Application summary

Application title
This should be the title of your proposed project.

Proposed duration of funding (months)
The maximum period of support is two years (24 months).

Proposed start date	
You should allow at least two months between the submission of the proposal and the proposed start date.	

Name of administering organisation
Please enter the name of the organisation where you intend to hold the award. If your application is successful, this is the organisation that will be responsible for administering the award.

Lead applicant's address at administering organisation	
Department/Division	
Organisation	
Street	
City/Town	
Postcode/Zipcode	
Country	
Please enter the address where you will be working at the administering organisation. If your application is successful, this is the address that will be used in the award letter.	

Research funding area Please select from the drop-down list the funding area that you consider your research falls under
The research funding area selected is used to automatically route your application form to the appropriate Wellcome Trust grants team when it arrives at the Trust. Please note that, when received, we may reallocate your application to another research funding area if we consider it appropriate.

Lead applicant

Lead applicant details	
Full Name	
Department	
Division	
Organisation	
Address Line 1	
City/Town	
Postcode	
Country	
Telephone No.	
Email Address	

ORCID iD	
ORCID iD	

Lead applicants must add their ORCID iD. Find out more about ORCID on our website.

Career history (current/most recent first)				
From	**To**	**Position**	**Organisation**	

Please provide details of your current position (if applicable) and all previous posts held, listing most recent first.

You are expected to be in receipt of salary funding for the duration of the grant requested.

Education/training				
From	**To**	**Qualification**	**Subject**	**Organisation**

Please provide details of relevant education/training, listing the most recent first.

Type of personal salary support

Source(s) of personal salary support for the proposed duration of award

Your source of salary may have an impact on your eligibility to apply for Wellcome Trust funding. Please, therefore, state the source of funding of the salary of your post (for example, if it is funded through your organisation's block grant from a Higher Education Funding Council). If your salary is being funded from more than one source, please provide details of all funding sources, including their relative contributions. If there are any ties on intellectual property rights or publications arising from the research you undertake, please contact the Wellcome Trust for advice. Restrictions on intellectual property may affect your ability to apply to the Wellcome Trust.

Clinical status	

Do you have a medical/veterinary degree?	

Please note that this includes dental and clinical psychology degrees.

Please specify

Are you clinically active?	

What is your specialty?

Please choose your specialty from the dropdown list – if it is not on the list, select 'Other' and specify.

Please specify

Career breaks Have you had any career breaks or periods of part-time work, for example parental or long-term sick leave?	

We encourage applications from researchers who have taken career breaks, and wish to ensure that any such breaks are duly taken into account when considering your track record. Please state when and for what period of time you took a break, or were working on a part-time basis. We are not seeking any information on the reasons for this break so please do not provide this here, including sharing any sensitive personal health information.

Please provide details

Do you wish to undertake this award part time?	

If you wish to undertake this award part time, you must be employed on a part-time basis. Please contact the Trust to discuss your requirements.

Career contributions
What are your most important research-related contributions to date? These may include contributions to health policy or practice, or to technology or product discovery and development. (350 words max.)

The examples you choose can be taken from any stage of your research career. In each case, please state what the achievement was, when it came about, why you think it is important and what impact it has had.

Research outputs
List up to 20 of your most significant research outputs, ensuring that at least five of these are from the last five years. For 10 of these outputs, provide a statement describing their significance and your contribution (up to 50 words per output).

Research outputs may include (but are not limited to):

- Peer-reviewed publications and preprints
- datasets, software and research materials
- Inventions, patents and commercial activity

For original research publications indicate those arising from Wellcome-funded grants in **bold**, and provide the PubMed Central ID (PMCID) reference for each of these. Please refer to guidance notes.

Publications should be in chronological order with the most recent first. Please give citation in full, including title of paper and all authors. Citations to preprints should state "Preprint", the repository name and the articles persistent identifier (e.g DOI).*

*(*All authors, unless more than 10, in which case please use 'et al', ensuring that your position as author remains clear.)*

You should include here systematic reviews (e.g. Cochrane Reviews) and meta analyses, but exclude abstracts and literature reviews. We encourage the inclusion of articles published via open research publishing platforms, such as Wellcome Open Research, providing they have passed peer review.

Preprints, i.e. complete manuscripts that have been submitted to a preprint repository or service (e.g. bioRxiv, PeerJ Preprints, arXiv, SocArXiv or PsyArXiv), can be included only if they have a permanent identifier such as a DOI or arXiv identifier.

