



Submission of a clinical trial for access to ECRIN services Notice to the Applicant

BEFORE SUBMITTING YOUR PROTOCOL

Please, contact the European Correspondent (EuCo) in your country. The list of EuCos and their contacts details are available [here](#). The EuCo can provide you more information about the submission to the ECRIN Scientific Board and its evaluation, as well as on the ECRIN organisation, type of services provided, etc. Please, note that the ECRIN evaluation comprises two aspects:

- A) scientific merit and methodology (by the ECRIN Scientific Board);
- B) logistical feasibility (by the network of EuCos).

Please, prepare the following documents for the submission:

- A cover letter specifying the services requested from ECRIN in the different ECRIN countries involved.
- Funding sources, or planned funding application.
- Curriculum vitae of the Coordinating Investigator.
- ECRIN checklist filled in and signed (ask the EuCo in your country).
- The full protocol written in English (no specific template is required, however ECRIN highly recommends the SPIRIT guidelines for the protocol writing).

If your protocol has already been evaluated by one or more ethics committees, regulatory authorities, or other entities you may wish to submit also their reviews. The ECRIN Scientific Board takes into consideration these evaluations.

Please, read carefully the ECRIN Scientific Board eligibility criteria, that are checked by the ECRIN Scientific Board Secretariat in order to start the evaluation process.

ELIGIBILITY CRITERIA

1. Multicentre trial run in at least two ECRIN-ERIC members or observer countries

2. Rules for transparency:
 - a. Commitment to register the trial in a public register before inclusion of the first participant. +
 - b. Commitment to post trial results in a public register one year after the trial is completed, i.e. last follow up of the last patient for the primary outcome. +
 - c. Commitment to publish results irrespective of findings.
 - d. Commitment to make raw anonymised data sets available to the scientific community upon request. *
 - e. Declaration of conflicts of interest.

+ according to the WHO ICTRP or ICMJE recommendations, for example on EudraCT or Clinicaltrials.gov.

* unless documented justification.

3. Commitment to fairly describe the contribution of ECRIN and its national partners in the publications.

Your signature on the ECRIN checklist is intended as a commitment to fulfil the eligibility criteria. Please, ensure that your trial protocol fulfils these criteria before submitting it. If the version of the protocol you are going to submit does not comply with each and all the eligibility criteria and cannot be changed at this stage (e.g. it has been already approved by ethics or regulatory authorities), you should commit to include them on the occasion of the earliest protocol amendment.

You may also want to consider the evaluation criteria that form the basis of the assessment by the ECRIN Scientific Board.

<p>EVALUATION CRITERIA</p> <p><i>Projects having already undergone scientific evaluation are invited to provide previous evaluation reports</i></p>
<p>Rationale for the trial - including the choice of the experimental intervention and the comparator - based on extensive and up-to-date review and analysis of relevant clinical and preclinical data. *</p>
<p>Suitable overall trial design appropriate to the clinical question</p>
<p>Clinical relevance for patients and public health</p>
<p>RECOMMENDATIONS</p> <p><i>You may wish to consider the following recommendations when preparing your protocol for submission to the ECRIN Scientific Board. These features are well accepted standards for high-quality multinational clinical trial protocols.</i></p>
<p>Relevant patient population (inclusion and exclusion criteria), setting, and duration of treatment and follow up.</p>
<p>Randomised superiority design is preferable for benefit assessment, rather than non-inferiority.</p>
<p>Use of the best available comparator.</p>
<p>Primary outcome measure most suitable for patient and public health's interests. Outcome measures for efficacy and safety clinically meaningful for the patient.</p>
<p>Adequate sample size with supporting calculation. Sample size calculation based on the primary outcome measure, and power calculation for secondary outcomes.</p>
<p>Adequate recording of adverse events.</p>
<p>Adequate strategies to reduce or control possible biases, for example central randomisation; blinding of all parties (at least assessors whenever possible, and the statisticians); intention-to-treat analysis for efficacy in superiority trial; blinded conclusions drawn before breaking the allocation code; and interpretation of, and decision to publish results, independent of funding source.</p>
<p>Adequate strategies to reduce the risks of random error ("play of chance"), i.e. problems with multiplicity due to multiple outcome comparisons and sparse data.</p>
<p>Description of potential risks and how to handle them, including involvement of and charter for independent data monitoring and safety committee.</p>
<p>Description of governance structure of the project including responsibility for coordination, data analysis, and independent monitoring.</p>
<p>Involvement of pertinent patient organisation (if available) or patient representatives in the protocol design.</p>
<p>Plan to make raw anonymised datasets available to the scientific community upon request.</p>

* In essence this aims to ensure that the study hypothesis addresses an open clinical question, meaning a question never addressed or convincingly answered before, which only justifies the involvement (and possibly the randomisation) of patients in the study. This mainly applies to comparative phase III or IV trials.

