Clinical Proof of Concept: pre-proposal template

*Important: see Appendix 1 for CPoC programme aims and review process*

*Note: hold your mouse cursor over the* ***(i)*** *for instruction notes.*

1. Project title, applicants, and abstract
   1. Project title

*Provide a short title that can be used as an easy reference for the project.*

* 1. Support from your assigned Oncode Business Developer:

It is mandatory to work together with your assigned Oncode Business Developer on this project.

My assigned Oncode Business Developer is:

Saharla Ahmed  Ian Bell  Harma Feitsma  Amber Liu  Yuva Oz  Emil Pot  Alexander Turkin

* 1. Applicants *([[1]](#endnote-1))*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Role** | **Name email address** | **Institute** | **Contribution** | **Expertise/ Role in project** |
| Choose an item. | John Smith  j.smith@domain.com |  | Choose an item. |  |
| Choose an item. |  |  | Choose an item. |  |
| Choose an item. |  |  | Choose an item. |  |
| Choose an item. |  |  | Choose an item. |  |
| Choose an item. |  |  | Choose an item. |  |
| Choose an item. |  |  | Choose an item. |  |
| Choose an item. |  |  | Choose an item. |  |
| Choose an item. |  |  | Choose an item. |  |

Project is discussed with/supported by (e.g. clinicians, patients, statistician, PI, key leader in the field, tumor working group, industry):

Mention the name(s) and expertise: …………………………………………………………………………………….

### 

### Main contact person:

### Conflict of Interest statement

It is recognized that an applicant might be engaged with other organizations, sponsors or companies which may give rise to certain Conflict of Interest. It is important that any (potential) real or perceived Conflict of Interests of any applicant is disclosed, in order to allow for the resolution or management of such Conflict of Interest. [[2]](#endnote-2)🛈

Check as applicable.

I confirm that none of the applicants has a potential Conflict of Interest.

I confirm that one or more of the applicants has a potential Conflict of Interest.

If applicable, please describe the (potential) conflict of interest per person:

* 1. **Submitted to other funding organization?** ([[3]](#endnote-3))

Check as applicable.

The proposal has been previously submitted to another funding scheme:

No, we think this project is best suited for an Oncode CPoC project because ….(please explain)

Yes, we previously have submitted this project to …. (include the review report and discuss with your assigned Business Developer how to address any comments or feedback received)

### Synopsis *(max 1,5 A4)*

* + 1. Goal of current proposal in 2-3 sentences.
    2. Clinical impact ([[4]](#endnote-4))
    3. Scientific basis of project & high-level plan of current proposal **([[5]](#endnote-5))**
    4. What innovation from the Oncode Investigator’s lab is underlying this proposal? Are any aspects of these innovations protected by intellectual property rights? If applicable provide a brief overview of the IP behind the technology proposed in the application.
    5. What are the differentiating factors of the projects , considering what treatment options are already available, potential treatments in early or advanced stages of development in the pipeline and what this project potentially contributes over and above the current state of the art? **([[6]](#endnote-6))**

### Nederlandse samenvatting

*Schrijf een duidelijke Nederlandstalige lekensamenvatting inclusief het doel van het onder-zoek, context en specifieke mechanisme van de tumor/kankersoort, de voor-en nadelen van het onderzoek en waarom jullie dit onderzoek willen doen.*

1. Goals and context of the project ([[7]](#endnote-7))

*The Target Product Profile (TPP) describes what benefit the new product will bring to patients. From the TPP it will be clear what attributes of the new product are necessary for its success and what attributes might cause it to fail. The goal for a CPoC project is to generate the necessary data to allow a decision that it is “reasonably likely” that the key attributes for success are present and the key causes of failure are absent. The workplan should make explicit how the proposed study/ -ies will generate those necessary data. In order to reach a decision, the decision criteria to declare or refute Proof of Concept need to be very explicit (quantitative). A key element for confidence in decision making is to be sure that you have actually tested the research hypothesis underlying your project.*