The Wellcome Trust's open access policy requires all original peer-reviewed research papers, supported in whole or in part by Trust funding, to be made available through PubMed Central (PMC) and Europe PMC as soon as possible and in any event within six months of the journal publisher's official date of final publication.

The PubMed Central ID (PMCID) is the unique identifier assigned to every full text paper in PubMed Central (PMC) and Europe PMC.

Please note that:

> *We actively monitor compliance with our open access policy and successful applicants will be asked to provide a full list of all their Wellcome-funded research papers, and confirm compliance by providing the PMCID identifier for these, before the award letter can be issued.*

For further guidance, please refer to the Trust's open access policy statement and authors' information

Total number of peer-reviewed publications which you have authored/co-authored. Please exclude abstracts and literature reviews.	

You should include here systematic reviews and meta analyses. We encourage the inclusion of articles published via open research publishing platforms, such as Wellcome Open Research, providing they have passed peer review.

Current and recent research funding (including Wellcome Trust grants)
Please list all held in the last five years and any key prior grants (list the most recent first). State the name of the awarding body, name(s) of grantholder(s), title of project, amounts awarded, your role in the project, and start and end dates of support. For all active grants, indicate the number of hours per week that are spent on each project. For grants where you are a co-investigator, indicate the amount of funding you receive.

In addition to research grants, please include details of any recurrent or core funding support that you have held in the last five years, including any Wellcome Trust awards. Please state clearly your role in obtaining the awards, for example, whether you held them in your own right as lead applicant, co-applicant, or as part of a consortium. Please state the value of your own component of the award and the percentage of your time spent on the research.

Organisational support Please provide details of any support (space, facilities, equipment, infrastructure, technical, financial or other assistance) that will be available to you at your organisation (200 words max.)

Collaborators

Will you require any key collaborators for this proposal?	
*These are collaborators who will be making a **significant** contribution towards the proposed research, for example, assisting with specific elements of the research, or providing access to key resources, reagents or samples. If the answer is 'Yes', you will be asked to provide information of these collaborators and to confirm their willingness to participate in the proposed research.*	

Please list any key collaborators* (name and organisation) and provide a very brief outline of their role in the proposed research. **The collaborators named may be replaced with suitable alternatives should it be necessary or appropriate to do so.*

I confirm that the collaborators named above have agreed to be involved, as described, in the proposed research and are willing for their details to be included as part of this application.

Related applications

Is this or a similar application for funding currently under consideration elsewhere?	

Please provide name(s) of funding organisation(s) and decision date(s)

Is this a resubmission of an application submitted to the Trust within the last 24 months?	
Please see the scheme page on the Wellcome Trust website for guidance before resubmitting an application.	

Project summary

Please provide a summary of your proposal, including key goals. (200 words max.)

This will be used as a short form 'abstract' and is necessary to enable the Trust to classify your proposal by subject area. This synopsis may be disclosed on the Wellcome Trust website and may be used for other publishing purposes. For all our awards, we publish the synopsis as part of the grant details made available externally.

The summary should be as complete as possible within the word limit, and should include key words which best describe the proposal to enable text searching.

Lay summary

Please provide a summary of your proposed research that people who may not be familiar with the subject can understand. We may edit your summary and then use it to describe your research on our website and elsewhere.

You don't need to oversimplify your research, but try to explain it as clearly as possible. You should write in the first person ("I" and "we") and structure your summary in this order:

- *background to the research problem*
- *your approach*
- *expected impact of your work.*

Example of a lay summary

In response to stress and environmental changes, bacteria generate hundreds of small RNA molecules that have key roles in regulating gene expression. This process of riboregulation involves chaperone proteins that facilitate the actions of regulatory RNAs, and enzymes that affect RNA transcript lifetimes. I aim to understand the molecular basis of riboregulation by taking a multidisciplinary approach. I will use biochemical and structural analyses, including cryoEM and cryoET, to visualise how RNA transcripts are captured and channelled to active sites, either for degradation or processing. I will also identify the RNA targets of chaperone proteins and the degradative machinery, and explore whether the patterns change with physiological state or during the cell cycle, and why. These studies will help to explain how small RNAs enhance the speed and accuracy of bacterial genetic regulation, enriching the capacity of the simplest organisms to exhibit complex behaviour.

