Investigator Initiated Clinical Trials, Call for Proposals 2021

**PROPOSAL**

**INSTRUCTIONS**

*The deadline for the submission of the full proposal is on* ***1 November 2021 at 5pm*** *Swiss local time.*

*For the submission of your application, the use of this proposal form is mandatory. The structure of the form must not be changed, but subtitles may be added and formatting can be changed.*

*The research plan must not exceed* ***25 pages****; this includes synopsis, abstract, footnotes, illustrations, formulae, tables (and, if applicable, the table of contents), but not the bibliography. A minimum of point 9 font size and 1.15 line spacing must be used.* ***No annexes are permissible.***

*Delete the INSTRUCTIONS on the first page and in each textbox before submission.*

*Make sure that pages are numbered.*

*Upload a PDF-file (not write-protected) of your proposal to the data container “IICT Proposal” in mySNF.* *Name the file as follows: IICT2021\_proposal\_[Name of responsible applicant].pdf (e.g.IICT2021\_proposal\_Smith.pdf).*

*This proposal form is based on the* ***SPIRIT 2013 Statement****: Defining Standard Protocol Items for Clinical Trials. It was adapted by the SNSF and is used with the permission of the SPIRIT group.*

*Please take note of the following publications when completing the proposal form:*

*Chan A-W, Tetzlaff JM, Altman DG, Laupacis A, Gøtzsche PC, Krleža-Jerić K, Hróbjartsson A, Mann H, Dickersin K, Berlin J, Doré C, Parulekar W, Summerskill W, Groves T, Schulz K, Sox H, Rockhold FW, Rennie D, Moher D. SPIRIT 2013 Statement: Defining standard protocol items for clinical trials. Ann Intern Med 2013;158:200-207.*

*Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ 2013;346:e7586.*

*When planning your clinical trial, please consider the following points:*

***Patient and public involvement (PPI)***

*We would like to draw your attention to the importance of PPI in all aspects of a clinical trial. The applications submitted for the IICT Call 2021 are for the second time evaluated by members of the public.*

*In this context please also consider the SPIRIT-PRO Extension: Calvert M, Kyte D, Mercieca-Bebber R, Slade A, Chan A-W, MD, King MT, and the SPIRIT-PRO Group. Guidelines for Inclusion of Patient-Reported Outcomes in Clinical Trial Protocols. The SPIRIT-PRO Extension. JAMA. 2018;319(5):483-494.*

***Trial management***

*All projects are encouraged to appoint a dedicated trial manager.*

***CTU involvement***

*It is advisable to involve experts of the Clinical Trial Units or similar institutions at an early stage to develop the study protocol and ensure the quality of data collection.*

1. **Trial Synopsis**

|  |  |
| --- | --- |
| Title of trial | *Insert a descriptive title identifying the study design, population, interventions, and, if applicable, study acronym. Maximum 180 characters, incl. spaces.* |
| Responsible applicant | *Indicate the name, institution, position, role, phone number and e-mail address of the applicant responsible for communication with the SNSF.*  |
| Other applicants | *Indicate the name, institution, and position of each applicant, as well as her/his specific role and responsibility in the project.* *The number of applicants (including the responsible applicant) is limited to 5 persons.* |
| Project partners | *Indicate the names, institutions and roles of the project partners (please refer to the IICT call text for definition of project partners).*  |
| Clinical trial unit involvement | The SNSF highly recommends involving your local clinical trial unit (CTU) in the conception, design and execution of the trial[ ]  Yes - Name of clinical trial unit:[ ]  No - Please explain:*Type of involvement during proposal preparation (check appropriate box and please specify contribution of the CTU)*[ ]  Grant writing[ ]  Literature review[ ]  Study design[ ]  Statistics[ ]  Monitoring plan[ ]  Data management plan[ ]  Other: *Planned involvement during trial*[ ]  Project management[ ]  Statistics[ ]  Monitoring[ ]  Data management[ ]  Data monitoring[ ]  Regulatory support[ ]  Other:  |
| Project management | The SNSF highly recommends appointing a dedicated, experienced project manager*Describe role and employment level of project manager* |
| Sponsor | *Indicate the sponsor or sponsor investigator of the planned study including the contact information.* |
| Re-submission | [ ]  Yes – Application number:[ ]  No |
| Medical field(s) |  |
| Trial type | [ ]  Interventional (according to Article 2 letter a [ClinO](https://www.admin.ch/opc/en/classified-compilation/20121176/index.html))[ ]  Prospective[ ]  Randomized[ ]  ControlledNote: only trials that fulfill all the above mentioned criteria are eligible for the call |
| Trial duration  | * (if applicable) Preparatory phase (months) max. 12 months:
* First patient in to last patient in/Recruitment period (months):
* Follow-up per patient (months):
* Duration of the entire trial (preparatory phase, recruitment, follow-up, analysis) max. 60 months:
 |
| Endpoints  | Primary endpoint:Secondary endpoint: |
| Sample size  |  |
| Recruitment sites  | No. of centres to be involved:Names of cities and centres: |
| Funding requested from the SNSF | Total amount: CHF |
| Co-funding, contributions and donations from third parties | [ ]  Co-funding – Type:[ ]  Donation – Type: Name of third party: Amount: CHFNote: all contributions and donations from third parties need to be confirmed in writing at the time of submission. Additionally, all points listed in the IICT Call text under 6.2 must be confirmed. |

