidelines and the IFPMA Code of Practice

Principles of transparent reporting of clinical research studies

Clinical research is undertaken with the goal of developing new medicines and healthcare products that help people live healthier and longer lives. Clinical research studies (or clinical trials) are a vital part of establishing whether a medicine or healthcare product is safe and effective and include studies that are conducted in humans. Investigators involved in clinical trials are obliged to report the trial in a timely and non-biased manner. There is a moral responsibility to both the study participants and society to share results freely – and thus assist in the development of further research involving better trial design, fewer patients and to avoid unnecessary duplication.

Specifically, this means:

1. Investigators should ensure that the methods and plans for their clinical study or trial are recorded on a publicly accessible register within 21 days of initiation of patient enrolment in the trial and that this information is kept up-to-date. Investigators participating in commercial clinical trials and investigations should be aware of the special registration arrangements set out in the NHS-ABPI-BIA and NHS-ABHI model agreements².
2. For commercial pharmaceutical trials, investigators should make available the methods and results of their trial within one year of the product gaining market authorisation and available on the market in any country in the world. Investigators participating in commercial clinical trials and investigations should be aware of the special reporting arrangements set out in the NHS-ABPI-BIA and NHS-ABHI model agreements³.
3. If the product failed to gain market authorisation, but the results are of significant medical importance, you should make those results available within a year of completion of the trial, in a publicly accessible website or journal.
4. For all other studies or trials, investigators should make available the methods and results of their trial within one year of completion in a publicly accessible website or journal.
5. Investigators should report the trial fully and transparently following appropriate reporting guidelines, in particular the recommendation in the current version of the CONSORT statement.
6. Investigators should ensure that no important aspect of the trial results has been omitted, and any deviations from the study protocol are explained.
7. Investigators should ensure that interpretation of their clinical trial accurately reflects the research questions, study design and results, and is without bias.
8. Investigators should report their clinical trial in adequate detail to allow other researchers to extract the trial design and data for use in meta-analyses and systematic reviews.
9. Investigators listed as authors on publications arising from clinical trials have responsibility for all content and should ensure they adhere to the ICMJE guidelines to qualify for authorship.

2. For commercially-sponsored trials, the requirements of the mCTA, CRO mCTA, mCIA and CRO mCIA take precedence – with the obligation to register falling to the commercial sponsor, as stipulated in the contract; and to prevent duplication of registration.

3. For commercially-sponsored trials, the requirements of the mCTA, CRO mCTA, mCIA and CRO mCIA take precedence – with the obligation to report outcomes falling to the commercial sponsor, as stipulated in the contract.

Frameworks supporting clinical research transparency

These principles are based on a solid commitment from the stakeholders involved in clinical research. Disclosure of clinical trial information has become the standard, and transparency guidelines are more robust than ever. This means that information about clinical trial methodologies and outcomes is collected prospectively and in most cases is available to healthcare professionals and the public.

- The European Medicine Agency established the EudraCT clinical trial database in 2004. Prospective registration of trial details on EudraCT is required in order to apply to the UK Medicines and Healthcare products Regulatory Agency (MHRA) for clinical trial authorisation and Research Ethics Committee approval for a study.
- Data extracted directly from EudraCT was made available to the public in March 2011 as the fully searchable EU Clinical Trials Register. Guidelines issued by the European Commission cover not only which data are stored in the EudraCT database, but also which of these data should be made available to view by the public. As a result, comprehensive information about trials conducted in the UK is collected, including descriptive data about the study. Plans for the future include the publication of summaries of results. This feature is planned for late 2012.
- Member journals of the International Committee of Medical Journal Editors (ICMJE), including prestigious titles such as the BMJ and Lancet, require trials to be entered in a public trials registry at or before patient enrolment. The chosen registry must be publicly accessible and free-of-charge, open to all registrants and managed by a not-for-profit organisation.
- The Association of the British Pharmaceutical Industry (ABPI) first published a best practice model in 2007 to promote open access to clinical trial information and results; with the aim of setting a 'gold standard' for making these facts accessible to patients and the general public which it views as the main 'stakeholders' in the outcomes of such studies.
- The UK General Medical Council supports good practice in research and its guidance states that investigators must report research results accurately and objectively. Research should be properly attributed and not contain false or misleading information. Wherever possible, research results should be published, including adverse findings, through peer-reviewed journals. This guidance is also reflected in the ABPI Code of Practice, which states that reports of clinical trials must be factual and never promotional.
- IFPMA and reputable registries such as EudraCT state that outcomes from listed trials should be reported. In 2005, IFPMA proposed a position whereby "the results of all clinical trials in patients at a minimum, conducted on a medicinal product that has been approved for marketing and commercially available in at least one country should be publicly disclosed, regardless of outcome" meaning all outcomes. Study sponsors are therefore encouraged to post trial results for an investigational product that has failed in development but has significant medical importance.
- The CONSORT Statement was first published in 1996 and is an evidence-based tool to help researchers, editors and readers assess the quality of the reports of trials. It is intended to improve the reporting of a randomised controlled trial, enabling others to understand a trial's design, conduct, analysis and interpretation, and to assess the validity of its results. It emphasises that this can only be achieved through complete transparency from investigators.
- According to the International Committee of Medical Journal Editors (ICMJE), to qualify as an author all 3 of the following conditions should be met: (1) substantial contribution to conception or design, or acquisition of data, or analysis or interpretation of data; (2) drafting the manuscript or revising it critically for important intellectual content; (3) final approval of the version to be published. All other contributors who do not meet these authorship criteria, including professional medical writers, should be listed in the acknowledgements section.

Further information

- i. The EudraCT clinical trials database can be accessed at <https://eudract.ema.europa.eu> and the EU Clinical Trials Register at <https://www.clinicaltrialsregister.eu/>
- ii. The WHO ICTRP portal for evaluated clinical trial registries can be accessed at <http://www.who.int/ictrp>
- iii. UK Medicines and Healthcare products Regulatory Agency can be accessed at <http://www.mhra.gov.uk/Howweregulate/Medicines/Licensingofmedicines/Clinicaltrials/index.htm>
- iv. The ABPI *Best Practice Model for the Disclosure of Results and Transparent Information on Clinical Trials* can be obtained from: <http://www.abpi.org.uk/our-work/library/guidelines>
- v. The General Medical Council Guidance on good clinical practice can be accessed at http://www.gmc-uk.org/guidance/good_medical_practice.asp
- vi. Schulz KF, Altman DG, Moher D, for the CONSORT Group. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010;340:c332.
- vii. ICMJE Uniform Requirements for Manuscripts can be obtained from: http://www.icmje.org/urm_main.html
- viii. The Faculty of Pharmaceutical Medicine Guiding Principles for Pharmaceutical Physicians includes a section on Clinical Trial Transparency and it can be found here: www.fpm.org.uk