

Guidance for Applicants on Ethical and Scientific Issues

This guidance document provides essential information for all applicants preparing SFI grant applications. While applicants are advised to be cognisant of all the information provided in this document, it is recognised that certain applications may not need to directly address all of the issues outlined herein (e.g., applications to programmes where clinical trials are not permitted need not address the requirements described in Section 4).

Sections

1	Ethical and Regulatory Requirements	1
2	Animal Studies	1
3	Human Studies	3
4	Clinical Trials	6
5	Ethical Issues Table	7

1 Ethical and Regulatory Requirements

All investigators and research bodies must ensure that, before the research commences and during the full award period, all the necessary ethical, legal and regulatory requirements in order to conduct the research are met, and all the necessary licences and approvals have been obtained. All research bodies are responsible for ensuring that a safe working environment is provided for all individuals associated with a research project.

Those applicants proposing research that involves the use of animals must consult with **Section 2** (Animal Studies) of this document. For studies involving human participants or material, applicants must consult with **Section 3** (Human Studies) of this document. Where applicable, additional requirements concerning clinical trials, are outlined in the ‘Clinical Trials’ Section of this document (**Section 4**).

Science Foundation Ireland requires evidence that relevant ethical and regulatory approval has been granted for studies involving human or animal subjects as well as human cells/tissues prior to research commencing.
Submission of an application to SFI represents an agreement by the applicant to obtain the relevant approval for any research which requires ethical and/or regulatory approval prior to the commencement of the research.

2 Animal Studies

Where animals are to be used in research projects, applicants must comply with the **SFI Use of Animals in Research Policy**¹ and the Health Products Regulatory Authority’s (HPRA)²

¹ <http://www.sfi.ie/funding/grant-policies/sfi-policy-on-the-use-of-animals-in-research.html>

² <https://www.hpra.ie/homepage/veterinary/scientific-animal-protection>

position on the use of animals in research. SFI will only support research using animals that is fully compliant with the requirements of the HPRA, has been independently peer reviewed and where consideration has been given to the use of alternative approaches not involving the use of live animals and addressing the principles of the 3R's (replacement, reduction, refinement). Additional external sources of guidance include the HPRA and **ARRIVE (Animal Research: Reporting In-Vivo Experiments)**³ guidelines produced by the UK National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs). In order to allow for the appropriate evaluation of the scientific merit of applications for funding involving animal use, applicants submitting proposals must provide the information outlined in **Table 1** below within the description of their proposed research and methodology.

In addition, as part of an SFI grant proposal, applicants are required to complete a questionnaire relating to ethical issues see **Section 5** (Ethical Issues Table) of this document.

Table 1– Information required for research involving the use of animals*

Information	Details to be provided in the main body of your Grant Proposal
Ethical Statement	Indicate the nature of the ethical review permissions, relevant licences and national or institutional guidelines for the care and use of animals that cover the research. SFI will require evidence that relevant ethical and regulatory approval has been granted prior to the award commencing.
Study Design	For each experiment, give brief details of the study design including: <ol style="list-style-type: none"> The number of experimental and control groups. Any steps taken to minimise the effects of subjective bias when allocating animals to treatment (e.g. randomisation procedure) and when assessing results (e.g. blinding). The experimental unit (e.g. a single animal, group or cage of animals). The number of times each animal will be measured.
Experimental animals	<ol style="list-style-type: none"> Provide details of the animals used, including species, strain, sex, developmental stage and weight. Include a sound scientific reason for these choices. Provide further relevant information such as the source of animals, international strain nomenclature, genetic modification status (e.g. knock-out or transgenic), genotype, health/immune status, drug or test naïve, previous procedures, etc.

³ <https://www.nc3rs.org.uk/arrive-guidelines>

Sample Size	<p>a) Specify the total number of animals used in each experiment, and the number of animals in each experimental group.</p> <p>b) Explain how the number of animals was arrived at. Provide details of any sample size calculation used.</p> <p>c) Indicate the number of independent replications of each experiment, if relevant.</p>
Experimental Outcomes	Details regarding the experimental outcomes to be assessed.
Planned statistical analysis	<p>An explanation of how the number of animals was arrived at, including power calculations, if appropriate, or other supporting information to demonstrate that the findings will be robust.</p> <p>A brief overview of the planned statistical analyses in relation to the choice of sample size, along with details of any statistical advice available.</p>

*Table adapted from the **UK NC3Rs ARRIVE** Guidelines³

3 Human Studies

For studies involving human participants or human material, ethical approval must be obtained from the relevant national or local ethics committee prior to the start of the project. SFI only permits early stage regulated clinical trials (Phase I or combined Phase I/II) and investigations to be undertaken under the scope of the following SFI programmes: SFI Research Centres, Spokes, and Strategic Partnerships in addition to SFI Research Professorship where the successful candidate will become a Co-Principal Investigator within an SFI Research Centre. Clinical trials and investigations requiring approval by the Health Products Regulatory Authority (HPRA) will not be permitted through other SFI funding programmes.

