**Rules of Procedure of the Clinical Research Committee**

**Princess Máxima Center for Pediatric Oncology**

1. **Definitions**
	1. Clinical Research Committee: the committee installed by the Princess Máxima Center responsible for the scientific review and approval of all proposals for clinical research studies (including LATER) and/or clinical trials to be implemented by the Princess Máxima Center (either in its role as site, national coordinator or sponsor of the study/trial).
	2. Clinical research: Clinical research contains any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes, or any research study that prospectively or retrospectively evaluates health outcomes within human participants or groups of humans, however excluding biobank and research data as defined in the “Rules of Procedure of the Biobank and Data Access Committee” of the Princess Máxima Center for Pediatric Oncology.
	3. Principal Investigator (PI): the person responsible for the structure and execution of the scientific research for which the Request for Review is made. The PI is the point of contact for the Clinical Research Committee in the context of the Request for Review.
	4. Independent Reviewing Committee: a designated independent Ethics Committee, and/or the competent authorities, who need to approve a scientific medical research protocol in the Netherlands.
	5. Scientific content: the scientific content is defined as a synopsis/protocol/research proposal discussing how the study fits into the Máxima strategy, the rationale and design (including background, hypothesis, objectives and endpoints), the eligibility criteria, the statistical aspects, ethical and risk/benefit aspects, any correlative studies, the set-up and feasibility, regulatory aspects (‘WMO-plichtigheid of genees-middelenstudie’) and the time-lines of a study/trial submitted for review. See e.g. the CCMO website for a template protocol with further explanation.
	6. Research proposal: A research proposal at minimum contains a (synopsis of) a proposed research protocol (scientific content as mentioned in 1.7), plus a budget proposal and an application form.
	7. Trial and Data Center: The Trial and Data Center (TDC) is the infrastructure available in the Máxima to support the implementation of Phase I-IV trials and studies in the Princess Máxima Center, with the exception of the ‘Later program’ of the Máxima. The implementation of the LATER studies is supported by the trial and data center of the LATER department. All studies are to be implemented through the TDC or LATER department after approval from the Clinical Research Committee.
2. **Composition of the Clinical Research Committee**
	1. The Board of Directors of the Princess Máxima Center appoints the members of the Clinical Research Committee.
	2. The Clinical Research Committee is composed as follows:
* The head of the TDC
* The head of the one of the 4 units (Hem-onc; solid, brain, LATER)
* A Statistician (one of the statisticians from the TDC)
* A clinical PI
* A preclinical PI (translational research)
* A data representative
* Someone with the patient perspective nominated by the ‘clienten raad’
	1. The Scientific Research Committee is supported by a Secretary, who is not a member of the committee.
	2. The head of the TDC is appointed as chairman.
	3. The members are appointed for a period of three years and may be reappointed but preferably no more than twice.
	4. Members who are not employed at the Princess Máxima Center sign a confidentiality statement before the start of the membership.
1. **Meeting and decision-making**
	1. The Clinical Research Committee itself determines the meeting frequency. In principle, the Clinical Research Committee meets at least once a month.
	2. Meetings can take place physically or by conference call.
	3. Members can also communicate their views through the Secretary by e-mail.
	4. If a member is not available a delegate attendant can participate in the meeting
	5. The Clinical Research Committee makes decisions on the basis of consensus.
	6. If no consensus is reached, the Clinical Research Committee will decide by means of a vote. Decisions are made by a majority of votes cast, in the course of which at least three members must be present at the meeting or must have made their views known in advance.
	7. If the Clinical Research Committee fails to arrive at a decision, the CMO and CSO of the Board of Directors of the Princess Máxima Center will decide.
	8. Before taking a final decision, the Clinical Research Committee may ask the PI for clarification in writing or ask the PI to present the research in a Committee meeting before a decision is made.
	9. In case of doubt whether a proposal should be reviewed by the Clinical Research Committee or the Biobank and Data Access Committee the chairs of the Committees will allocate the proposal to the right Committee.
2. **Tasks and powers**
	1. The Clinical Research Committee reviews and approves proposals for clinical research studies/trials to be implemented by the Princess Máxima Center for Pediatric Oncology.
	2. If only a synopsis is approved the PI should submit the full protocol for final approval.
	3. Approval from the Clinical Research Committee must be obtained prior to submission to other Independent Reviewing committees such as the ethics committee or competent authorities. These submissions will be taken care of by the Trial and Data Center/LATER data center.
	4. It is recommended not to submit to a grant funding body prior to approval by the Clinical Research Committee, to avoid a situation where funding is obtained but no approval from the Clinical Research Committee.