1. Summary for general public

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| Please provide a brief summary of your proposal with a clear explanation of your research, which will help members of the public who evaluate your application to understand your project. This summary is targeted at an interested audience but not specialists. Therefore please write it similar to a newspaper article and avoid using jargon, abbreviations, technical terms and generally complicated English words without providing a clear explanation.Max. 4000 characters including spacesWhen writing the summary consider including the following information where appropriate:Aim(s) of the research* What are you aiming to find out?
* How will patients / carers / members of the public and services benefit from your research - either directly or in the longer term?

Background to the research* Why does this research need to be done now?
* What is the scale of the issue?

Design and methods used* What design and methods have you chosen and why?
* Who are your participants? (if appropriate)

Patient and public involvement* How have patients / the public been involved in developing this research to date?
* How will patients / the public be involved in the conduct / management of the research?

Dissemination* Who will the findings be communicated to and how?
 |

1. Scientific abstract

|  |
| --- |
| Insert an abstract of your proposal. *Maximum 4000 characters, incl. spaces.**This abstract, compared to the summary for the general public above, is targeted at an audience of specialists.* |

1. Background and rationale
	1. Research question

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| --- |
| Insert a description of the research question and justification for undertaking the study, including a summary of relevant studies (published and unpublished) examining benefits and harms for each intervention. Explain the mechanism of action of the proposed treatment or state what experiments are planned to better understand this mechanism.  |

* 1. Choice of comparators

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| Insert an explanation for the choice of comparators.  |

* 1. Importance

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| Explain the importance of the study for the public and its potential value for an insufficiently researched field and/or its significance for clinical research in Switzerland. Explain the impact of the study on future research questions or clinical trials. State what follow-up studies are planned.  |

* 1. Commercial interest

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| --- |
| Describe any potential commercial interest of a company or an individual in the results of the study (patents, planned commercialization, etc.), or explain why no such interest exists. Please note that studies conducted for directly commercial purposes are excluded from support by the IICT program. |

* 1. Patent protection

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| --- |
| Describe if the investigational medicinal product, medical device or any other product under investigation is patent protected. Name the owner of the patent and the duration of patent protection. |

1. Objectives and hypothesis

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| --- |
| Insert the specific objectives and hypotheses.  |

1. Study design

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| Insert a description of the study design, including the type of study (e.g., parallel group, crossover, factorial, single group), allocation ratio, and framework (e.g., superiority, equivalence, non-inferiority, exploratory). |

1. Study phase

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| For pharmaceutical studies, indicate the study phase. Be aware that studies with safety endpoints only are excluded from support by the IICT program. |

1. Inclusion and exclusion criteria

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| --- |
| Define the inclusion and exclusion criteria for study participants.  |

1. Intervention
	1. Interventions

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| Describe the interventions for each study group with sufficient detail to allow replication; including how and when interventions will be administered. |

* 1. Criteria for discontinuing or modifying interventions

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| Insert criteria for discontinuing or modifying allocated interventions for a given patient (e.g., drug dose change in response to harms, patient request, or improving/worsening disease).  |

* 1. Adherence

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| Insert strategies to assure adherence to intervention protocols, and any procedures used to monitor adherence (e.g. drug tablet return, laboratory tests).  |

* 1. Concomitant care

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| Describe all relevant concomitant care and interventions that are permitted or prohibited during the study.  |

1. Outcomes

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| Insert primary, secondary, and other outcomes, including the specific measurement variable (e.g., systolic blood pressure), analysis metric (e.g., change from baseline, final value, time to event), method of aggregation (e.g., median, proportion), and time point for each outcome. An explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended.  |

