HNN 3.0
HEALTH-NCP-NET

Health NCP Net

Information on Clinical Studies

Annotated Template

www.healthncp.net

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DISCLAIMER

The comments of the Health NCPs are just recommendations and suggestions. Please always follow all instructions of the European Commission.

For the application, use only the currently valid template from the European Commission issued application form (template). For a successful application, it is advisable to read the entire application template carefully. The given structure should be followed exactly.

The basis for this annotated version of the application template is the document "Information on clinical studies (HE)", published by the European Commission, version 4.2 of April, 1st 2023.

HNN3.0
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Health-NCP-Net (HNN3.0) is a European project of the Horizon Europe programme funded by the European Commission. The network facilitates trans-national cooperation between National Contact Points (NCPs) for Cluster 1 "Health" (CL1) within the pillar "Global Challenges and European Industrial Competitiveness". The aim is to align and enhance the services that NCPs provide applicants of European funding for Health research across Europe and to optimize the support for applicants. Our services are tailormade to the needs of NCPs and applicants and are free of charge. Find out here what support we can offer.

Recommendation for applicants

INFORMATION ON CLINICAL STUDIES

(For calls that involve clinical studies[1], project participants must add this document to the application and upload it as a separate annex to the proposal part B in the Submission System.)

This template **has to be used** for any clinical studies addressing scientific questions related to the understanding, prevention, diagnosis, monitoring or treatment of a disease, mental illness, or physical condition. These include:

- Clinical trials,
- Clinical studies,
- Investigations,
- Cohorts,
- Systematic prospective collection and analysis of health data,
- Retrospective analysis of health data obtained from individual patients or healthy persons.

! Please be advised that almost every time, when you are planning to collect human data or biological samples, you need to fill out this template.

Here are some examples for which you need to fill out this template:

- Phase I trial of a vaccination,
- Clinical Investigation of a medical device,
- New analysis of blood samples of a closed trial,
- Survey on well-being,
- Retrospective analysis of patient data.

Clinical study costs can be declared as:

- Actual costs,
- Subcontracting costs, or
- Costs for internally invoiced goods and services.

Clinical studies have a number of methodological, operational and regulatory specificities. Information on these issues is crucial for evaluators to assess the scientific quality and operational feasibility of the proposal. The following set of section headings guide applicants to provide essential information on clinical studies in a standardised format.

[1] Clinical study covers clinical studies/trials/investigations/cohorts and means, for the purpose of this document, any systematic prospective or retrospective collection and analysis of health data obtained from individual patients or healthy persons in order to address scientific questions related to the understanding, prevention, diagnosis, monitoring or treatment of a disease, mental illness, or physical condition. It includes but it is not limited to clinical studies as defined by Regulation 536/2014 (on medicinal products), clinical investigation and clinical evaluation as defined by Regulation 2017/745 (on medical devices), performance study and performance evaluation as defined by Regulation 2017/746 (on in vitro diagnostic medical devices).

Applicability:

For **HE collaborative research and innovation:**

Single-stage and stage-2 proposals: The use of this template is mandatory for single-stage or stage-2 proposals, if the application includes a clinical study[Fehler! Textmarke nicht definiert.] AND it concerns a topic including clinical studies[2].

For these topics, you will have the possibility to upload the completed template as a separate part of your application in the submission system.

Stage-1 proposals: In the limited frame of a stage-1 proposal, not all methodological details of clinical studies can be fully elaborated. Depending on the characteristics of the study, however, key aspects of a clinical study have to be convincingly addressed already at stage 1. This template cannot be uploaded as a separate document at stage 1, but relevant aspects of this information should be integrated in part B of the stage 1 proposal template.

For **HE IHI Joint Undertaking and Global Health-EDCTP3 Joint Undertaking:**

Single-stage and **stage-2** proposals: The use of this template is mandatory for all clinical studies. You can upload the completed template as a separate part of your application in the submission system.

