



ECCRN Clinical Trials Group

Mission

To foster European collaboration in collaborative investigator-driven clinically oriented research to improve the outcome of critically ill patients

Goals

To promote investigator-initiated intensive care research in a number of ways
This includes establishing networks of investigators and research teams, providing forums for discussion of research projects, development and implementation of clinical trials and programs of study. It should also offer opportunities for education and collegial support for emerging investigators and fostering communication among the ICU research community.

Spirit and intent

Investigators commit to collaborate for the advance of science. Self promotion should be discouraged. The intellectual property of the data remains under the responsibility of the ECCRN TG.

1/ General principles

Any ESICM member proposes to the Network Board a research proposal. After approval by the Network Board, the study will be discussed at the ECCRN TG meetings. If TG decides that a study is worth to be conducted, a steering committee for the study is constituted among the members of the network willing to participate into the trial, proposed by the PI and nominated by the Network Board. This steering committee includes at least one member of the Network Board and, if possible, one methodologist. The study is promoted by Network Board and PI to ESICM members (identified through ERIC registry)

The network belongs to ESICM, ESICM membership is mandatory to propose a study (PI).

2/ Network composition

The network is open to any ESICM member (full-members and in-training members). Registration to the network is mandatory (as well as filling out ERIC registry for the unit). All network members are voting members. Non ESICM members health care professionals are allowed to participate in network activities (meeting, studies) but are not allowed to present proposals and to vote.

The ECCRN TG is lead by a Board (named ECCRN TG Board), which will be responsible for elaborating the research projects. A Finance committee may provide, if needed, an independent evaluation of feasibility of the large-scale projects (and evaluation of adequacy of use of financial resources)

2.a/ ECCRN TG Board

Goals: to discuss research proposals

Composition: 10 members, including 5 ESICM representatives and 5 members elected from the ECCRN TG. The Chairman of the Research Committee will chair the ECCRN TG board. Excepted for the ESICM representatives, all other members should be elected (this would not be feasible initially; the first committee will be under invitation).

For the first committee, we would propose a mixed committee of 5 ESICM representatives (the chairman of ESICM Research Committee, the chair of Division of Scientific Affairs, the chair of the Ethic section plus 2 active members of the research committee) and 4-5 established investigators for starting (short time). One methodologist should be included in the ECCRN TG board.

Pediatricians would be welcome. First replacement of elected members after 3 years and then replacement of one third of the committee every 2 years. Replacement by elections inside the network, with validation by Council after approval by ESICM Ex Com. Members of the ECCRN TG board, leaving the committee at the end of their mandate, continue their duties in the studies in which they were nominated up to the termination of the study.

This committee should discuss scientific issues but also should pay attention to political issues (potential conflicts of interest with other societies-ongoing studies, within ESICM,...).

2.b/ Finance Committee

Independently raised by ESICM treasurer and Research Committee chairman. This committee is composed of several well known investigators, accustomed to drive large RCT (investigator or industry driven), some members with political responsibilities in ESICM, treasurer and chair of Research Committee. In addition, one or two experts are designated for a specific study (researchers in the field who do not have conflict of interest with the specific project / investigator). With exception of Treasurer and Chairman of Research Committee, none of these members should also be member of the ECCRN TG Board. This committee should only be raised when large scale RCT are proposed, especially when a large financial contribution of ESICM is expected. The ECCRN TG decides whether or not the Finance Committee should be consulted.

3/ ECCRN Trial Group meetings

Meeting 2(-3) times a year (one to two days meeting, depending on the number of projects to discuss). Meetings should occur at locations allowing conviviality at reasonable costs. All participants pay for their own travel expenses (travel, lodging and food). ESICM is responsible for covering the costs of the hosting facility. During that meeting, the PI presents the study proposal. The study proposal should be sent in advance to the ECCRN TG Board (for agenda), one to two members are selected for in depth evaluation of the proposal (literature review, evaluation of methods, relevance of study endpoints, plausibility of study expected effects and power analysis). At meeting, the proposal is discussed in depth by all members, after presentation of critical analysis by 2 pre-selected members (and answer to relevant questions by PI). Decision at meeting (agreement / rejection / postponed and need for further information). During this meeting, educational activities (centered on methodological aspects) will also be implemented.

The meeting is open to any health care professional involved in research (including CRA).