### Target Product Profile ([[8]](#endnote-8))

### Success factors and Risk assessment

* + 1. Key drivers of Success **([[9]](#endnote-9))**
    2. Key risks and mitigation **([[10]](#endnote-10))**
    3. Key enablers **([[11]](#endnote-11))**

### Proof of Concept criteria, knowledge gaps and hypothesis testing

* + 1. Description of PoC criteria **([[12]](#endnote-12))**
    2. Key Knowledge Gaps that will be filled by the proposed study/-ies **([[13]](#endnote-13))**
    3. Essential data required to verify the scientific concept underpinning your invention **([[14]](#endnote-14))**

1. Approach & Workplan

### Integrated operational plan of study(-ies) that will generate the necessary data for a PoC decision

Study design **([[15]](#endnote-15))**

## 

## Table A: Clinical study synopsis

|  |  |
| --- | --- |
| Mono- or multicentre study? |  |
| Current stage of clinical development |  |
| Primary objective(s) |  |
| Secondary objective(s) |  |
| Exploratory objective(s) |  |
| Methodology: double/single blind or open trial, type of control (placebo, comparator, none), randomization |  |
| Test Product, Dose, Mode of Administration |  |
| Control Product, dose, Mode of Administration |  |
| Summary of Trial Design |  |
| Primary endpoint |  |
| Secondary endpoint(s) |  |
| Number of Subjects (planned) |  |
| Treatment duration |  |
| Estimated trial duration (First subject in – last subject out) |  |
| Main enrolment criteria | Main Inclusion criteria:  1.  2.  …  Exclusion criteria  1.  2.  … |
| Recruitment strategy and expected accrual |  |

* 1. **Patient Engagement and impact ([[16]](#endnote-16))**
     1. Describe the involvement of patients (individual and patient organisations) in the different phases of the study (e.g. set-up, design, follow up steps)[[17]](#endnote-17)🛈
     2. What is the burden for the patient (additional hospital visits, side effects and treatments)? And how does this burden deviate from the normal standard of care? [[18]](#endnote-18)🛈

### **Project status**

Indicate status by checking as applicable.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **In place** | **In progress** | **Start after funding approved** | **Need support** | **n/a** |
| Availability of clinical expertise |  |  |  |  |  |
| Ethical approval |  |  |  |  |  |
| Availability of materials required for study (e.g. chemicals, drugs…) |  |  |  |  |  |
| Data management plan |  |  |  |  |  |
| Patient information form (PIF) |  |  |  |  |  |

### Partners and additional expertise ([[19]](#endnote-19))

### Possible next steps ([[20]](#endnote-20))

### Budget ([[21]](#endnote-21))

See the excel sheet provided with this template.

*We need the financial controller of your department/Institute and from the department of the clinical PI to check the budget and sign for approval.*

**Appendix I: CPoC aims and review process**

**Aims & scope of the CPoC programme**

Oncode Institute's mission is to accelerate breakthrough discoveries and speed up their translation into new diagnostics and treatments for cancer patients, by supporting the development of novel treatment strategies based on innovations arising from Oncode Institute groups. To enable this, Oncode Institute has set-up a clinical proof-of-concept (“CPoC”) programme with the aim to answer whether the concept is worth pursuing further. The programme includes expert support and funding for Oncode Investigators to study their most promising innovations in the clinic. These CPoC studies are defined as early, clinical studies to understand whether the innovation elicits the expected response in individuals, and to determine whether the concept warrants further studies, e.g. dose-escalation, efficacy trials etc., and whether there is a promising route towards implementation/commercialisation.

**Outline**

The CPoC programme will provide funding and expert support for early stage, clinical studies with a high-risk, high-gain profile, based on innovations developed by an Oncode Investigator, with the aim to create impact for patients. In general, the CPoC program is focused on projects for new or repurposed therapies, where relevant in combination with (existing) biomarker research. Development of innovations to improve patient stratification approaches may also be considered. Eligible projects require a clear route to the clinic and/or market. Research focused *only* on the *discovery* of novel biomarkers is excluded.