	5. When significant changes to the proposal are requested the PI will be asked to submit an updated version of the proposal before approval.
	6. Proposals that are rejected by the CRC will not be implemented in the Máxima; the PI will be provided with the arguments for rejection in writing.
	7. If a PI does not agree with the decision of the Clinical Research Committee, the PI can submit an appeal to reconsider the decision. In case of a second rejection, the PI can make an appeal to the CMO and CSO of the Board of Directors.
	8. The Clinical Research Committee keeps a research proposal registry of approved and rejected proposals and proposals under consideration. Proposals will be tagged with a Clinical research Committee unique number for administrative reasons. The registry will be published on the Intranet of the Princess Máxima Center (titles of final approvals only).
	9. The Clinical Research Committee will report on its activities by means of the annual scientific report.
3. **Procedure on the application of research**
	1. The Clinical Research Committee reviews research proposals according to the procedure as described in article 6 through 7.
	2. Research proposals are submitted to the Clinical Research Committee by the PI, using the digital application form intended for this purpose.
	3. External research proposals need to be submitted by an investigator from the Máxima for consideration
	4. The Clinical Research Committee assesses research proposals submitted at least one week before the meeting.
	5. When reviewing research proposals, the Clinical Research Committee may seek further internal or external advice, e.g. a statistician or medical ethicist (see also article 2.6).
	6. The Clinical Research Committee can ask the PI for further clarification or request the PI to adapt the research question or design, etc.
4. **Review criteria for research proposals**
	1. Requests for Review of clinical research at the Princess Maxima Center takes place by the means of a research proposal as defined in paragraph 1.6.
		1. The Clinical Research Committee considers a research proposal if the following criteria have been met:
5. The proposal fits within the mission statement of the Princess Máxima Center: ‘cure every child with cancer, and provide optimum quality of life’;
6. The proposal has sufficient priority in consideration of the Máxima research portfolio;
7. The research question has sufficient scientific value, and the proposed research methodology is sound;
8. The proposal does not interfere with (ongoing) research projects within the Princess Máxima Center or research projects part of international collaborations; for instance, by influencing the endpoints of ongoing studies in the same population;
9. The number of participants is feasible and supported by a statistical power analysis;
10. The proposed statistical analyses and endpoints are in line with the research question;
11. The budget attached to the research proposal is sufficient for the expected costs. Note that the Trial and Data Center may withhold implementing studies if the approved funding is not obtained;
12. There are no logistical barriers for the implementation of the study.
	1. In addition to art. 6.1, for an Internal Request for Review the protocol will be presented in synopsis format prior to establishing the full protocol; an External Request for Review (e.g. a pharma protocol submitted by an internal PI) may be discussed in final format with a full protocol.
	2. In addition to art. 6.1, the Clinical Research Committee only agrees with an External Request for Review from a commercial party, when clear agreements are made between the Princess Máxima Center and the requesting party about the distribution of revenue (in-) directly resulting from the research proposal. On the basis of these agreements, at least a reasonable amount of that revenue will flow back to the Princess Máxima Center for the purpose of financing new scientific research. These agreements are included in a Clinical Trial Agreement, which should be reviewed and approved by the Máxima legal office.
	3. Any substantial amendments on the approved research proposal that contains major changes in the study objectives or the conduct of the study need to be applied as a new request for review to the Clinical Research Committee.
13. **Decision on Request for Review**
	1. After discussing a research proposal at the meeting, the Clinical Research Committee will arrive at one of the following decisions:
14. approval of the research proposal,
15. rejection of the research proposal,
16. request for additional information,
17. seeking external advice.
	1. If the Clinical Research Committee requests the PI for additional information, it will place the research proposal on the agenda for the next meeting again after receiving the additional information.
	2. If the Clinical Research Committee seeks external advice, it will place the research proposal on the agenda for the next meeting again after receiving the advice. External advisors will be asked to sign a confidentiality statement with regard to the research proposal.
	3. The Secretary will send the PI the decisions on the research proposal in writing within a week after the Clinical Research Committee meeting.
	4. In all situations not provided for in these Rules of Procedure, the Clinical Research Committee shall make a decision.
18. **Costs for provisioning**
	1. No costs for a Request for Review will be charged to PI’s.

Date 23-05-2018

Signatures

Drs D. Monissen, CEO Prof. dr.R. Pieters, CMO Prof. dr. H. Clevers, CSO