Publication Integrity and Ethics

PIE (π)

P.I.E. Guidelines: Clinical trials code of practice, conduct and reporting

Practice Guidelines

Please read the declaration at the end of this document before applying these guidelines

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Introduction

The issue of reporting clinical trials in biomedical research for medical doctors and dentists is of major public concern. One of the potentially contentious points for discussion, with regard to full reporting of the results obtained from clinical trials, is the sponsorship of trials by the drug companies, biological or device industries.

The challenge for debate broadens when academic researchers within the fields of medicine, dentistry and biomedical science and their institutions, have a key role to play in these trials. As a result, the objectivity and principles of the academic medical research teams are called into question against the integrity of the individual sponsors of the trials.

Detail

Although there have been peripheral attempts to raise reporting standards of clinical trial results for doctors, dentists and biomedical scientists, the concerns have not abated. This is largely due to the wide variation that exists in academic circles, in relation to the implementation of correct academic standards. The evidence can be seen in the significant differences seen in the analyses and reporting of results of sponsored clinical research; this is most apparent in clinical trials sponsored by industry, particularly the pharmaceutical companies.

Therefore, medical schools, teaching hospitals, and professional societies must be given standard guidelines; any principles and recommendations are to be developed in such a way that substantial and firm scientific ethics are embedded within these. In addition they should be widely dispersed across the breadth of the professional community.

A clear set of principles for academic medical research must guide institutions and their investigators appropriately. Any such guidelines must embrace operational elements for data access, ethical considerations, analysis and the reporting of clinical research studies. When such a document is understood and accepted, integrity, trust, credibility and honesty in the reporting of clinical trials can thus be assured.

Based on the assumption that widespread agreement is attained within academic medicine, the sponsors should aim to win acceptance of the prevailing governing principles. Agreement must run throughout the industry, embracing the whole spectrum of the medical community, including patient advocacy groups and non-profit making sponsors of clinical trials. Integrity and credibility are the key factors when documenting the results of clinical trials.

Any legal issues commonly associated with clinical trials such as indemnities, intellectual property and others should be avoided. Central to the core aim should be access to data and analysis, registration, reporting and subsequent publication and participation in studies. These guidelines can identify the items of concern and where agreement has been reached amongst all relevant stakeholders.

1 *Principles of agreement*

1.1 All clinical trials should follow certain pre-set principles when they are conducted within academic medical or dental institutions, whether on a single or on multiple sites; this must be external to any financial, or funding, aspects.

1.2 The definition of a clinical trial can be given as any research project that aims to divide human subjects into distinct groups of a) intervention and b) comparison - with the goal of analysing the underlying relationship between clinical intervention and the subsequent health outcome.

1.3 The term 'clinical intervention' alludes to any process used to modify a health outcome; this may include surgical procedures, drugs, medical tools, and behavioural treatments.

2 *Results of research for public scrutiny and publication*

Whilst the World Health Organisation (WHO) is at the head of an international drive for promotion of clinical trial registration, agreement has not yet been received regarding the 'masking' of certain areas of the minimum data requirements. The WHO strategy for registration requirements is therefore acknowledged but not yet included.

2.1 An obligation towards ethical conduct must be placed on research institutions and their team of researchers when involved in human research projects; they should strive towards a policy of transparency, with open publication of their results to the public, in accessible format.

2.2 When clinical trials are being conducted the institutions involved and their corresponding sponsors must draw up contracts that allow for a degree of good faith that results of any clinical trials will be published expediently with appropriate peer review.

2.3 Adequate funding for clinical trials for the full cost of the analysis and publication of the results should be stipulated in the contract. If, for any reason, termination of the study occurs prior to objectives being met, this principle still applies.

2.4 Results of trials that meet registration prerequisites are to be made available to the public with full transparency; the results will be posted to an accessible online file or be accessible via a link to a peer-reviewed publication. The results are to be available within 24 months from the completion of the clinical trial.

2.5 Post publication of results, the researchers, sponsors and organisations share, with a consistent formulaic approach, the data underpinning the publication, with allowance for permissible exceptions on the grounds of confidentiality or information pertaining to ownership or branding.

3 *Clinical trials and the necessity of registration*

3.1 A clinical trial covered by the aforementioned principles is to be registered in full according to current requirements. In addition, registration must afford a unique identification number to each clinical trial. Registration should be documented in a public, not-for-profits international registry with all required elements.

3.2 As far as possible, data for trial registration should be regularly updated; a link to relevant reports previously published and associated with the research being studied should accompany this.

4 *Lead researcher and principal committee*

Whereupon a clinical trial is conducted across multiple sites, from the commencement of the trial, a lead or principal investigator should be identified, together with a reliable and appropriate steering committee; these teams will represent the full body of investigators.