Details of proposal

Please detail the following information: (a) aims of the project; (b) the work to be carried out; (c) the expected outcomes; and (d) how this will lead to a larger study (1,400 words maximum).

*No more than **1,400** words should be used to describe the proposal, excluding figures. You may provide your answer to this question in text entry format or as a PDF attachment. If you are uploading your proposal, the uploaded document must be in 11 point Arial font and portrait format.*

You may submit up to three figures in support of the proposal. These may be embedded in the text or attached as supporting material.

You must provide all information pertinent to your grant proposal within the application form (it is not acceptable to refer to additional unpublished information on personal websites).

Approach and methods to be used
Details of experimental design for animal studies should be provided as part of the justification for animals in the 'Proposals involving animals' section of the form.

For epidemiological, demographic, case control, cohort and related studies, give a full and detailed analysis of the study design, including details of any validation already undertaken or rationale for using standard protocols. Particular attention should be given to power calculations, sample size justification and, where appropriate, case definition and inclusion/exclusion criteria.

Clinical trials applications
If you are requesting support for a clinical trial, you must provide full details, including study design, in the 'clinical trial' section of the form.

(1400 words max.)

Does your proposal involve a clinical trial?	

The World Health Organization defines a clinical trial as: "any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes. Interventions include, but are not restricted to, drugs, cells and other biological products, surgical procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc."

For further information, refer to the Wellcome Trust's clinical trials policy statement and information for applicants.

If your proposal involves a clinical trial, you should provide details of it within this application form. If your proposal involves more than one clinical trial, please contact the Wellcome Trust for guidance.

Clinical trial details

What are the proposed participating centres, and the roles of the clinical trial team members? Provide details of any activity to be undertaken by a third party, and comment on the plans to ensure the presence of a formal contract.
(200 words max.)

Please describe the study design, including planned interventions (experimental and control), duration of treatment, and any potential significant risks to participants. Details of any investigational product should be provided with particular regard to manufacture, quality and consistency.
(300 words max.)

Describe the inclusion/exclusion criteria. What are the proposed methods for protecting against sources of bias? What are the proposed arrangements for allocating participants to trial groups?
(200 words max.)

What are the envisaged primary and secondary outcome measures, and how will these be assessed at follow up? Describe the proposed frequency and duration of follow up and any anticipated problems with non-compliance and/or loss to follow up.
(200 words max.)

Detail and justify the sample size and proposed statistical analysis, including any interim analyses and/or subgroup analyses. Outline and justify the strategy for recruitment.
(200 words max.)

How have patients, patient advocacy groups or communities been involved in developing the clinical aspects of this proposal?
(300 words max.)

Describe anticipated regulatory and governance approvals, and the proposed arrangements for trial management. What is the proposed membership of the Trial Steering Committee and the Data Monitoring and Ethics Committees?
(200 words max.)

You may submit additional information of up to three figures in support of the proposal.

These figures may be embedded in the text of your file upload or attached here as a separate file. If you choose to embed this information, any text present can be excluded from the word count.

Please note that this form asks for all the information we require to consider your application. You should not provide additional information (e.g. letters of support) unless specifically requested in the form.

References
You should give the citation in full, including title of paper and all authors.

You may provide up to the equivalent of two A4 pages of references. Please ensure that all references included are pertinent to your research proposal and are cited in full, including all authors, the full title of each publication, journal title, year, volume and pages. Citations to preprints should state "Preprint", the repository name and the article persistent identifier (e.g DOI).

References with more than 10 authors may be shortened to et al, but please ensure that your position as author (if applicable) remains clear.

Are there any papers listed in your 'References' section as being "in press" that you wish to submit to us?	

Upload papers "in press"

Please submit papers "in press" as a single PDF.

Location of activity

Will the funded activity take place at more than one location?	

It is important that we are able to track the countries and organisations where research activity is taking place and the approximate proportion of the funds that will be spent at each location.

You should list any locations where you will be conducting research or redirecting funds outside of the administering organisation. This includes, but is not limited to, anywhere in receipt of indirect funding, fieldwork sites, and time spent working in another institution/laboratory. This does not include conference attendance.

Salary costs, if requested, should be attributed to the employing organisation.

For each location, select the country and, where applicable, state the organisation (please include the administering organisation). Indicate the approximate percentage of the total funds that will be spent in each location, entering zero for locations where activity will take place but no significant funds will be spent. Salary costs, if requested, should be attributed to the employing organisation.		
Country	**Organisation**	**Percentage of funds**

Costs requested and justification

Please select the currency in which you wish to apply.