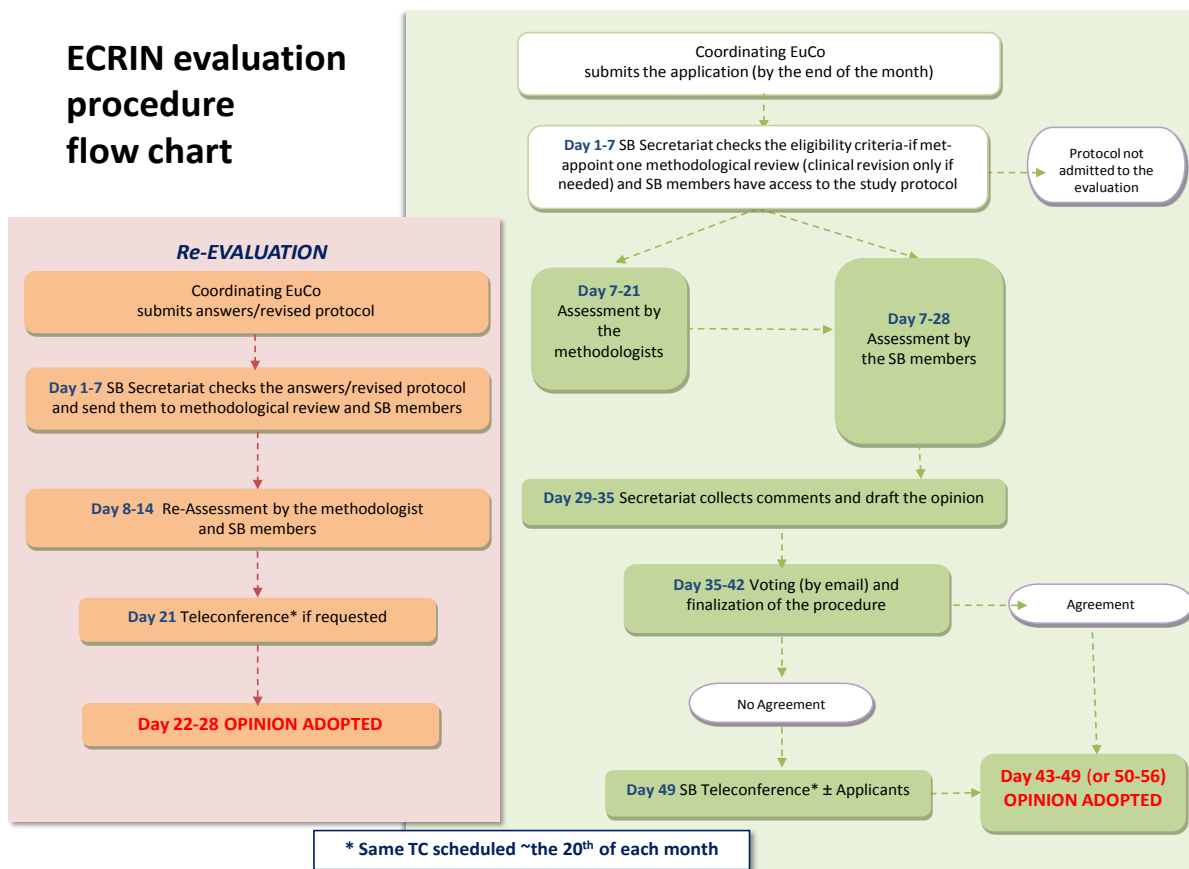
HOW TO SUBMIT YOUR PROTOCOL

Please, contact the EuCo in your country to submit the study protocol and all the relevant documents to the ECRIN Scientific Board Secretariat. The EuCo will take care of the submission. The protocol can be submitted any time before the end of each month.

HOW ECRIN EVALUATES YOUR PROTOCOL

A) Scientific Evaluation

The evaluation procedure by the ECRIN Scientific Board takes a maximum of 8 weeks (see flow chart). It starts the 1st Monday of each month (day 1 of the procedure)



SB: Scientific Board; NC: Network Committee; EuCo: European Correspondent

The ECRIN Scientific board checks the eligibility criteria (**Day 1-7**). If the criteria are not met, you will be informed of the grounds for non-acceptance through the EuCo. If they are met your project will be assessed by the members of the ECRIN Scientific Board and by one methodological expert selected from a panel of ECRIN methodologists (Day 8-28) and a draft opinion will be prepared (**Day 29-35**).

Then the Scientific Board members vote the opinion (**Day 36-49**):

1. If the qualified majority (two third of the voting members) agrees, the opinion is adopted and forwarded (including the reasons of the minority) to the ECRIN Management Office and the EuCo in your country.
2. If an agreement cannot be reached, the ECRIN Scientific Board discusses the open issues further in a teleconference, in which you (the applicant) might be invited. This teleconference is scheduled on the 20th of each month (or the next working day). In this teleconference the ECRIN Scientific Board adopts an opinion by absolute majority of the voting members. Thereafter, the procedure follows the steps described in section 1.

B) Logistical Evaluation

In parallel to the ECRIN Scientific Board assessment, the network of EuCos evaluates the logistical feasibility of the ECRIN support to the trial implementation in each country, including the estimation of the costs of requested services

OUTCOME

On the basis of the opinion of the ECRIN Scientific Board, the logistical assessment and, if requested the opinion of the Network Committee, the ECRIN General Director makes the final decision on the accessibility to ECRIN services.

The ECRIN Management Office informs you about the outcome of the evaluation.

RE-EVALUATION

If the outcome of the evaluation is negative because of scientific reasons, you can access the re-evaluation procedure, which lasts four weeks (see flow chart). Please, send the EuCo in your country a revised protocol taking into consideration the suggestions of the Board and/or a letter rebutting the points raised by the ECRIN Scientific Board which you disagree with.