1. Patient timeline

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
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| Insert a schedule of enrollment, interventions (including any run-ins and washouts), assessments, and visits for patients. A schematic diagram is highly recommended.Example:

|  |  |
| --- | --- |
|  | **Study Period** |
|  | **Enrollment** | **Allocation** | **Postallocation** | **Closeout** |
| **Time point\*** | **–t1** | **0** | **t1** | **t2** | **t3** | **t4** | **etc.** | **tx** |
| **Enrollment:****Eligibility screen****Informed consent****[List other procedures]****Allocation** |  |  |  |  |  |  |  |  |
| **X** |  |  |  |  |  |  |  |
| **X** |  |  |  |  |  |  |  |
| **X** |  |  |  |  |  |  |  |
|  | **X** |  |  |  |  |  |  |
| **Interventions:****[Intervention A]****[Intervention B]****[List other study groups]** |  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
|  |  |  |
|  |  | **X** |  | **X** |  |  |  |
|  |  |  |  |  |  |  |  |  |  |
|  |  |  |  |
| **Assessments:****[List baseline variables]****[List outcome variables]****[List other data variables]** |  |  |  |  |  |  |  |  |
| **X** | **X** |  |  |  |  |  |  |
|  |  |  | **X** |  | **X** | **etc.** | **X** |
|  |  | **X** | **X** | **X** | **X** | **etc.** | **X** |

Recommended content can be displayed using various schematic formats. See SPIRIT 2013 Explanation and Elaboration (BMJ2013;346:e7586 doi: 10.1136/bmj.e7586) for examples. This template is copyrighted by the SPIRIT Group and is reproduced with permission.  |

1. Sample size

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| Specify the estimated number of patients needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting sample size calculations.  |

1. Recruitment
	1. Recruitment strategies

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| Describe strategies for achieving adequate patient enrollment to reach target sample size.  |

* 1. Feasibility of recruitment

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| Insert a detailed explanation of the feasibility of recruitment. State how the planned patient numbers were estimated, for example by a retrospective analysis of cases within the last 12 months. Define the sources used to estimate the patient recruitment (individual estimate, patient registry, hospital data management system, etc.). Note that a “letter of commitment”, indicating the planned number of patients to be included in the study, has to be submitted for each recruiting site (see article 4.6 of the Investigator Initiated Clinical Trials (IICTs): call for proposals and instruction on mySNF “Letters of commitment”).Note that the feasibility of patient recruitment is crucial for the evaluation of your proposal. |

1. Assignment of intervention
	1. Allocation sequence

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| Describe the method of generating the allocation sequence (e.g., computer-generated random numbers), and list any factors used for stratification.  |

* 1. Concealment mechanism

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| Explain the mechanism of implementing the allocation sequence (e.g., central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned.  |

* 1. Implementation

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| Describe who will generate the allocation sequence, who will enroll patients, and who will assign patients to interventions.  |

1. Blinding (masking)
	1. Blinding

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| Describe who will be blinded after assignment to interventions (e.g., study participants, care providers, outcome assessors, data analysts), and how.  |

* 1. Emergency unblinding

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| If the study is blinded, describe circumstances under which unblinding is permissible, and the procedure for revealing a patient’s allocated intervention during the study. |

1. Data collection
	1. Data collection methods

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| Insert plans for assessment and collection of outcome, baseline, and other study data, including any related processes to promote data quality (e.g., duplicate measurements, training of assessors) and a description of study instruments (e.g., questionnaires, laboratory tests) along with their reliability and validity, if known.  |

* 1. Retention

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| Insert plans to promote patient retention and complete follow-up, including list of any outcome data to be collected for patients who discontinue or deviate from intervention protocols.  |

1. Data management

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| --- |
| Insert plans for data entry, coding, security, and storage, including any related processes to promote data quality (e.g., double data entry; range checks for data values).  |

1. Statistical methods
	1. Statistical method for primary and secondary outcomes

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| --- |
| Describe the statistical methods for analyzing primary and secondary outcomes.  |

* 1. Statistical methods for additional analysis

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| Describe the methods for any additional analyses (e.g., subgroup and adjusted analyses).  |

* 1. Analysis population and missing data

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| Insert a definition of analysis population relating to protocol non-adherence (e.g., as-randomized analysis), and any statistical methods to handle missing data (e.g., multiple imputation). |

