Guidelines for Submission of Full Proposals for Trials

Applicants please note that a full proposal should only be submitted if it has been formally invited following consideration of a letter of intent submitted in answer to the ESF call for proposals issued in June 2001.

General Points

- Please structure the **Case for Support** of your proposal using the headings listed in the full proposal form**.** These are an extension of those in the letter of intent form.
- **Make an entry under every heading**
- **The case for support for the proposal should not exceed 20 sides of A4 (11 point), including up to 2 pages of references.**
- **The case for support should include a list of further information available, either as appendices or as additional information lodged with ESF/EMRC Department.**

The Amount of Information Required

In presenting your full proposal it is important to strike a balance between, on the one hand, clearly demonstrating that all the important issues have been fully addressed and on the other, the desire to bury the peer-reviewer in an avalanche of detail. There are three levels of information that can be included in a full application:

1. Case for Support (20 x A4 maximum)

This should be used to demonstrate clearly that all the major issues have been addressed. No more than two pages of references should be included. It should refer, where necessary, to further details in the appendices or information lodged with ESF/EMRC Department. **It should include a list** of further information available in the appendices or in information lodged in the ESF/EMRC Department.
*Example: **-** A statement on the number of centres involved in the proposed trial*

2. Appendices

These should be limited to information that peer-reviewers may wish to consult on matters of detail.
Example:- A list of those centres that have agreed to participate in the study

A copy of the draft patient information leaflet and consent form based on the guidelines for the country of the principal applicant **must be submitted with the full proposal**. It should be kept in mind that this patient information leaflet might need to be modified to fit with local guidelines in each participating country.

Additional submissions should be kept to a minimum, but may include information that you would wish peer-reviewers to know was available but which they were unlikely to require.
Example:- letters from centres agreeing to collaborate in the proposed trial

Completing the full proposal

When completing the **case for support** of the application form, please structure your application using the headings provided in the full proposal form. This is divided **into 5 sections**, each with a series of **headings** (**bold type**). The headings on the form are structured to ensure that the key information required to assess the trial is present (further explanations expected are asked under *sub-headings in italic*). Listed below are key questions that should be taken into account when completing each section of the form.

■ Section 1 – Trial identifier

1.1 Full title of the trial

The full title of the trial should aim to be a useful description of the study (not just an acronym) and should not exceed 120 characters.

1.2 Acronym (if applicable)

■ Section 2 - The need for a trial

2.1 What is the problem to be addressed?

- *The importance of the issue should be adequately explained in terms of e.g.:*
  - *i) burden of disease*
  - *ii) potential impact of the results (for this disease and others)*
  - *iii) present and future resource implications for European Health Services and the European economy in general*

2.2 What are the principal research questions to be addressed?

- *The therapeutic model and the hypothesis(ses) should be presented and documented*

2.3 Why is a trial needed now?

- *Justify that it is the right time to conduct the trial with respect to current knowledge of the intervention and current use of existing technologies*
- *Explain the reasons for the study and the changes that might be implemented as a result of the study*

2.4 Background and systematic reviews

- *What evidence is available to inform the need for and design of this trial (e.g.: systematic reviews)?*
- *Is the proposed research compatible with the extent of the available knowledge, nationally and internationally?*

2.5 Added value of the expected benefit

- *Given the available knowledge, what will be the added value (compared to other available interventions for the same disease) of the anticipated results?*

2.6 How will the results of the trial be used?

- *How will you address the dissemination of the results?*
- *What impact will the results have on clinical practice or our understanding of the proposed intervention or underlying disease?*
- *Do you intend to look for subgroups with particular response to the intervention? How?*
- *Do clues exist that the results of the trial will be generally applied beyond the immediate research setting of the trial in a way that will maximise the impact of the results?*

2.7 Risks to the safety of the participants

- *Review the potential hazards of the intervention(s) and of being participant in the trial*

