GUIDELINES ON THE STRUCTURE OF A FORMAL AGREEMENT TO CONDUCT SPONSORED CLINICAL RESEARCH

Introduction

Advice on relationships between the medical profession and the pharmaceutical industry published in June 1994[1] referred to the need for a formal agreement between a pharmaceutical company and an investigator in conducting sponsored clinical research. The Higher Education Funding Council for England[2] and a briefing by the Committee of Vice-Chancellors and Principals of the universities of the United Kingdom[3] both lay emphasis on collaboration with the pharmaceutical industry as a means of generating income in order to support basic research. Hospital trusts have also become aware of such collaboration as a source of revenue.

This document reiterates the need for formal agreements and suggests items to be included in the interests of containing research costs and ensuring value for money. It may also be appropriate for a separate formal agreement to be signed by other service providers to the clinical trial and by the responsible member of the company (e.g. pharmacy departments, radiological departments and laboratories).

In consideration of such collaboration and the provision of services to the sponsoring pharmaceutical company, the company should offer an indemnity in respect of third party claims in the form agreed with the Department of Health.

Standardise the structure of the formal agreement

- A formal agreement should be signed by the investigator, a Company Senior Manager or the company person to whom authority for the trial has been properly delegated before the trial commences. Service providers must be able to sign with the delegated authority of their employer (e.g. Hospital Trust).
- It may also be appropriate for a formal agreement to be signed by other service providers to the clinical trial and by the responsible member of the company, (e.g,. pharmacy departments, radiological departments and laboratories). Service providers must be able to sign with the delegated authority of their employer (e.g. Hospital Trust).
- Brevity is important wherever practical but precision and clarity is essential to avoid misunderstanding since non-compliance with the protocol or with agreed standards is likely to affect payments and may affect patient safety. Extra information can be included as a schedule to the agreement (e.g. synopses of EU guidelines, clinical trial protocol information).
- The formal agreement should refer to the following which may also be covered in detail in the protocol or a separate financial agreement:
  - A description of the clinical trial (e.g. Title of the Protocol). Any Company identifying number for the study and the Medicines Control Agency approval number may be added, as appropriate.
  - Standards of conduct to which the clinical trial will be performed by the investigator and the consequences if these standards are not met. This should contain as a minimum:
    - Agreement to adhere to the protocol, procedures for changes to the protocol, notification of serious adverse events associated with treatment, withdrawal of subjects from the trial and cooperation in verification of source data.
    - Agreement that the trial will not commence without the approval of an appropriate ethics committee constituted and operating in accordance with prevailing UK guidelines[4,5] (a Local Research Ethics Committee where the patient is being treated under the NHS) and the responsibilities of the investigator for provision of information concerning approval to the sponsor and for updating information to the ethics committee.
    - Specification that the clinical trial will be conducted according to the EU guidelines for Good Clinical Practice or such guidelines as are subsequently developed by ICH.
  - Payment terms, when appropriate, for carrying out the defined clinical trial to the agreed standards. These should specify the circumstances under which payment will or will not be made bearing in mind that the protocol specifies the eligibility of patients or non-patient subjects for the trial and the criteria by which treatment outcome will be judged. Guidance on payment for subject withdrawal and the consequences of termination of the trial may be appropriate. In addition the name and number of the account into which monies should be paid and a payment schedule should be included.
  - A statement outling the period of time over which the agreement is to run.
  - The subject recruitment rate expected.

- A statement relating to:
  - confidentiality.
  - retention of records.
  - ownership of study materials and records and return to sponsor on completion or termination of the study.
  - the respective obligations of the parties in relation to disclosure of potentially price sensitive information and publication of results.
  - the intellectual property rights attaching to any documentation provided by the sponsor and any study findings.
- Where equipment is provided for the purposes of the study, the terms of such provision should be included.
- The grounds, as appropriate, for termination of the study prior to completion such as regulatory action, recruitment difficulties etc and the consequences of such termination.
- Agreement of the sponsor to abide by the ABPI guidelines[6] governing compensation for injury to research subjects and to provide an indemnity to the investigator in the form agreed with the Department of Health.

Matters relevant to the costs of clinical research in the United Kingdom

- It is in the interests of both the NHS and British academic institutions that charges to the sponsor of commissioned clinical research remain not only good value for money but also ensure that such research endures in the United Kingdom.
- Data confirm that the costs of performing sponsored clinical research in the UK are among the highest in the EU.[7]
- It is in the interests of the community as the consumer of pharmaceutical products that the costs of clinical research be contained.
- Proper costing of clinical trials is an essential adjunct to the ethical conduct of such trials.
- The financial benefit to the investigator/service provider under the agreement with the sponsoring company or (as the case may be) contract house should be declared to the appropriate ethics committees prior to initiation of the trial.
- Costs of clinical trials include the following elements:
  - Attendance at and travel to specified investigators' meetings.
  - Medical, nursing or researcher's time spent interviewing, examining and investigating the patient/non-patient volunteers.
  - The time spent recording the data in the Case Record Form.
  - The costs of tests, investigations and pharmacy services specific to the protocol which should not differ in cost from those performed identically for the NHS.
  - The costs of subjects attending purely for the purposes of the clinical trial, including travel expenses, documented loss of earnings and, where there is no therapeutic benefit or required attendances involve material inconvenience, reasonable participation fees.
  - The administrative costs arising out of the clinical trial and borne by the institution conducting the trial.
  - The overheads charged by the institution or service provider as a reasonable profit upon the provision of services. This item should not be added to items where profit is already included, e.g. investigators' fees, patient costs, clinical investigations where the overhead is already added in to the charge.

References

1. Relationships between the medical profession and the pharmaceutical industry. ABPI June 1994.
2. Research Assessment Consultation Document CP/93 of the Higher Education Funding Council for England 1993.
3. A briefing by the Committee of Vice-Chancellors and Principals of the universities of the United Kingdom. Briefing November 1994.
4. Guidelines on the Practice of Ethics Committees in Medical Research involving Human Subjects. Royal College of Physicians of London 1990.
5. Local Research Ethics Committees; Department of Health 1991. HSG(91)5.
6. For patient volunteers, the ABPI Guidelines Clinical Trials – Compensation for Medicine-Induced Injury (1991) and for healthy volunteers, the ABPI Guidelines for Medical Experiments in Non-Patient Human Volunteers 1988 (amended 1990).
7. Data provided to ABPI by Data Edge Inc 1994/95/96.

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