| **Title:** | **Guideline for initiating a HOVON trial** | |
|---|---|---|
| Version: | 04 | |
| Effective date: | 01-JUNE-2016 | |
| *Author name* | *Signature* | *Date* |
| P. Westveer | | 04- May -2016 |
| *Approver name* | *Signature* | *Date* |
| Prof Dr J.J. Cornelissen | | 23 May 2016 |

The purpose of this guideline is to clarify for HOVON working group members and specifically Principal Investigators the steps to follow in order to initiate a new trial.

## Procedure for initiating a new HOVON trial.

1. An investigator submits a trial concept to the working group for discussion.

2. The working group appoints the Principal Investigator (PI) and co-investigators of the trial (see HOVON policy on “Investigator terminology” and “PI responsibilities and qualifications”), and a writing committee is formed.
   For a trial where HOVON is the co-sponsor, the HOVON Coordinating Investigator is appointed by the working group. This Coordinating Investigator has the same role as described for the PI in this guideline.

3. The working group discusses the trial design, consulting the trial statistician.

4. The PI writes a protocol synopsis. A protocol synopsis should outline the proposed patient population, treatment schedule, objectives, study design (e.g. phase III, randomized), specific tests and side studies and an estimate of the number of patients.
   For a trial where HOVON is the co-sponsor, the synopsis or (draft) protocol should be provided to the PI by the sponsor.

5. The PI and co-investigators discuss the proposed trial with other HOVON investigators, for example at the general HOVON protocol meeting (“HOVON protocollen dag”)

6. The PI informs the HOVON management bureau that a new trial is initiated, by sending an e-mail to the HOVON management bureau that includes the name of the trial and the contact details of the PI. The HOVON manager will contact the PI to draw up a trial budget.

7. The PI informs the HOVON Research Program Manager that a new trial is initiated, by sending an e-mail to the HOVON Research Program Manager that includes the name of the trial and the contact details of the PI. The Program Manager contacts the team managers at the HOVON Data Center (HDC). Within one week after the initial contact by the PI, the HDC team managers will appoint an “intake team” to the project, including a senior trial manager, who will contact the PI to arrange a project intake meeting.

8. Prior to the intake meeting, the PI will draw up a first version of the Project Proposal Form for the trial.
   The project proposal is an outline of the plan how the trial will be executed. It includes proposed time lines for important milestones such as submission to the Ethics Committee and first patient included. The purpose of the project proposal is to get an understanding of how much work and time the trial will take from start to end. It enables the HDC to make an estimate of the feasibility in terms of available capacity at the HDC, and it enables the HOVON management bureau to verify the planned activities with the trial budget and trial agreements.
   The template for the form is provided to the PI by the Program Manager. If necessary, the PI can ask the Program Manager for advice how to complete the form.

9. The HDC intake team discusses the operational aspects of the trial with the PI and the HOVON Program Manager. The aim is to gain a better understanding of the activities needed to successfully prepare and execute the trial, and to identify any issues that need to be addressed before trial preparation can start.
   The HOVON Program Manager assists the PI in following up any required actions resulting from the meeting. The PI updates the project proposal accordingly and sends the updated form to the Program Manager.

10. The HOVON Research Program Manager sends a copy of the project proposal to the HOVON management bureau and to the HDC team managers. The HOVON Research Program Manager contacts the HDC team managers for a check on the feasibility of the

proposed trial in terms of available capacity, and ensures that the PI updates the project proposal accordingly, if applicable.

11. The PI will draw up a first version of a trial specific document that specifies which tasks and responsibilities are delegated by HOVON to another party, using HOVON policy document "Template for recording delegation of HOVON sponsor responsibilities"
    This is only applicable if HOVON is the sponsor of the trial.
    The template for the form is provided to the PI by the Program Manager. If necessary, the PI can ask the Program Manager for advice how to complete the form.