It is expected that costs within the application will be submitted in the currency which, in the view of the applicant(s), best enables the activity to be undertaken. In the majority of cases, the currency specified is likely to be the local currency. Where this is not the case, please explain the reasons for selecting the chosen currency.

Please refer to the Wellcome Trust's website for further information regarding selecting a currency.

If at any point, the Wellcome Trust is unable to award in the currency requested, discussions will be held with the administering organisation to decide whether an alternative currency should be used. If you have any concerns that the currency you would like to request may not be readily available, please contact the Wellcome Trust by e-mailing: grantpayments@wellcome.ac.uk.

Is the selected currency your local currency?	

What is your local currency?	

Please state clearly the reasons for requesting costs in the selected currency and the exchange rate used (100 words max.)

Synchrotron radiation sources Will the proposed research require access to a synchrotron source?	

We wish to collect data on access to synchrotron sources for information purposes.

Applicants should apply directly to the synchrotron facility they wish to use. These facilities are normally free at the point of access for researchers who are prepared to publish their results in the public domain. If this is not the case for the facility that you have selected, access costs may be requested from the Wellcome Trust.

Which source(s) will you be applying to? (Please select all that apply)

Please specify:

Are you requesting costs from the Trust?	

These facilities are normally free at the point of access for researchers who are prepared to publish their results in the public domain.

In instances where the costs of travel and subsistence will not be met by the facility, they may be requested from us. Please include these costs under 'Travel and subsistence'.

Are you requesting research management costs under the miscellaneous costs heading? (for applicants from low- and middle-income countries only)	

Please upload a letter from the Finance Director of the host organisation confirming that your request for research management costs is a true representation of the costs incurred.

Justification for resources requested
Please provide a brief justification for the resources requested.
(300 words max.)

Full economic costing

Is your organisation based in the UK?	

Is your organisation calculating the full economic cost of this proposal?	

What is the total full economic cost (£)?	

*Please provide the **total** full economic cost of your research proposal. Costs should be inflated at the recognised percentage rate currently used by the organisation.*

Research involving human participants, human biological material and identifiable data

Does your project involve human participants, human biological material, or identifiable/potentially identifiable data?	

The following notes relating to 'Research involving human participants, human biological material and identifiable data' are intended to provide guidance and advice in completing the form, rather than a comprehensive review of the legal and regulatory environment in which the application is made.

The World Health Organization defines research with human subjects as "any social science, biomedical, behavioural, or epidemiological activity that entails systematic collection or analysis of data with the intent to generate new knowledge, in which human beings i) are exposed to manipulation, intervention, observation, or other interaction with investigators either directly or through alteration of their environment, or ii) become individually identifiable through investigator's collection, preparation, or use of biological material or medical or other records."

The Wellcome Trust policy position on research involving human participants can be found on the Wellcome Trust website (www.wellcome.ac.uk/wellcome-trust-policy-position-research-involving-human-participants)

Ethical approval (usually from the appropriate National Health Service (NHS) research ethics committees) is required for all Wellcome Trust funded research involving human participants, biological samples or personal data. Personal data, in the context of the 1998 Data Protection Act (Section 3.2, and Annex 3), comprise information about living people who can be identified from the data, or from combinations of the data and other information which the person in control of the data has, or is likely to have in future. Any use of personal data or biological samples, relating to living or dead persons,

should conform to MRC guidelines available at: http://www.mrc.ac.uk/documents/pdf/personal-information-in-medical-research/ and http://www.insight.mrc.ac.uk/2015/02/12/getting-the-best-out-of-biological-samples/.

Approval from other regulatory bodies such as the Human Fertilisation and Embryology Authority (HFEA) or the Gene Therapy Advisory Committee in the UK should also be sought where necessary, e.g. research involving human embryos may require a licence from the HFEA (please refer to www.hfea.gov.uk for more information). If your proposal involves research on gene therapy which requires regulatory approval, approval should be sought from your Local Research Ethics Committee, the University's Genetic Manipulation Committee, the Gene Therapy Advisory Committee and the Medicines and Healthcare products Regulatory Agency (MHRA).

The organisation must ensure that ethical approval is in place at all relevant times during the project. For research carried out at multiple sites, ethics committee approval must cover each site.