The CPoC process consists of 3 steps:

1) discuss ideas for potential CPoC projects with your dedicated business developer at an early stage to explore the possibilities for development in a pre-proposal. Additionally, a pre-discussion meeting with the OEDES team will be planned to discuss whether the project is likely to meet the criteria of the CPoC programme, and to provide advice and support for the pre-proposal.

2) Submission of the pre-proposal to determine whether the project meets the goals of the CPoC programme, and to select high-potential ideas

3) OEDES workshop and submission of the full proposal (see below for more details of the process)

The maximum funding available for a CPoC study is 400.000 Euro, however exceptions can be discussed and will be judged based on quality of the proposal and possibilities for additional funding. Full project proposals require a detailed and well-justified budget in the Oncode template.

*‘Proof-of-Concept is the earliest point in the development process at which the weight of evidence suggests that it is “reasonably likely” that the key attributes for success are present and the key causes of failure are absent.’* Cartwright *et al*. [[22]](#footnote-1)

**Eligible criteria full project:**

*This eligibility criteria is for the final full project. Some of these criteria will be asked during the pre-proposal stage to see if the project fits in the programme. Oncode Institute aims to aid in the complete clinical validation process!*

* Pre-clinical studies are not eligible for this programme. However, some preclinical work needed to enable a clinical trial can be considered on a case-by-case basis.
* CPoC project must:
  + Detail the early phase clinical study that aims to obtain clinical proof-of-concept for an innovation arising from or developed by an Oncode Investigator.
  + Be a collaboration between at least one Oncode Investigator and one practicing medical specialist with proven expertise in the field of the proposed study, and the project must be supported by clinical groups or clinical experts outside of the main Oncode Investigator’s institution. Of note, support to organize this can be provided.
  + Have an impact on patients with cancer that is unlikely to be met by currently available treatment options or by treatments that are already in more advanced stages of development; Improve the quality of life; change the standard of care; and/or have a significant impact on health care costs.
  + Contain clear milestones with timelines, ultimately leading to the proof-of-concept decision with well-defined go/no- go criteria (typically these milestones include, METC approval, opening of first center, first patient included, 50% + 100% of patients included, time for follow up and final report of study).
* Patients or patient organisations need to be involved during the development of the proposal and clinical protocol.
* It must be explicitly clear how the proposed CPoC programme will result in risk reduction for later (more expensive) stages of development. In support of this criterion, the proposal should have a well-defined valorisation perspective and downstream development plan. The output of successful CPoC projects should comprise sufficient evidence to make the project results, intellectual property and outcomes attractive to follow-on developers, e.g. biotech or pharmaceutical companies. Also here Oncode Institute provides support.
* At the full proposal stage a letter of intent is necessary from the project partners.
* The budget of the project proposal is justifiable, filled out correctly and checked and approved by the Oncode Investigator’s home institution’s finance department and the finance department of the clinical PI.
* If an external party is involved in the study, a letter of intent is required with the full proposal.

We may need to ask for additional documents on request from our funders, this will be clear at the full proposal stage (e.g. letters of commitment on behalf of project partners, consortium agreement, use of specific budget formats).

**Oncode support**

Before submitting a pre-proposal, it is necessary to inform your assigned BD about your intent to apply to the CPoC progamme. Together you will discuss with the Oncode Explorative Development Expert Support (OEDES) team whether the project is likely to meet the criteria of the CPoC programme and they can provide advice and support for the pre-proposal. This will save you a lot of preparation time.

Additional support is provided by your assigned Business Developer and the OEDES team during the preparation of the pre-proposal, OEDES workshop and full proposal. You can contact Programme manager Marlinde Smit ([marlinde.smit@oncode.nl](mailto:marlinde.smit@oncode.nl) ) for program and review related questions or if you need other additional support from Oncode.

**Review process**

Potentially suitable projects can be submitted to the CPoC programme as pre-proposal first and as full proposal in a following stage. The review of both pre-proposal and full proposal is driven by a panel of experts.

Review of the pre-proposal by:

* The Clinical Advisory Board (CAB) for its feasibility and clinical value;
* The Research Management Committee (RMC) for its scientific rationale and innovative approach; and
* The Valorization team for the opportunities and challenges of bringing the innovation to the market.