Stage-1 proposals: see under Horizon Europe collaborative research and innovation

For each[3] clinical study performed within the scope of the proposal, essential information according to the structure below should be provided and compiled into one single document per proposal. Each section must be addressed briefly and concisely. In case one or more sections do not apply to a particular study, please provide a short explanation.

When the requested information is currently not available (e.g. a clinical study is planned for a later stage of the project and it will be based on or influenced by future results of other studies), the source and the collection of the relevant input should be described.

Information provided in this template does not need to be repeated elsewhere in the proposal but can be referred to.

There are no page limitations for this template, but explanations should be as concise as possible.

You can refer to this template in Part B, if it concerns the planned (clinical) study or analysis, and explain it here in more detail, because there are no page limitations for this template compared to Part B. But, please, be as concise as possible.

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[2] For proposals containing clinical studies submitted to topics *not* foreseeing clinical studies, you may use the section headings of this template as an orientation and provide the related information in sections B.1 and B.3 of the proposal, if the submission system does not provide the possibility to upload the template.

[3] If the proposal contains more than one clinical study, each study should be described separately, e.g. study A, study B, etc.

Information outside the scope of this template will not be considered in the proposal evaluation. No other chapters or annexes (e.g. complete study protocols) can be added to this template. Section headings should not be changed.

> **!** Do NOT add any other chapters or change the existing chapter.
>
> **ALL chapters need to be filled out**, even if they do not fit your specific clinical study. If this is the case, you can mention that this chapter is not applicable for your study, but don´t leave any subchapter unanswered and do not delete it.

Ethics considerations have to be addressed in the appropriate section of the proposal. Similarly, risks and mitigation measures have to be addressed in the respective section of the proposal (part B.3.1 and table 3.1e) and not in this template!

> Do not forget to include the ethical aspects of your clinical study in the **Ethics Self-Assessment** section in Part A of your proposal. Among other possible ethical issues, a planned clinical study or analysis of human data will always require the Ethics Self-Assessment section to be completed.
>
> Additionally, do not forget to add the **risk and mitigation measures** concerning your clinical study in Part B 3.1. and table 3.1e.

The following three **mandatory deliverables** apply to each clinical study included in the proposal:

1. Study initiation package (before enrolment of the first study participant) including:

   - Registration number of the clinical study in a registry meeting WHO Registry criteria[4] (see also references given in subheading 1.1 of this template)

   - Final version of study protocol, as approved by the regulator(s) / ethics committee(s)
   - Regulatory and ethics (if applicable, institutional) approvals required for the enrolment of the first study participant. (In case of multicentre clinical studies, submission of approvals for the first clinical site is sufficient.)

2. Midterm recruitment report

   This report is due when 50% of the study population is recruited. The report shall include an overview of the number of recruited participants by clinical sites, any problems in recruitment and, if applicable, a detailed description of implemented and planned measures to compensate for any incurred delays.

3. Report on the status of posting results

   Irrespective of the successful completion of the clinical study, summary results must be posted in the applicable registry/ies (where the study was registered) even if the timing of the posting of results falls outside of the grant period. The report is to be scheduled for the time when the results are expected to be posted or for the last months of the project, whichever comes earlier.

[4] https://www.who.int/clinical-trials-registry-platform/network/registry-criteria

Please include the **three deliverables** (study initiation package, midterm recruitment report, report on the status of posting results) in Part B 3.1. In case your study is not a “classical” clinical trial, please try to think what would be appropriate for your clinical study.

Here is an example for a survey on well-being, which *does not need to be registered anywhere:*

1. *Study initiation package:*
    a. *The survey is prepared and finalized; the ethics committee has agreed to it.*
    b. *The target groups of the survey are defined, including (but not limited to): the amount of people, sex, gender, and countries.*
    c. *Interviewers are trained and ready to start and timelines are defined.*
2. *Midterm recruitment report:*
    a. *Half of the people were questioned/have completed the survey.*
3. *Report on the status of posting results:*
    a. *Report on performed survey including: number, sex, gender, countries.*

1 Description of the clinical study

1.1 Title, acronym, unique identifier (e.g. EudraCT Number[5], or identifier from ISCRTN[6], ClinicalTrials.gov[7] if available) of the clinical study

[insert text]

In case you have a **unique identifier**, please be sure to provide it together with the **study title and acronym**, which can be different from the proposal acronym.