5 *Publication and analysis committee*

5.1 From its inauguration, a clinical trial that is being conducted as a multisite programme needs to form a publication and analysis committee. This must be made up of authorised and appropriate personnel and be independent from control by the sponsors of the study.

There must be an easy accessibility to all data and information by members of the publication and analysis committee. Its members are required to understand the pre-set plan for analysis and be willing and prepared to implement the specifics of this plan, for publication purposes, with adequate resources, knowledge and skill sets.

5.2 Additional to this requirement, the members must have the necessary ability to interpret the findings from the analysis and if necessary, formulate and submit additional analytical material. This approach is fundamental to success in order to prevent any overshadow of undefined influence from sponsors.

The publication and analysis committee should also be comprised of members of whom the majority are participating investigators but not employed by the sponsors. They must be trained and skilled to a relevant level in analysis of clinical trials and the resultant interpretation. Members of the steering committee may also be members of the publication and analysis committee.

5.3 The publication and analysis committee involved in multisite clinical trials or, in the case of a study on a single site - the principal investigator, should appoint an appropriately qualified expert person who is preferably already serving as a member on that committee and this specified individual should have the unopposed right to be able to access data which has been duly produced during the designated study.

This should be of a nature, however, which the committee states is necessary to ensure proper codes of integrity and validity of the study and its subsequent full reporting.

5.4 It is the responsibility of the publication and analysis committee in a multisite trial, or the principal investigator in a single site trial, who request that the sponsors of the study have a set parameter of time in which to perform the analysis.

5.5 Either the principal investigator, or the committee in a multisite trial, should have the facilities and ability to perform their own independent analysis by a designated selected person of their own election. This should be conducted to the level and depth deemed essential. However, this person who will necessarily be of exceptional knowledge, should be appointed on agreement by the publication and analysis committee and the corresponding sponsor.

5.6 The publication and analysis committee should be invited to share knowledge of the analysis received from the relevant sponsor in all areas of the study; the aforementioned sponsor will have been responsible for conducting the study whereby biological materials, pertaining to medical and dental clinicians and biomedical scientists, have been received and implemented during the course of the study.

5.7 The principal investigator or the publications and analysis committee must be relied upon to disseminate the results of the study, in trust and good faith, via the respected peer review channels.

6 *Publication of an individual nature*

6.1 Whereby a trial involving clinicians and biomedical scientists is multisite and there is a site which is specific for publication, there may arise a potential towards bias. This bias may be wholly unavoidable.

However, as such site specific publications would not have constituted part of the plan for analysis; this can be a nebulous area open to misinterpretation or detrimental outcomes. This situation needs to be avoided as far as possible.

6.2 However, an analysis which is specific to a certain site should be permitted, in order to maintain a degree of respect for an academic facility, providing there are pre-set conditions imposed therein.

6.3 With respect to the above point, a researcher from an individual site, whereupon the trial is multisite, should be afforded the liberty to make the necessary analysis from the trial and publish data from that site. However, the analysis must be consistent with the protocol of the principles for scientific study and only after review and report by the publication and analysis committee. It must also only be allowed after the complete study has been published or, if this is not possible, then within a two-year time lapse from the designated close or termination of the study.

7 *Authorship*

7.1 It is inappropriate to authorise ghost or guest authors. A signatory as author implies significant input of independent, open and honest participation in the programme of study and subsequent creation of the manuscript.

7.2 An employee of the sponsor may be involved in draft work and publication of the manuscript; however, their input and role must not be nebulous in nature and should be fully clarified. Any authorship arising should have full conflict of interests declared

7.3 A facility or institution conducting a trial concerning medics, dentists and biomedical scientists is to implement strict standards of authorship in an honest and fully disclosed manner.

7.4 Researchers and investigators should use high principles pertaining to defined levels of protocol in publication of clinical trial results.

7.5 An investigator of a clinical trial pertaining to medics, dentists and biomedical scientists must be prepared to declare any appropriate financial interests or consultancy work. This should be apparent in all communications regarding the results of the trial; the aforementioned principles should include publication by journals.

7.6 The role of individual authors, when involved in a study and creation of the final manuscript to be submitted for publication, must be made transparent. This information, where practical and applicable, should be made open to public view, whereupon there is public presentation of the results of the trial.

7.7 Whereby a manuscript is submitted for publication it should declare all former publications pertaining to the same data base or principles.

7.8 A manuscript which is submitted for publication must include submission of the relevant principles and protocol underpinning a pre-set plan for analysis. All amendments and corrections must have the date stated; any deviations to this pre-specified analytical plan need to be identified and afforded relevant discussion.

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Declaration

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