Support will be provided by the OEDES team and your assigned Business Developer.

Purpose of this step is to provide suggestions for improvement of the project, and to select high-potential ideas for the full proposal stage that can contribute to Oncode’s mission of translating fundamental knowledge into patient benefit. The pre-proposal review takes 4-5 weeks. At the end of the review period, the decision made by Clinical Advisory Board and supported by the Research Management Committee, will be communicated to the investigator. A positive outcome will result in an invitation to attend a face-to-face project-oriented workshop (2 hours), led by the OEDES team (including the assigned Business Development expert), with the goal of working the pre-proposal into a full proposal. The full proposal will be reviewed by the CAB and Valorization team, followed by a final decision of the Oncode Managing Board.

**Deadlines call 2025**

* **Call open: January 6, 2025**
* **Deadline pre-proposal:** pre-proposals can be submitted and will be processed on a rolling basis, but ultimately **before March 3rd , 2025.** (send your pre-proposal to [marlinde.smit@oncodeinstitute.nl](mailto:marlinde.smit@oncodeinstitute.nl))
* **Deadline full proposal: June 20, 2025**
* **Start project:**  we aim to start allocated projects before the end of 2025.

**Appendix II: Trial Flow Chart (example)**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **Screening** | **Baseline** | **Treatment period** | | |
|  |  | **V1**  **D1** | **V2**  **Dxx** | **V3**  **Dxx** | **V…**  **Dxx** |
| **Administrative Procedures** |  |  |  |  |  |
| Informed Consent | X |  |  |  |  |
| Inclusion/Exclusion Criteria | X |  |  |  |  |
| Urine Drug/ Alcohol Screen | X |  |  |  |  |
| Medical history | X |  |  |  |  |
| Concomitant medication | x-------------------------------------------------------x | | | | |
| **Clinical Procedures/Assessments** |  |  |  |  |  |
| Physical Examination | X |  |  |  |  |
| Height | X |  |  |  |  |
| Weight | X |  |  |  |  |
| 12-Lead Electrocardiogram | X |  |  |  |  |
| Vital signsx | X |  |  |  |  |
| Adverse event recording | x-------------------------------------------------------x | | | | |
| **Laboratory Procedures/Assessments** |  |  |  |  |  |
| Haematology x | X |  |  |  |  |
| Chemistry x | X |  |  |  |  |
| Urinalysisd | X |  |  |  |  |
| HIV, Hepatitis B and C serology | X |  |  |  |  |
| β-hCG in serum of women of childbearing potential | X |  |  |  |  |
| Urine Pregnancy Test in women of childbearing potential |  |  |  |  |  |
| Serum FSH (if applicable)x | X |  |  |  |  |
| **Efficacy/PD endpoint evaluation** |  |  |  |  |  |
| xxxx |  |  |  |  |  |
| **Pharmacokinetics** |  |  |  |  |  |
| Blood for Plasma xx /metabolites x |  |  |  |  |  |
| Blood for Future Biomedical Research |  |  |  |  |  |
| Blood sampling for genotypoing/RNA/serum/..x |  |  |  |  |  |

V=Visit, D=Day

x….

**Instruction notes**

1. An Oncode Investigator (main applicant) and at least one (lead) clinician is required.

   The lead clinician(s) may be associated with any Dutch institution. If applicable, please list other researchers

   involved. [↑](#endnote-ref-1)
2. 🛈 A Conflict of Interest (CoI) may occur as a result of personal involvement with other organizations,

   corporations, institutions or businesses, based on a personal interest, a personal relationship, a professional

   relationship and/or an economic interest. For example, a Conflict of Interest arises when an applicant of the

   proposal is engaged with a certain commercial organization that also will be providing paid services as part of the proposed project. Please refer to the Oncode CoI policy for details. In case of doubt or questions, please discuss with your dedicated Oncode Business Developer. [↑](#endnote-ref-2)
3. The CPoC programme aims to fund projects that are high-risk high-gain proof-of-concept projects, which are