1. Interim Analysis

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| Insert a description of any interim analyses and stopping guidelines, if any, including who will have access to these interim results and make the final decision to terminate the study.  |

1. Dissemination policy
	1. Dissemination of study results

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| --- |
| Insert plans to communicate study results to patients, health care professionals, the public, and other relevant groups (e.g., via publication, reporting in results databases, or other data-sharing arrangements).  |

* 1. Reproducibility

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| Insert plans, if any, for granting public access to the full protocol, patient-level data set, and statistical code. |

1. Patient and public involvement

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| --- |
| Insert a description what has been or is planned to be done to actively involve patients, members of their family, carers, the public or respective organisations in the design and delivery of the project. If no patient or public involvement was or will be possible, the reasons need to be outlined in the research plan. Describe the effect of the patient and public involvement on planning and designing the trial. For example, patients, carers and members of the public may work with researchers to: ▪ Help select research topics that are important ▪ Devise relevant research questions ▪ Identify outcomes that matter most to patients ▪ Design studies so they are easier to take part in ▪ Develop clear information about research studies ▪ Help create plain English summaries of studies ▪ Co-produce consent forms ▪ Make sure communication is sensitive and appropriate for participants ▪ Help collect research data, for example through interviews ▪ Analyse research findings from a patient perspective ▪ Raise awareness amongst the public of what research is taking place ▪ Share findings of important research ▪ Help make sure research is reported in understandable ways ▪ Be part of a research project steering group  |

1. Study schedule and milestones

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| Adapt the below provided study schedule (see also example below) according to your plans complying with the following guidelines:* Maximum duration of entire project 60 months
* If applicable, a preparatory phase of max. 12 months can be part of the project

Please also mention here whether you plan to assess endpoints beyond the 60 months funding period (see article 4.3 in the IICT Call Text).Funding by the SNSF critically depends on the study progression according to milestones. A scientific report on the predefined milestones is due every 6 months.In order to complete the preparatory phase and start recruitment, the following milestones have to be fulfilled:* Trial protocol finalized and made publicly available
* Required approvals and authorizations (Swissmedic, ethics commission, etc.) for at least the first Swiss study site
* Registration of trial on SNCTP Portal as well as clinicaltrials.gov, WHO or other
* Contracts/agreements signed
* Data management system ready
* QA/monitoring system ready
* Safety reporting system ready

Please note that in case your grant proposal does not include a preparatory phase, the funds will only be released once all above mentioned points are fulfilled.After start of recruitment, the report will focus on:* Number of patients included compared to number planned; in case of a delay, an explanation of the reasons including the measures to be taken is necessary
* Recruitment centres opened including the submission of authorisations obtained
* Follow-up status and patient retention
* Mention of important events such as changes in personell or other
* Mention of major deviations from the research proposal

Marked in yellow are the parts to be completed according to your project. Additionally, in the row marked in grey, please enter the numbers of patients included at the predefined timepoints.Example

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| *Months* | *1-6* | *7-12* | *13-18* | *19-24* | *25-30* | *31-36* | *37-42* | *43-48* | *49-54* | *55-60* |
| Preparatory phase; 12 months | x | x |  |  |  |  |  |  |  |  |
| Recruitment24 months |  |  | x | x | x | x |  |  |  |  |
| # of patients recruited; n=120  |  |  | 30 | 60 | 90 | 120 |  |  |  |  |
| Follow-up; 12 months |  |  |  | x | x | x | x | x |  |  |
| Analysis12 months |  |  |  |  |  |  |  |  | x | x |
| Comment |  |  | First patient in |  |  | Last patient in |  | Last patient out |  |  |

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Months | 1-6 | 7-12 | 13-18 | 19-24 | 25-30 | 31-36 | 37-42 | 43-48 | 49-54 | 55-60 |
| Preparatory phaseXX months; max. 12 months |  |  |  |  |  |  |  |  |  |  |
| RecruitmentXX months |  |  |  |  |  |  |  |  |  |  |
| # of patients recruited; XX total |  |  |  |  |  |  |  |  |  |  |
| Follow-up; XX months per patient |  |  |  |  |  |  |  |  |  |  |
| AnalysisXX months |  |  |  |  |  |  |  |  |  |  |
| Comment |  |  |  |  |  |  |  |  |  |  |

1. Further comments

|  |
| --- |
| Insert further comments and additional information important to your study.  |

1. Bibliography

|  |
| --- |
| List of publications, including unpublished work, relevant to the study. Please upload unpublished manuscripts to the corresponding data container in mySNF.  |