Where the research, or part of the research, is to be performed outside the UK, independent ethics review must be obtained. For research involving people living in low and middle income countries, see the Wellcome Trust's website (www.wellcome.ac.uk/funding/managing-grant/guidance-notes-research-involving-people-low-and-middle-income-countries).

Please confirm that you have read the Trust's guidance on the feedback of health-related findings in research and that you are in the process of considering your approach to this.

The Wellcome Trust's guidelines on the feedback of health-related findings in research can be found on the Trust's website.

Please state by whom and when the ethics of the project has been, or will be, reviewed and specify any other regulatory approvals that have been obtained, or will be sought.

We reserve the right to see relevant approval documents at any point during the lifetime of the grant, in accordance with our policy position on research involving human participants.

The following notes relating to 'Research involving human participants, human biological material and identifiable data' are intended to provide guidance and advice in completing the form, rather than a comprehensive review of the legal and regulatory environment in which the application is made.

The World Health Organization defines research with human subjects as "any social science, biomedical, behavioural, or epidemiological activity that entails systematic collection or analysis of data with the intent to generate new knowledge, in which human beings i) are exposed to manipulation, intervention, observation, or other interaction with investigators either directly or through alteration of their environment, or ii) become individually identifiable through investigator's collection, preparation, or use of biological material or medical or other records."

The Wellcome Trust policy position on research involving human participants can be found on the Wellcome Trust website (www.wellcome.ac.uk/wellcome-trust-policy-position-research-involving-human-participants)

Ethical approval (usually from the appropriate National Health Service (NHS) research ethics committees) is required for all Wellcome Trust funded research involving human participants, biological samples or personal data. Personal data, in the context of the 1998 Data Protection Act (Section 3.2, and Annex 3), comprise information about living people who can be identified from the data, or from combinations of the data and other information which the person in control of the data has, or is likely to have in future. Any use of personal data or biological samples, relating to living or dead persons, should conform to MRC guidelines available at: http://www.mrc.ac.uk/documents/pdf/personal-information-in-medical-research/ and http://www.insight.mrc.ac.uk/2015/02/12/getting-the-best-out-of-biological-samples/.

Approval from other regulatory bodies such as the Human Fertilisation and Embryology Authority (HFEA) or the Gene Therapy Advisory Committee in the UK should also be sought where necessary, e.g. research involving human embryos may require a licence from the HFEA (please refer to www.hfea.gov.uk for more information). If your proposal involves research on gene therapy which requires regulatory approval, approval should be sought from your Local Research Ethics Committee, the University's Genetic Manipulation Committee, the Gene Therapy Advisory Committee and the Medicines and Healthcare products Regulatory Agency (MHRA).

The organisation must ensure that ethical approval is in place at all relevant times during the project. For research carried out at multiple sites, ethics committee approval must cover each site.

Where the research, or part of the research, is to be performed outside the UK, independent ethics review must be obtained. For research involving people living in low and middle income countries, see the Wellcome Trust's website (www.wellcome.ac.uk/funding/managing-grant/guidance-notes-research-involving-people-low-and-middle-income-countries).

Is the proposed clinical trial covered by The Medicines for Human Use (Clinical Trials) Regulations in the UK?	

Under the Medicines for Human Use (Clinical Trials) Regulations 2004, applicants must identify a sponsor (which will normally be either a university or NHS Trust) who fully understands the responsibilities and costs associated with assuming this role. Please note that the Wellcome Trust cannot act as sponsor.

Please confirm that the trial will be registered on the International Standard Randomised Controlled Trial Number Register (ISRCTN), ClinicalTrials.gov, or on another register listed on the WHO International Clinical Trials Registry Platform (ICTRP).

In the course of your project, do you propose to use facilities within the National Health Service (NHS) or to involve patients being cared for by the NHS?	

By agreeing to fund work which requires NHS support, the Wellcome Trust is agreeing to abide by the Statement of Partnership on Non-commercial R&D in the NHS in England (and the corresponding statements in Northern Ireland, Scotland, and Wales). Researchers must therefore meet the obligations of the Partnership and may not carry out any research until the NHS has given its consent.

The Research Governance Framework for Health & Social Care, published by the Department of Health in England can be downloaded from the Department of Health website http://www.dh.gov.uk/health/category/research. Please note that the Wellcome Trust cannot act as sponsor.