12. The PI will draw up a first version of the quality risk management plan (QRMP) for the trial. Quality management activities following from the QRMP are incorporated into the trial documents, project planning and trial budget.
    See HOVON policy "Risk Based Quality Management of Clinical Trials" and "HOVON Template for Quality Risk Management Plan"
    This is only applicable if HOVON is the sponsor of the trial.
    The template for the form is provided to the PI by the Program Manager. If necessary, the PI can ask the Program Manager for advice how to complete the form.

13. After approval of the project proposal and the trial budget by the PI, the HOVON Program Manager on behalf of the PI submits the trial to the HOVON executive board for approval. The protocol synopsis, the preliminary budget, the draft QRMP and the draft sponsor delegation log should be sent as an attachment with the project proposal.
    The QRMP and sponsor delegation log are only applicable if HOVON is the sponsor of the trial.

14. The HOVON executive board decides if the trial is eligible for further development. If approved by the executive board, the HOVON Research Program Manager assigns the HOVON trial number.

15. After assignment of the HOVON trial number, the HOVON Research Program Manager inform the HDC team managers who appoint a trial team. The project is transferred from the intake team to the trial team. The Program Manager sends the final version of the Project Proposal Form to the HDC trial manager.

16. The PI, co-investigators and writing committee compose a first version of the full protocol and the patient information and informed consent form and submit these to the HDC trial manager.
    The PI should use the HOVON templates for protocol and ICF. All applicable sections of the templates have to be completed.
    For a trial where HOVON is the co-sponsor, the protocol should be provided to the PI by the sponsor.

    Please note that discussion regarding critical design issues (such as treatment schedule or endpoints) should be concluded at this stage of preparation. Major revisions of the design of the trial or operational aspects (such as number of sites, participating countries) after this point are possible but will necessitate an adaptation of the project proposal regarding the proposed time lines or required resources, and may require a revised trial budget and renewed approval by the HOVON executive board.
    The PI should consult the HOVON Research Program Manager and the HOVON management bureau to determine if a change is to be considered substantial and requires renewed approval.

17. The HDC trial team draws up an overview of the trial activities with timelines. This overview is based on the project proposal. It includes a detailed planning of all stages of the trial,

from preparation for Ethics Committee submission until the final analysis.
This overview will be the point of reference to check if the trial activities are still on track or if adjustments need to be made.

18. The HDC trial manager organizes a “kick off meeting” with the trial team and the PI, where they discuss the proposed trial planning, mutual expectations for their cooperation as a team, lines of communication and relevant details about the study design (to be regarded as study specific training of the trial team by the PI)

19. The HOVON management bureau draws up contracts with involved parties (such as central labs, study groups, companies) Input is provided by the PI, the HOVON Program Manager and the HDC trial team.

20. The PI ensures the composition of a first version of supporting documents for the protocol, such as the lab manual, and submit these to the HDC.

21. The PI completes the final version of the QRMP.
This is only applicable if HOVON is the sponsor of the trial.
The HDC trial team will provide input and assists the PI.

22. The trial documents are submitted to the HOVON “protocol uitvoerbaarheids commissie” (PUC) for review. This includes the final version of the protocol, ICF and CRF, and, if applicable, the QRMP. The reimbursement form for the trial is also submitted to the PUC.

23. The PI will complete the final version of the trial specific document that specifies which tasks and responsibilities are delegated by HOVON to another party, using HOVON policy document “Template for recording delegation of HOVON sponsor responsibilities”, before the trial is opened for inclusion of patients.
This is only applicable if HOVON is the sponsor of the trial.
The HDC trial team will provide input and assists the PI.

24. The PI, with the assistance of the HDC trial manager, will forward the quality risk management plan (QRMP) to the HOVON executive board for approval.
This is only applicable if HOVON is the sponsor of the trial.

25. The HDC trial team executes the activities for the trial according to the overview.
The trial manager will keep the PI informed of the progress of the trial. Any changes to the agreed planning and time lines will first be discussed with the PI.

26. The PI executes the PI responsibilities.
The PI is the project leader for HOVON. The PI will take all decisions regarding medical and scientific aspects and will collaborate with the trial manager to solve any issues with the progress of the trial.

27. The HOVON management bureau executes the HOVON management responsibilities.
This includes all legal and financial aspects of the trial.