However, in case there is no unique identifier available at this stage or there is no identifier, if the project is not a "classical" clinical trial, but rather a survey or data analysis, please explain that it is not currently, or not applicable for your study.

1.2 Study rationale

Please clearly outline the clinical study methodology and justify its need. Be sure to demonstrate the need for the clinical study as well as provide a thorough and critical review of the currently available knowledge, linked to the scientific questions of the study or investigation. You should ensure that there is congruence between the study rationale and your Horizon Europe proposal methodology.

Please provide the overall rationale for conducting the proposed study.

Explain why the clinical study is needed to answer the scientific questions addressed.

[insert text]

1.2.1 Extent and evaluation of current knowledge directly linked to the scientific question(s) to be answered by the clinical study

Briefly outline the current knowledge and state-of-the-art of the questions that you wish to answer with the clinical study. You should demonstrate the credibility of your study by providing other relevant clinical data such as surgery reports, social media, or data on outcomes reported by patients to support your study.

[insert text]

1.2.1.1 Outcomes (efficacy, safety) of completed and number of ongoing clinical studies utilising the same intervention in the same indication (including review of public registers)

Describe whether the current knowledge is based on previous clinical studies and what the outcomes of the studies were.

[insert text]

[5] https://www.clinicaltrialsregister.eu/
[6] https://www.isrctn.com/
[7] https://clinicaltrials.gov/

1.2.1.2 Level of evidence related to the mechanism of action of the intervention in the planned clinical study population

Evidence should be presented related to the intervention that you will be using. Describe the current understanding of the mechanism to support the study rationale.

1.3 Objective(s) of the clinical study

Please differentiate between primary and secondary objective(s)

Please describe the primary and secondary endpoints of your clinical study.

[insert text]

1.4 Characteristics of the study population (size, age group, sex distribution, inclusion and exclusion criteria; all items with justification!)

Provide information on all the characteristics of the study population and justify each of the attributes.

[insert text]

1.4.1 Details on sample size and power calculation

It is expected that clear details will be provided on the calculation of the study sample size and the power of the study.

[insert text]

1.5 Design of the clinical study (controlled / uncontrolled; randomised; open / blinded; parallel group / cross over / other, including innovative trial designs e.g. for personalised medicine, small study populations, or adaptive platform trials; please justify the appropriateness of the selected design)

Details should be provided regarding the design of the clinical study. It should also be made clear why the chosen study design is appropriate. The study design must correspond to the scientific questions and the expected impact of the study results.

[insert text]

1.6 Type of intervention (medicinal product / advanced therapy medicinal product / medical device / in vitro diagnostic medical device / surgical or other invasive procedure / other medical intervention, including, e.g., counselling)

Clearly state the type of intervention. It determines the regulatory and ethical frameworks.

[insert text]

1.7 Description and timing of study procedures

Please provide an overview, preferably in a tabular format, about the schedule of study procedures. Please give a simple statement on how long individual patients or healthy volunteers participate in the clinical study.

Present information in a table and provide clear details on how long patients or healthy individuals will stay in the clinical study.

In a “classical” clinical trial this overview is given in the study protocol in terms of “visits”.

[insert text]

2 Preparedness status

Describe clearly how far the planning of the study has progressed, i.e. how possible it is that you can start the study as planned if the project is funded. If you plan to start the study later in the project, describe when you will have documentation ready to apply for regulatory and ethical approval. It is very likely that during this stage you may not have everything prepared yet, which is not a problem.