Is a formal sponsor required for the project, for example under the Medicines for Human Use (Clinical Trials) Regulations or the Research Governance Framework for Health and Social Care and equivalent guidance?	

Please indicate which organisation(s) has/have agreed to fulfil this role. Please note that the Wellcome Trust cannot act as sponsor.

If any potentially commercially exploitable results may be based upon tissues or samples derived from human participants, please confirm that there has been appropriate informed consent for such use.

Please answer 'not applicable' if no potentially commercially exploitable results (based on human tissues or samples) will be produced during the course of the proposed research.

Proposals involving animals

Please indicate which of the following apply: *(Proposal involves the use of animals, Proposal involves the use of animal tissue, Neither of the above)*

The following notes relating to 'Proposals involving animals' are intended to provide guidance and advice in completing the form, rather than a comprehensive review of the legal and regulatory environment in which the application is made.

Applicants must refer to the Wellcome Trust's policy on the use of animals in medical and veterinary research on the Trust's website.

In all animal experiments supported by the Wellcome Trust, the principles of reduction, replacement and refinement will apply. In all experimental studies, it is the responsibility of the applicants to actively consider:

- *the complete replacement of live animals with tissues derived from either animals or humans;*
- *the possibilities of reducing the numbers of animals that need to be used;*
- *refining the experimental design in order to obtain the maximum amount of information from the minimum number of animals.*

Refined methods in animal research are those which alleviate or minimise any adverse effects for the animals involved, and/or enhance animal welfare. Refinements may be applied at any stage in the life of an animal. Thus, refinement encompasses all aspects of a procedure, including:

- *the source, transport, husbandry and environment of the animals involved;*
- *the experimental design (e.g. the choice of species and the group size employed);*
- *the techniques applied;*
- *the end points of the procedures; and*
- *care of the animals before, during and after a procedure.*

For further information regarding the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs), please see www.nc3rs.org.uk

Monoclonal antibodies
The use of ascitic animals for monoclonal antibodies (mAb) production in vivo should only be proposed when in vitro attempts at mAb production have failed or the use of animals is considered justified for specific diagnostic or therapeutic products. If in vitro production methods are not considered to be suitable, a full explanation must be given.

Indicate which of the following species will be used
(Primate, Cat, Dog, Equidae, Pig, Genetically Altered Animals, Other animals)

All applications involving the use of primates, cats, dogs and equidae animals, or their tissue/data will be further reviewed by the NC3Rs.

All proposed research projects involving genetically altered mice are expected to consider the principles of welfare assessment set out on the NC3Rs website: https://www.nc3rs.org.uk/generation-and-breeding-genetically-altered-mice.

Click 'Add...' to enter details of the animal species and numbers required

Animal species	**Strain (if appropriate)**	**Total number required to carry out proposed work**
-		

Please provide details on any animal species which are to be used in the proposed project. Please provide the total number to be used (this may differ from the number to be purchased, maintained etc.)

Please justify the animal numbers. A justification of the proposed sample size must be given along with details of the planned statistical analyses. Describe experimental design, including any plans to reduce bias such as blinding or randomisation if appropriate. Power calculations must be included in this section if appropriate. (1,000 words max.)

You may provide your answer to this question in text entry format or as a PDF attachment. If you are uploading your answer, the uploaded document must be in 11 point Arial font and portrait format.

For each species, please ensure that adequate experimental detail is provided to justify both the use and number of

animals. This should include:

- *definition of unit of analysis (i.e. N referring to animal or sample number);*
- *means of avoidance of bias (e.g. blinding or randomisation);*
- *statistical analysis to be used and explanation of how sample and/or group size was derived;*
- *where repeated measures are used, the number of time points;*
- *an indication of number of replications of each experiment to mitigate spurious non-replicable results.*

Tables and figures may be included in this section to help justify animal numbers. For additional guidance on designing animal experiments please see the NC3Rs Experimental Design Assistant: https://www.nc3rs.org.uk/experimental-design-assistant-eda

(1000 words max.)

Why are the species to be used the most appropriate?
(250 words max.)

It is particularly important to justify the species when an animal is being used as a model for a human physiological or pathological condition.

Does your proposal include procedures to be carried out on animals in the UK which require a Home Office licence? If yes, refer to notes.	

The organisation must ensure that research involving the use of animals complies at all times with UK laws and regulations.

If your proposal involves the use of animals, what would be the severity of the procedures?