4/ Network rules

4.a/ Responsibilities of PI (member proposing the project) and of ECCRN TG Board

Project presented to ECCRN TG by PI, after preliminary approval by ECCRN TG Board. PI looks for grant and comes back to ECCRN TG Board for final approval. Grants and authorship (see table for details).

PI: responsible for grant – submission for ethical agreement –acceptance or refusal of centers willing to participate into the study (any refusal of a center should be justified to ECCRN TG Board). PI analyses data with statistician (DSMB), presentation to steering committee. Presentation of the advancements of the trial and final data at ECCRN TG meetings, after approval of the agenda by ECCRN TG Board. Name of ECCRN TG should be mentioned in grants / manuscript, after agreement of network. A letter of support will be provided by the chairman of ECCRN TG for each grant or manuscript submission.

4.b/ ECCRN TG Board

Address book for identification of recruiting centers (ERIC registry + personal contacts) – discussions on quality and feasibility of project, nomination of DSMB. Participation in writing committee and data analysis (through designated members), approval of grant proposal and final manuscript (both before submission).

The chair of the ECCRN TG Board liaise with other important networks to prevent duplicate studies.

4.c/ Access to network facilities

Once the project is accepted by the group, it will have access to all facilities of the network. Groups of investigators not desiring to open their study to other collaborators but desiring some support may and studies for which the network consider that involvement of the network is not a priority

may still benefit from ECCRN endorsement/support. Electronic CRF and randomization facilities should be provided for ECCRN TG studies.

4.d/ Discussion of new studies (general lines)

Based on the following principle/sequence (for non randomized trials, the same sequence may be applied but point 4 may be deleted):

1-Discussion of the literature

2-Meta-analysis (when studies are available) => publish it, if not already done

3-Observational study performed to evaluate the incidence of the problem locally, evaluate mortality, calculate sample size (and publish it!)

4-Small run-in RCT: using the same inclusion/exclusion criteria as the main study. Mostly for evaluation of feasibility, as reported above (and publish it) The analysis focus on feasibility-technical problems- recruitment but the primary endpoint is not evaluated in most cases.

If a small run in study is not feasible, it is proposed that the e-CRF and data acquisition procedures are tested for each study in "dummy" patient (patients not included in the study, prior to launching the study). This may help to identify problems in data acquisition and recording.

This procedure may be extended to other parts of the study (randomization – supply of material....). This should be done in a few selected centers (on a voluntary basis).

5-Large RCT: To prevent centers to stop recruitment and thus demotivation, sometimes the small run-in is incorporated in the large one, this may raise issues or registration of the trial (they usually amend it) but there is no need for adjustment of statistical analysis as long as primary endpoint has not been evaluated).

At each step the project is presented by PI, evaluated in advance by one/two reviewers from the board and discussed in meeting. General agreement is required before going further. Points 1-2 and sometimes 3 can be merged. At any point the project can be stopped (lack of interest, questionable feasibility or lack of funding).

Each project is submitted for acceptance to the members present at meeting. At the meeting the chairman always ask who may be interested to participate (include patients) and who may be interested in collaborate to design the study (steering committee). Small working groups are built at each step. When reaching step 5 (large RCT) then the study is open to other researchers through ERIC registry.

Each step of a project should include a time-line and financial description.

5/ Projects frame

Project steering committee

PI + members of the network actively contributing in the design of the project. Should be composed by at least 5 but no more than 10 persons.

Authorship rules

The PI, the ECCRN TG Board agree on authorship order (or at least rules) in advance. Each study should include the name of the network in authors name (For the ECCRN Trial Group). Including all members of the project steering committee is not mandatory, as often some are less active than others and should therefore not appear in authorship. Collaborators including the highest number of patients and contributors active at each step of the project (design-inclusion-analysis-writing) should be prioritized. The statistician should not be included in authors name, unless agreed otherwise.

DSMB

Proposed by PI and need to be approved by board.

Financial committee (for large studies, when applies, on request of ECCRN TG Board)

Analyzes the feasibility of the study and evaluates costs as proposed in budget plan (ensure that no excess occur as well as most costs seems to be included in budget proposal). Check at each step that project budget is fitting with expectations.

6/ Data analysis

6.1/ eCRF and randomization facility

Centralized and provided by ESICM

The eCRF is tested either in run-in study or in "dummy" study. If a small run in study is not feasible, it is proposed that the eCRF and data acquisition procedures are tested for each study in "dummy" patient (patients not included in the study, prior to launching the study). This may help to identify problems in data acquisition and recording.

