University Hospitals Bristol NHS
NHS Foundation Trust

R&D Information Sheet No.1[b]
Guide to writing an Observational Study Protocol

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The aim of this guide is to help researchers with the content and structure of protocols for observational (cross-sectional (prevalence), cohort (longitudinal) and case control) studies. It indicates the information that should generally be included in a protocol and has been constructed to cover important methodological considerations and requirements specified under Good Clinical Practice.

Advice of the methodological aspects of designing a research study and writing a protocol can be obtained from the Research Design Service on 0117 342 0233.

Where University Hospitals Bristol (UH Bristol) is the sponsor of the research study suggested standard wording is available for the sections of the protocol marked with a *, please refer to Research Guidance Sheet No 3b available from the Research website.

General Information

Title

- It is useful to specify both a full title and short title.
- The titles specified must be consistent across all documents relevant to the study.

Names (titles), roles and contact details of:

- Name and address of sponsor(s)*.
- Name, title, address and telephone number of the Chief Investigator.
- Name, address, title and telephone number of all other Investigator(s) (if applicable).
- Address and telephone number of study site(s).

Protocol details

- Version number and date, e.g. v2 12.09.2010.
- Final/draft.

List of abbreviations and definitions

Background

The detail given in this section should be backed up by a full literature review and should make reference to relevant papers, previous clinical experience and pilot work.
This section should include:

- A clear explanation of the main research question.
- Detailed justification for the study including:
  - A statement indicating the size of the problem and an explanation of why the study is appropriate.
  - Potential benefits to patients and the NHS.
  - Service, relevance to current policies and priorities.
  - Description of the indication, its diagnosis, incidence, current treatments and their limitations.
  - An explanation of what your study will add to the body of evidence already available.
  - A discussion of the feasibility of the study in terms of subject and data availability as well as length.

Aims and Objectives

- State the purpose of performing the study (e.g. student project, commercial/non commercial study, licensing).
- State the primary and secondary objectives.

Study Design – the scientific integrity of a study and the credibility of results obtained are largely dependant upon the study design. A description of the study design should include the following:

- The type/design of the study e.g. Case-Control, Cohort, Cross sectional (Prevalence)
- A description of the study groups.
- The expected length of time each subject will participate in the study for and the sequence and duration of all study periods
- The criteria for discontinuation of parts of the study or the entire study

Subject selection

- Source of subjects (where they come from and why this group is appropriate).
- Number of centres involved.
- Expected number of eligible participants available per year and proportion of these expected to agree to the study.

Inclusion Criteria

- List the inclusion criteria defining who is eligible for the study.

Exclusion Criteria

- List the exclusion criteria; consider incompatible concurrent treatments, recent involvement in other research.

Subject recruitment

- Details of recruitment process including:
  - Method of recruitment (e.g. via adverts, clinics) and details of enrolment procedure.
  - Payment of participants.
  - Details of procedures, tests, and screenings carried out to assess study suitability.
  - Provision of patient information sheet.
  - Gaining patient consent (how consent will be obtained, who will gain consent, whether a witness will be present, how long the subject will have to decide, the arrangements for non-English speakers and special groups (e.g. mentally ill, children, those suffering from dementia).
  - Detail of enrolment procedure.

Subject compliance

- Recording of patient compliance information (what will be recorded, when and where).
- Detail of follow-up of non-compliant subjects.

Withdrawal of Subjects

- Subject withdrawal criteria and procedures identifying:
  - When and how to withdraw subjects.
  - The type and timing of any data to be collected for withdrawn subjects.
  - Whether subject should be replaced and if so the methods for doing this.
  - The follow up procedures for withdrawn subjects.
  - Documentation to be completed on subject withdrawal.

Sample size calculation

- Study sample size, for multi-centre studies the projected sample size for each site.
- The power of the study.
- The level of significance to be used.
- Statistical criteria for terminating the study

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Data collection

- Provide a detailed list of all data (outcome variables, explanatory variables etc) to be collected, with each description including:
  - Source of the data, the time point for collection (baseline, during treatment, at follow-up point) & who will collect the data.
  - Why data are being collected (e.g. baseline comparison data, main outcome, important prognostic/ explanatory variable).
  - Whether data are from a standardised tool (e.g. McGill pain score)/involves a procedure in which case full details should be supplied).
  - What form the data will take (e.g. binary, continuous (numeric), time to event).
- Describe methods used to maximise completeness of data (e.g. telephoning patients who have not returned postal questionnaires).
- Include data collection forms as appendices.

Data handling and record keeping

- State who is responsible for data collection, recording and quality and describe procedures for data collection and recording (software to be used, location of the data etc).
- Detail methods implemented to ensure quality of data (e.g. double entry, cross validation etc).

- Describe procedures for security/storage of data.
- Describe procedures for retention of source data including the duration and location*.
- Include statement on adherence to Data Protection Act 1998*.
- Plans for archiving at the end of the study and details of where documentation will be archived.

Statistical analysis

- Description of the type of analyses to be performed.
- Methods of analysis (e.g. t-test, logistic regression) and how the results will be reported.
- Details of adjustments for pre-defined confounders.
- Details of how any planned subgroup analyses will be done.
- Details of any non-statistical methods that might be used (e.g. qualitative methods).
- The selection of subjects to be used in the statistical analyses. e.g. all eligible subjects all dosed subjects etc.

Safety Assessments

- Specification of safety parameters and the methods for timing, assessing, recording and analysing safety parameters.
- Definition of serious adverse events for the study that are expected e.g. hospitalisation in terminally ill patients.
- State which serious adverse events (if any) will not be reported.
- Detail the procedures that will be followed in the event of adverse events in the study* including who has what responsibility
- Describe the type and duration of follow up of subjects required after and adverse event/adverse reaction.

Stopping/discontinuation rules

- Define completion and premature discontinuation of the study.
- Describe procedure regarding decisions on discontinuation of the study (e.g. interim analyses).
- State documentation to be completed if part/all of the study is discontinued.

Research Governance, Monitoring and Ethics & R&D approval

- A statement that the study will be conducted in compliance with the Research Governance Framework for Health and Social Care and Good Clinical Practice (GCP)*.
- Arrangements for monitoring/auditing conduct of the research* & the use and role of data monitoring groups and steering groups etc.
- Detail of any other steps taken to ensure quality of research.
- Description of ethical issues related to the study.
- A statement that the study will be conducted in accordance with approvals from relevant groups (e.g. MREC, MHRA, Trust(s) and other specialist approvals e.g. NIGB)*.

Finance

- Provide any details of the financial arrangements for the study if not assessed in a different document.
- Provide details of any payments to be made to participants.

Indemnity

- Describe arrangements for providing cover for non-negligent and negligent harm*.

Reporting and dissemination

- Detail of plans for publicising the results of the study.

Tables, figures and references

Appendices

For example:

- Patient information sheet.
- Patient consent form.
- GP letter.
- Data collection forms.
- Case Report Forms,
- Adverse Event/Serious Adverse Event reporting form.