■ Section 3 - The proposed trial

3.1 Brief summary of the trial proposed (max 100 words)

3.2 What is the proposed trial design? Describe it

- *Justify that the study design is appropriate to answer the research questions posed*
- *Justify that sufficient account has been taken within the study design of the issues of generalisability and representativeness*
- *Have the measures been validated specifically for the target population(s)?*
- *Are the control groups appropriate?*

3.3 What are the planned trial interventions?

- *Describe in details the tested intervention*
- *Justify the choice of the control intervention*

3.4 What are the proposed practical arrangements for allocating participants to trial groups?

- *Describe the allocation process and explain why it will be unbiased*

3.5 What are the proposed methods for protecting against other sources of bias?

- *Endpoints*
- *Delayed randomisation*

3.6 What are the planned inclusion/exclusion criteria?

- *Inclusions*
- *Exclusions*
- *Has the study sample been defined adequately in relation to the target population so that the results will have meaning?*

3.7 What is the proposed duration of treatment period?

3.8 What is the proposed frequency and duration of follow-up?

3.9 What are the proposed outcome measures?

- *Primary endpoints*
- *Secondary endpoints*

3.10 How will the outcome measures be measured at follow-up?

3.11 Will health service research issues be addressed?

3.12 What are the proposed sample size and the justification for assumptions underlying power calculations?

3.13 What is the planned recruitment rate?

- *On what these estimates are based?*

3.14 Are there likely to be any problems with compliance?

- *How will they be addressed?*

3.15 What is the likely rate of loss to follow-up?

- *How will they be addressed?*

3.16 How many centres will be involved?

- *On what criteria will they be selected?*
- *Outline the selection processes and monitoring of sites*

3.17 Are there any planned subgroup analyses?

3.18 Details of the planned analyses

3.19 Is there any efficacy and/or safety monitoring process planned?

- *Outcomes to be monitored*
- *Organisation of the monitoring process*
- *What is the proposed frequency of analyses?*

3.20 Has any pilot study been carried out using this design? If yes, please give the results if there was any

3.21 Over what period is funding required?

■ Section 4 - Trial Management

4.1 What are the arrangements for the day to day management of the trial?

4.2 What will be the responsibilities of the named participants

4.3 What will be the roles of the named collaborators

4.4 Who is the trial statistician?

4.5 Trial organisation

4.6 Trial Steering Committee: proposed membership

*A Trial Steering Committee (TSC) should be set up. The membership should include an **independent** Chairman (not involved directly in the trial other than as a member of the TSC), other independent members and principal investigators or applicants. Applicants should propose TSC **membership**, in their full application. The ESF reserves the right to advise on the appropriateness of the proposed membership.*

4.7 Data Safety and Monitoring Committee (see 3.19): proposed membership

*A Data Monitoring and Ethics Committee (DMEC) independent of the investigators and the Steering Committee should be set up. Applicants should propose DMEC **membership**, in their full application.*

4.8 Quality issues and good clinical practices

- *Identify all the quality issues and address them appropriately*
- *Explain how the good clinical practices issues have been solved*

4.9 How the interventions will be provided?

- *Who will pay for the intervention? Give the appropriate documents supporting these claims in the appendices*
- *How will the material(s) for the interventions be distributed to the clinical sites?*
- *If the trial is double-blind, explain how the interventions will be masked*

■ Section 5 - Financial details of the trial

5.1 Financial summary

- *One financial summary per applicant (country)*
- *One financial summary covering the co-ordination costs*

■ Section 6 - Application History

6.1 State how this proposal has been modified since submission of the letter of intent

6.2 Has the proposal been submitted to other funders?

■ Section 7 - Other Issues

7.1 Is a health economics component included? If not, justify

7.2 Is a quality of life component included? If not, justify

7.3 Ethics (see also 2.7)

- *Address all the ethical issues in details and explain the adopted solutions*
- *Give the required advice(s) of the Ethical Review Board(s) or how they will be obtained*
- *Explain how the consent form processing will meet the local requirements*

7.4 How will the data be processed?

- *Detail the data collection, circulation, control and storage*