Funding requests for early stage research involving human volunteers and/or human samples that does not require regulatory approval are permitted under SFI funding programmes. Where there is any doubt, applicants are advised to contact the HPRA prior to submission to ensure eligibility and are required to indicate in their application that the proposed study does not require HPRA approval.

Furthermore, in line with a current directive from its parent Government Department, research funded by SFI must not comprise any component of the following:

- Research intended to create human embryos solely for the purpose of research or for the purpose of stem cell procurement, including by means of somatic cell nuclear transfer
- Research using human embryonic stem cells or tissues.

In order to allow proper evaluation of the scientific merit of applications for funding, applicants who propose research involving human participants and/or biological material must provide the information requested in **Table 2** below within the description of their proposed research.

In addition, as part of an SFI grant proposal, applicants are required to complete a questionnaire relating to ethical issues see **Section 5** (Ethical Issues Table) of this document.

Table 2-Information required for research involving the use of human participants or material

Information	Details to be provided in the main body of your Grant Proposal
Ethical Approval	Ethical approval is required for all research work funded by SFI that involves human participants or human material (including tissue). Applicants should state by whom and when the research programme will be reviewed and specify any other regulatory approvals that have been obtained, or will be sought. Applicants should allow sufficient time to obtain Ethical approval. SFI will require evidence that relevant ethical and regulatory approval has been granted prior to the award commencing.
Study Recruitment	Applicants are asked to provide specific details on study recruitment procedures including inclusion and exclusion criteria and informed consent procedures. These should include relevant, additional details for specific groups including children/minors, patients and vulnerable groups.
Clinical Research Infrastructure	Applicants are asked to provide specific details where they have access to, or plan to access, the support/services of a Clinical Research Facility/Centre (CRF/C) at study design and/or implementation phase. The following information must be provided: <ul style="list-style-type: none"> • Name and address of the CRF/C • Information on the nature and stage/s of the input/advice/collaboration/service • Rationale for the choice of facility/centre Information on the costs of providing the service/input, setting out where this is provided in-kind, from additional funding or requested from the project budget Evidence of this support/service must be provided to SFI in the form of a letter from the Director of the facility at the time of application for funding.

Clinical Trials	<p>SFI will only support trials that are fully compliant with the SFI Clinical Trial and Clinical Investigation Policy⁴ and the requirements of the HPRA. For applications including clinical studies that fall within the scope of the EU Clinical Trials Directive, approval from the HPRA is required. Necessary authorisations for trials involving medical devices differ depending on the device. Applicants are responsible for ensuring that all necessary approvals are in place and provided to SFI prior to study initiation.</p> <ul style="list-style-type: none"> • Sponsor: Plans for appropriate sponsorship arrangements must be included in the application i.e. Letters of Support must be provided from sponsors or potential sponsors. Please note that SFI cannot act as sponsor. • Steering Committee: Applicants should provide details on the establishment and membership of an independent Trial Steering Committee. If any other type of independent monitor is to be implemented, please indicate and provide any relevant details. • Study Registration: Applicants are asked to outline plans for the registration of their trial or investigation on a publicly available, free to access, searchable clinical trial or investigation registry such as the International Standard Randomised Controlled Trial Register (ISRCTN) or ClinicalTrials.gov. • Multi-Jurisdictional Studies: Subject to pre-approval from SFI, applicants should provide relevant details in relation to clinical research activities outside of the Republic of Ireland or partnerships with international Collaborators.
Human Cells/Tissues	<p>Applicants are asked to provide details on the cells or tissues types, including the source of the material.</p>
Biobanking	<p>Applicants are asked to describe how they will comply with international best practice for biobanking components in this research programme⁵⁶⁷⁸, with particular regard to quality of sample collection, processing, annotation and storage, and describing data protection measures where appropriate. Please also reference relevant guidelines/standards you will use.</p>

⁴ <http://www.sfi.ie/funding/grant-policies/sfi-clinical-trial-and-clinical-investigation-policy.html>

⁵ <http://www.oecd.org/science/biotech/44054609.pdf>

⁶ <http://www.isber.org/?page=BPR>

⁷ <http://www.molecularmedicineireland.ie/resources/biobanking-guidelines/>

⁸ <https://biospecimens.cancer.gov/bestpractices/2011-NCIBestPractices.pdf>

Protection of Personal Data	Compliance with legislation and EU rules on data protection is required. Applicants are asked to provide that appropriate safeguards will be put in place and provide examples e.g. details of their procedures for data collection, storage, protection, retention, transfer, destruction or re-use (including, collection methodology (digital recording, picture, etc.), methods of storage and exchange.
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4 Clinical Trials