   innovations developed in the lab of the OI and not likely to be funded through conventional mechanisms (e.g. KWF, ZonMW). [↑](#endnote-ref-3)
4. Indicate the unmet clinical need addressed by this project and the potential contribution to the standard of care? What is the benefit for the target patient group? [↑](#endnote-ref-4)
5. The scientific theory that is at the basis of this project. What is the status of the work that needs to be

   completed before the clinical study described in your current proposal can start? Short description of what you will do, and how. [↑](#endnote-ref-5)
6. Ask your dedicated Business Developer for support to answer this question. [↑](#endnote-ref-6)
7. In this section, you will describe what you are aiming to achieve with your overall project– how will the final ‘product’ look like in terms of benefit, risk, convenience, and how does the clinical profile of a patient look like who benefits from your product? This defines the Target Product Profile. More information on purpose and use of a Target Product Profile can be found at the FDA website: <https://www.fda.gov/media/72566/download> [↑](#endnote-ref-7)
8. Describe the indication for the drug. Quantify the level of benefit you target with the drug. This should be done

   relative to the current Standard of Care. For a drug, benefit can be gained in: efficacy safety, tolerability,

   convenience, and /or cost. [↑](#endnote-ref-8)
9. What factors or conditions will be key to the success of this project? Define the cut-off criteria for the SuccessFactors, i.e. what are the criteria that would mean stopping the project? [↑](#endnote-ref-9)
10. What are the key risks for the project e.g. in the area of safety, feasibility, cost, competition, formulation,

    availability of study participants, test samples, analytical issues? [↑](#endnote-ref-10)
11. What other work needs to be available before the study for which you ask funding can be initiated? Think of

    results from other studies, facilities, tools, formulation, toxicology, biomarkers etc. [↑](#endnote-ref-11)
12. For clinical PoC, describe in quantitative terms what in your opinion would constitute a positive outcome. [↑](#endnote-ref-12)
13. Which are the key knowledge gaps with respect to the Critical Success Factors, criteria to stop the project,

    target, competition, formulations etc. that must be filled before Proof of Concept? [↑](#endnote-ref-13)
14. For a drug: How will you know you have sufficient exposure of the target? Describe pharmacokinetic and/or pharmacodynamic analysis that needs to be done and target levels herein [↑](#endnote-ref-14)
15. Please fill in table A and append a Trial Flowchart. See Appendix II for example. [↑](#endnote-ref-15)
16. 3.2.1. Describe the involvement of patients (individual and patient organizations). How are they involved in shaping the project and how will they be engaged during the study? Please mention any connections you may already have with any relevant group(s). Is the treatment of the study standard of care or do the patients get

    additional treatments or procedures?

    Note that the Clinical Advisory Board, which includes patient representatives, will critically review this section. [↑](#endnote-ref-16)
17. *🛈* Please describe how patients are involved in the setup and design of the study, in follow up steps and how patients will be informed after finishing the study. [↑](#endnote-ref-17)
18. *🛈* To what extent does the study imply an extra burden compared to the standard treatment, which interventions are part of the standard of care? [↑](#endnote-ref-18)
19. Multi-disciplinary projects are encouraged. Please indicate any other partners involved that may not be listed as co-applicants, and describe their contribution to the project.

    If not identified yet, please indicate what additional expertise you require to execute the project. Such expertise might be provided with help from Oncode. [↑](#endnote-ref-19)
20. When successful, describe briefly what follow-up research and other activities are anticipated? Think of IP, commercial strategy, marketing, valorization strategy. You can ask your Business Developer to help with this. [↑](#endnote-ref-20)
21. Please provide a budget of the proposed study, using the xls template. Please make sure the costs for the study are calculated in full and the financial controller of your department or institute has checked and signed for the budget. [↑](#endnote-ref-21)
22. Cartwright ME et al, [Proof of concept: a PhRMA position paper with recommendations for best practice](https://www.ncbi.nlm.nih.gov/pubmed/20130568).; Clin Pharmacol Ther. 2010 Mar;87(3):278-85. doi: 10.1038/clpt.2009.286. [↑](#footnote-ref-1)