This procedure may be extended to other parts of the study (randomization – supply of material....). This should be done in a few selected centers (on a voluntary basis).

Generation of enrollment list (+site)-country): available online (for the steering committee)

Generation of SAE on line, made available for DSMB. Automatic warning every X events to be defined for each study.

6.2/ Statistician

Each study should have its own statistician. It can be nominated by the PI or the ECCRN TG. If collaboration is acquired, this may limit the costs. Discussion in the ECCRN TG with study statistician and methodologists to ensure that the analytic plan is appropriate as well as sample size calculation.

The statistician involved in DSMB and final data analysis is present at investigator meeting (physically or through webinar)

7/ Data quality control

By CRA, whenever available, or by National Coordinators. Ten percent of the CRF need to be checked. This check should focus on ensuring that entry criteria (inclusion and exclusion criteria) were respected and that the primary outcome measurement is correctly reported. Other detailed information need not to be checked.

CRA may be hired, but it would depend on funding. Seems feasible later, but not actually.

Table 1: Meetings Organization

Visitors at ECCRN TG Meetings

- Are sponsored by Chair, Board or any member
- Fund themselves
- Have clear objectives (e.g., starting TG, participating in ECCRN TG study, not just seeking enrolment in their own study)
- Are invited by Chair in writing (including confidentiality / intellectual property clause)
- Are introduced to ECCRN TG (background, objectives)
- Address the ECCRN TG at the end of the meeting (observations, plans for future collaboration)
- Are limited to 1-2 visitors / meeting

Presentation Guidelines

- New Studies

- Brief background
- Question/Hypothesis
- Objective(s)
- Design
- Plans (implementation, timelines etc)
- Questions for the ECCRN TG?

- Ongoing Studies

- Brief review of background, question, hypothesis, objective(s), design
- Update

- Issues raised by group at last meeting
- Work done since last meeting
- Milestones
- Problems
- Solutions
- Plans
- Questions for the ECCRN TG?

Responsibilities of PIs to the ECCRN TG

- Pre-circulate documents in advance
- Follow presentation guides
- Explain responses to feedback
- Be clear on collaborator commitments
- Provide detailed study update
- Share challenges as well as successes
- Attend each meeting or send representative
- Develop & commit to (revised) timelines
- Ensure study completion

Responsibilities of the ECCRN TG to Each Study

- Read pre-circulated documents in advance
- Provide constructive feedback on rigor, relevance, ethics, feasibility & fundability
- Consider mentorship & partnership
- Problem solve during ongoing trials
- Share tips, study aids & other documents
- Ensure to study completion
- Help to interpret study results
- Review grants & manuscripts within 2 weeks

Responsibilities of PIs to the Site Investigators

- Provide all necessary study documents
- Provide initial training & ongoing feedback
- Communicate study progress & set-backs
- Advise on local feasibility issues
- Seek advice on study issues
- Follow through on commitments
- Develop & commit to (revised) timelines
- Publish scientific progress
- Ensure study completion

Responsibilities of Site Investigators to Each Study

- Understand collaborator commitments
- Problem solve local feasibility issues
- Communicate study progress & set-backs
- Advocate locally for the study
- Follow through on commitments
- Suggest improvements
- Collaborate on scientific progress reports
- Ensure study completion

Responsibilities of the Chair to PIs & Site Investigators

- Summarize ECCRN TG feedback
- Write support letters for ECCRN TG grants
- Advocate for each study across sites
- Help to problem solve
- Ensure the ECCRN TG honors commitments
- Ensure study completion
- Ensure publication
- Liaise with funding partners as necessary
- Liaise with other networks to prevent duplicate studies.

Table 2: ECCRN TG Authorship and grant rules

ECCRN TG authorship must be acknowledged in the grant proposal submitted for funding if all of the following criteria are fulfilled a) the protocol has been presented at a ECCRN TG meeting, b) support has been given to the project by the ECCRN TG membership at one of the meetings, c) explicit agreement regarding grant submission was obtained, and d) feedback on the grant itself was provided by the ECCRN TG Board. Without these 3 steps, investigators are requested not to make reference to the ECCRN TG in their proposal.

ECCRN TG authorship must be acknowledged in all manuscripts submitted for publication if in the opinion of the ECCRN TG Board and the investigators, substantial scientific support has been provided by the group at our meetings and between meetings. Without this agreement, investigators are requested not to make reference to the ECCRN TG in their manuscript.