SFI permits early-stage regulated clinical trials (Phase I or combined Phase I/II) and investigations to be undertaken **only** under the scope of the SFI programmes, outlined in **Section 3** of this document. Investigator(s) proposing to undertake clinical trials should avail of the input, advice, services and/or support of a Clinical Research Facility/Centre (CRF/CRC), a Clinical Trials Unit (CTU) or other specialist facilities at the study design stage and the clinical trial must be under the governance and oversight of an established Clinical Research Facility/Centre. SFI cannot take on the role of sponsor; therefore, appropriate sponsorship arrangements, satisfactory to SFI, must be made in compliance with relevant EU Clinical Trials Directives and related regulations, or, where relevant, the EU Medical Device Directives. Details of Sponsors, including Letters of Support from sponsors, must be provided to SFI prior to initiation of the clinical trial.

It is the responsibility of the Principal Investigator to ensure that the clinical trial is conducted in a manner that is compliant with all applicable legislation, regulations and guidelines, including the **Guidelines for Good Clinical Practice**⁹. Furthermore, evidence that the requisite ethical and competent authority approval has been secured, and that the appropriate insurance cover (including no-fault and legal liability insurance as deemed appropriate by SFI) is in place to cover the liability of all parties including the Principal Investigator, Research Body and Sponsor, must be provided to SFI prior to initiation of the clinical trial. Responsibilities of the Principal Investigator shall also include that the clinical trial will be well managed and monitored in respect of any inherent risks, that the principles of good clinical practice are applied effectively, and that sound safety reporting systems are put in place.

The award shall be subject to such terms and conditions for clinical trials at the discretion of SFI and notified to the Research Body. In the case of any clinical trials that may be multi-site, SFI may apply additional terms and conditions.

Please note that payment on awards involving clinical trials will not be issued until evidence of ethical and competent authority approval and the requisite insurance cover has been submitted to SFI.

Additionally, the host Research Body and/or Sponsor (as stipulated by SFI) must fully indemnify SFI from all claims and proceedings arising from the trial by submitting a signed indemnity to SFI using a template to be provided.

⁹ http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002874.pdf

5 Ethical Issues Table

As part of an SFI grant proposal, applicants are required to complete a questionnaire relating to ethical issues. These questions are outlined in the table below.

Section	Ethics Issues Table	
	Applicant Name	
	Proposal Title	
	Research Body of Applicant	
Use of Animals in Research		
1	Does your research involve the use of animals?	Yes <input type="checkbox"/> No <input type="checkbox"/>
Human Participants / Material / Data		
2	Does your research involve human participants, human biological material, or identifiable/potentially identifiable data?	Yes <input type="checkbox"/> No <input type="checkbox"/> If No, please review entire checklist but do not complete Sections 3-19. If Yes, complete all remaining sections.
Human Embryos/Foetuses		
3	Does your research involve Human Embryonic Stem Cells (hESCs)? <i>Research using human embryonic stem cells or tissues will not be supported by SFI.</i>	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
Humans		
4	Does your research involve human participants?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
5	Are they vulnerable individuals or groups, patients or persons unable to give informed consent (including children/minors)?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
6	In the course of your research programme, do you propose to use Clinical Research Facility/Centre (CRF/C) facilities?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
7	Is a formal sponsor required for the research programme?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
8	Does your research involve physical interventions on the study participants?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
9	Does your research involve a clinical trial or investigation?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>

10	Is the clinical trial or investigation covered by the EU Clinical Trials Directive?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
11	If yes, please confirm that HPRRA approval will be obtained prior to study commencement.	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
12	Will an independent Trial Steering Committee (TSC) be established?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
13	Will the trial or investigation be registered in a publicly available, free to access, searchable clinical trial or investigation registry?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
14	Will the requisite insurance cover be sought for the clinical trial or investigation and evidence of cover submitted to SFI prior to trial initiation?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
15	Does this clinical trial or investigation involve activities outside of the Republic of Ireland or partnerships with international Collaborators?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
Human cells/Tissues		
16	Does your research involve human cells or tissues?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
17	Does your application include an element of biobanking?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
Personal Data		
18	Does your research involve personal data collection and/or processing?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>
19	If any potentially commercially exploitable results may be based upon tissues or samples derived from human participants, will appropriate informed consent for such use be sought?	Yes <input type="checkbox"/> No <input type="checkbox"/> N/A <input type="checkbox"/>