2.1 Development of the clinical study protocol

Please describe how the below aspects have been or will be addressed in developing the clinical study protocol (if applicable):

2.1.1 Scientific advice from regulatory and health technology assessment bodies

Here you should outline whether you have sought advice from relevant regulatory and health assessment bodies. *Has there been any contact already? Have any documents been submitted yet? Were there problems at an earlier stage of the study? Has a similar study or questionnaire been approved recently by one of the consortium members?*

[insert text]

2.1.2 Clinical efficacy, safety, and methodological guidelines (including guidelines on statistics)

You should describe which clinical efficacy, safety, and methodological guidelines you have included in the planning of your (clinical) study. *For example*, ICH E2A-E2F, ICH E6, ICH E9. You should consider how your guidelines have been influenced by factors such as the range of diverse organizational models, or participatory co-design.

[insert text]

2.1.3 Involvement of citizens / patients, carers in drawing up the clinical study protocol

A clear overview should be provided of the key-stakeholders that you have involved when developing your clinical study protocol. *For example*, you should describe whether you have consulted with the users of the technology, the patients, specialist physicians or carers that you are targeting.

[insert text]

2.2 Regulatory intelligence to ensure timely regulatory approval and ethics clearance of the clinical study in all jurisdictions where its implementation is planned

You should demonstrate that you have the expertise in your consortium and the knowledge about regulatory expertise for your planned clinical study.

You should identify the legal framework which the clinical study falls in, and the legal obligations that have to be complied in the country(s) where the study will run. You should demonstrate that your consortium has the proper expertise and knowledge to deal with the any regulatory issues identified as being related to the planned clinical study.

Please provide information on the following regulatory and ethics aspects:

2.2.1 How the consortium will ensure access to regulatory expertise necessary to get advice on, and management of, regulatory affairs activities in all concerned jurisdictions?

You should outline whether you have consulted experts from these areas to ensure local law compliance. This is vital to obtain timely approval to start the study.

[insert text]

2.2.2 How the consortium will ensure access to ethics expertise necessary to get advice on current proceedings and documentation requirements of all concerned ethics committees?

Demonstrate how you will ensure continuous access to expertise which is particularly relevant for periods of changing regulation. Depending on the study, you may consider to appoint an ethics advisor for the duration of the project or include an ethics advisor in a Steering Bord.

[insert text]

2.3 How the scientific and operational governance of the clinical study will be ensured?

Within this section you should provide details of the sponsor of the study, the role of the governance boards, and their composition. You should highlight the strengths of your governance system, and the composition of experts' board/panel.

2.3.1 Please give details about the sponsor(s) (name, type of entity, seat or country of residence).

[insert text]

2.3.2 Please describe the composition, the role and the functioning of the planned board(s), governing bodies.

[insert text]

3 Operational feasibility

3.1 Please describe how the availability of the intervention(s) (including comparators) is secured throughout the entire implementation phase (give details on manufacturing, packaging / labelling operations, storage, logistical, import/export issues, etc.)

Describe how the availability of the intervention(s), i.e. drugs, medicinal products, and specially trained staff are secured. *For example*: *Does your intervention need a specific refrigerated transport? Do you include a temperature logger, which will be checked, before releasing the investigational product (IP)? Where is it stored and labeled?*

! In case different countries are involved in your clinical study, please be advised that there are country-specific labelling requirements for Investigational Product (IPs). You could add your expertise on this to section 2.2.

[insert text]

3.2 Please describe how the study population will be recruited

Please give details on the recruitment strategy, monitoring of progress and potential mitigation measures

! **This chapter is very important, because study recruitment is often a bottleneck. Please describe this chapter well.**

You should clearly outline the strategy and capability of the consortium to recruit enough patients or volunteers without too much delay. You should give a clear understanding of the planned number, and country distribution, of the clinical sites. Other aspects to be included include mitigation measures should the study population fall behind the original recruitment expectations. For a robust recruitment plan, it is more desirable to have a feasibility study that draws upon prior patient enrolment figures, rather than on rough estimates. *Is a clinical network (e.g. ECRIN), a CRO or an expert part of the consortium?*

[insert text]

3.2.1 How many clinical sites will contribute to the recruitment of the study population in which countries? Are these clinical sites part of an established clinical trial network? Please also describe the selection criteria of the clinical sites.