Before ECCRN TG authorship is finalized, the ECCRN TG Board must review all manuscripts to be submitted to peer-review journals. To allow for (inevitable) last minute preparation, abstracts of ECCRN TG projects may be submitted to scientific meetings without a priori review by the Board.

Figure 1: ECCRN studies

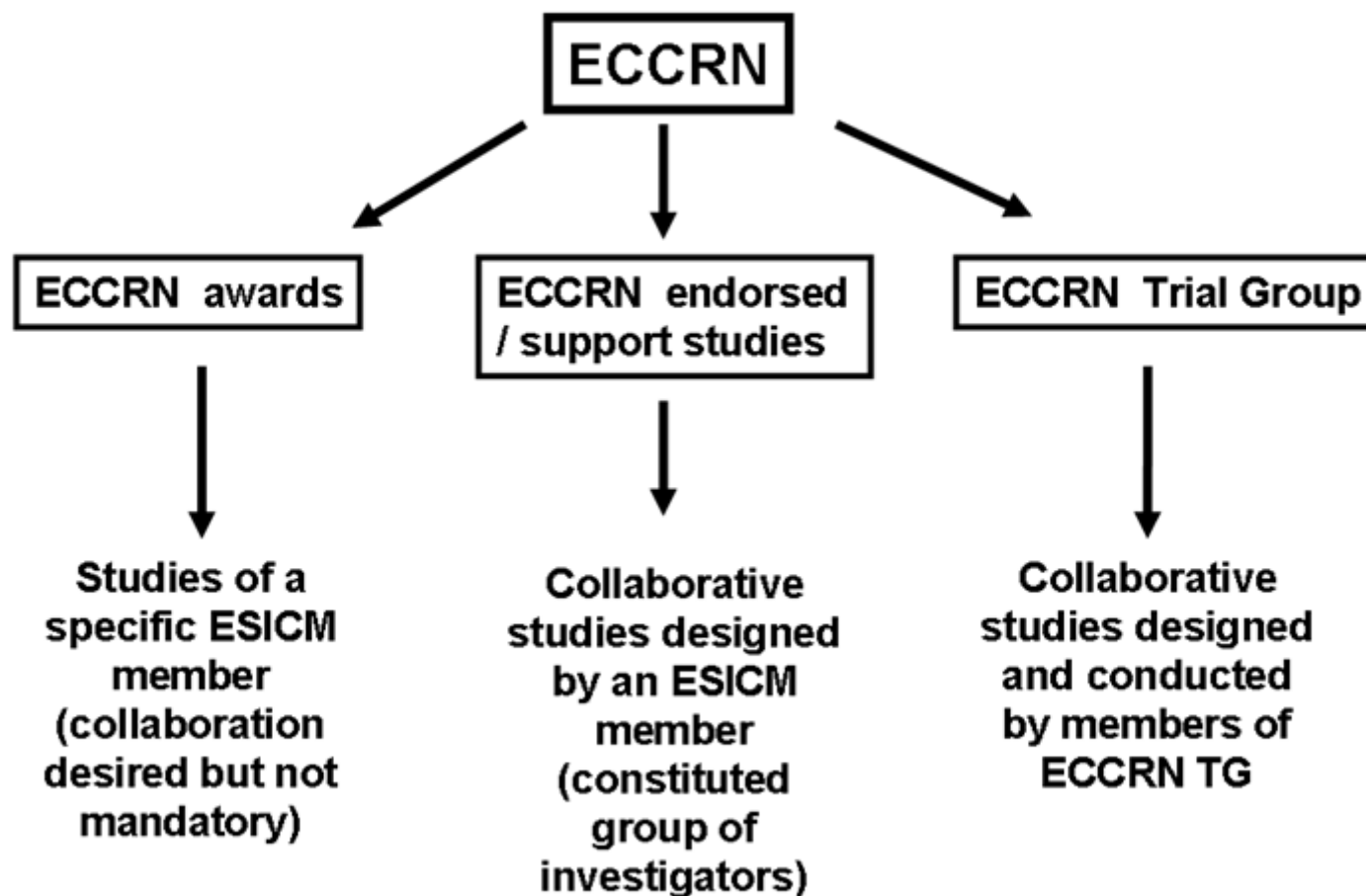


Figure 2: ECCRN Trials Group Board