Outline whether the clinical sites are part of an established clinical trial network. You should also describe the selection criteria of the clinical sites.

[insert text]

3.2.2 Will recruitment of the study population be of competitive nature between the clinical sites? (Please describe how underperformance of individual clinical sites in recruitment will be managed.)

Outline whether there will be clinical competition between sites and how they will manage difficulties such as one site being unable to recruit participants. *In case one site is not performing, can another site recruit more patients?*

[insert text]

3.2.3 What evidence supports the ability of the individual clinical sites to recruit the required number of study participants within the planned timeline (e.g. documented performance in previous clinical studies of similar complexity targeting very similar study population)?

Please explain the ability of the clinical sites to recruit the study participants. For example, you may give details of the previous experiences of participating clinical sites.

[insert text]

3.3 Please describe what additional supply (e.g. an electronic device for remote data capture, a specific instrument for administering the investigational product, etc.) is necessary to carry out the required study procedures and how this supply will be made available to the clinical sites

Additional supplies may include electronic devices for remote data capture; common characteristics of these supplies are that they are all required to carry out the study procedures. You should provide details on the description and means by which the sponsor will make these supplies available to the clinical sites.

[insert text]

3.4 Please provide plans on data management aspects (data standards, type of data capture, verification of data, central data collection, cleaning, analysis, reporting, security)

In this chapter you should describe your data management system and process of data capture, verification and cleaning concerning your clinical study.

Good to know: Please be advised that you can refer in Part B 1.2, which deals with data management within the project, to this template for any data management aspects concerning the clinical study. This will save you some space in Part B, which has limited pages.

[insert text]

3.5 Please give details on how reporting obligations (regarding study initiation, safety of study participants, ethical concerns, quality issues, integrity of data, study results) to regulatory bodies and ethics committees will be met.

Describe how obligations towards regulatory bodies and ethics committees are fulfilled in relation to reporting. *For example,* safety of study participants or quality issues.

[insert text]

3.6 Please list all items of the sponsor's responsibilities (e.g. monitoring clinical sites, meeting regulatory obligations, data management, etc.) that will be supported by entities that are not part of the sponsor's organisation. Please describe how the sponsor will ensure oversight of these activities.

Provide a list of sponsor responsibilities which were transferred from the sponsor to another entity e.g., a CRO. These responsibilities may include monitoring, pharmacovigilance, data management and statistics. It is important to give details on how the sponsor of the clinical study will have adequate oversight of the clinical study.

For further information about the sponsor's responsibilities, please have a look at ICH GCP E6.

[insert text]

3.7 What are the plans for major study milestones and what evidence supports its feasibility?

Please describe a realistic plan (based on prior experience) detailing the time necessary for (i) compiling the required regulatory and ethics submission package, (ii) receipt of regulatory and

ethics approval, (iii) initiation of clinical site(s), (iv) completion of recruitment of the study population, (v) final assessment of all study participants, (vi) analysis and reporting of the study results.

! Here you should demonstrate a realistic plan, ideally based on prior experience, that provides details on the time necessary to achieve the six major milestones above. You should ensure that you focus not only on the dissemination of results to clinical, industry and academic audiences, but also sufficiently address patient-specific dissemination strategies. **Do not forget to include these milestones in Part B table 3.1.d.**

[insert text]

HISTORY OF CHANGES		
VERSION	PUBLICATION DATE	CHANGE
1.0	24.03.2021	Initial version (included in the standard HE proposal template)
1.1	08.04.2021	Reference to 'sex distribution' added in section 1.4.
2.0	13.10.2021	Standalone template document.
3.0	15.01.2022	Reformatting changes and change of document name.
4.0	01.05.2022	Removed reference to specific topics for a more generalised template
4.1	13.05.2022	Added reference to Global Health-EDCTP3 Joint Undertaking
4.2	01.04.2023	Added reference to mandatory use of CTIS and complex trials