Guidance on assessing the severity of a procedure is available from the Home Office website: http://www.homeoffice.gov.uk/science-research/animal-research/

Please provide details of any moderate, severe or non-recovery procedures
(250 words max.)

Does your proposal involve the use of animals or animal tissue outside the UK?	

Animal research conducted outside the UK must, as a minimum standard, be carried out in accordance with the principles of UK law and regulation. Please confirm that proposed animal work outside of the UK will comply with these principles.
(1000 words max.)

Law and regulatory standards often vary from country to country. If experiments are to be carried out on animals outside the UK, the experiments proposed must be performed to standards which accord with the principles of UK legislation. Furthermore, the housing and care of animals must similarly accord with the standards and principles of UK legislation.

Please refer to NC3Rs guidance on carrying out work abroad and choosing contractors: https://www.nc3rs.org.uk/news/choosing-contractors-animal-research

Why is animal use necessary: are there any other possible approaches? (250 words max.)
Please specify if there are any other procedures of less severity that could be used.

Non-human primates

If you are exclusively using already generated tissue or data in the proposed experiments please answer all relevant questions as thoroughly as possible, in particular the questions relating to housing and procedures. Non-relevant questions can be answered with 'N/A', but please note that we may request additional information if necessary for assessment.

Do the facilities and practices, and the proposed research comply with the principles set out in the 'National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs) Guidelines: Primate accommodation, care and use' ?	

Please explain why not

Will it be necessary to transport the non-human primates (i.e. from breeding facility and within the host organisation environment)?	

Indicate approximate journey times and the measures that will be taken to minimise the potential stress during transport.

Please provide details of the housing for the animals, e.g. enclosure size, environmental enrichment.

Will single housing of the non-human primates be necessary at any time?	

Please provide details in terms of the justification for single housing, its duration, and what additional resources will be provided to the animals to minimise the impact on animal welfare.

Describe the experimental procedures involved and how any pain, suffering, distress and/or lasting harm will be minimised. Have the procedures been recently reviewed by the Named Veterinary Surgeon (NVS), Named Animal Care and Welfare Officer (NACWO) and Animal Welfare and Ethical Review Body (AWERB)?

Will any of the experimental procedures involve food and/or water restriction?	

Justify why this is necessary and outline what alternatives have been considered.

Will any of the experimental procedures involve restraint?	

What alternatives have been considered? Describe the nature of the restraint, its duration and frequency, and what will be done to avoid distress.

What prior experience and training in non-human primate use, care and welfare have the staff named in the application had? What provision is made for continuing professional development in these areas?

Will any of the staff involved require specific training for any of the procedures concerned?	

Please provide details of the training needed and where it will be undertaken.

Cats, Dogs, Equidae and Pigs

If you are exclusively using already generated tissue or data in the proposed experiments please answer all relevant questions as thoroughly as possible, in particular the questions relating to housing and procedures. Non-relevant questions can be answered with 'N/A', but please note that we may request additional information if necessary for assessment.

From where will the animals be sourced?

Will it be necessary to transport the animals?	

Indicate approximate journey times and the measures that will be taken to minimise the potential stress during transport.

Are animals to be imported?	

Where animals are to be imported, what journey times have been agreed with the Home Office? Describe the conditions for the animals at the breeding establishment and how the potential stress during transport will be minimised.

Please provide details of the housing for the animals, e.g. enclosure size, environmental enrichment.

Please see the NC3Rs guidance on animal housing and husbandry for further details: https://www.nc3rs.org.uk/3rs-resources/housing-and-husbandry

Will single housing of the animals be necessary at any time?	

Please provide details in terms of the justification for single housing, its duration, and what additional resources will be provided to the animals to minimise the impact of the single housing.

Describe the experimental procedures involved and how any pain, suffering, distress and/or lasting harm will be minimised. Have the procedures been recently reviewed by the Named Veterinary Surgeon (NVS), Named Animal Care and Welfare Officer (NACWO) and Animal Welfare and Ethical Review Body (AWERB)?

What adverse effects might the animals experience? List the clinical and other signs that will be monitored, the frequency of monitoring and, where relevant, the humane endpoint criteria established for the study. (1000 words max.)

Will any of the experimental procedures involve restraint?	

What alternatives have been considered? Describe the nature of the restraint, its duration and frequency, and what will be done to avoid distress.

What prior experience and training in animal use, care and welfare will be required of the staff named in the application? What provision is made for continuing professional development in these areas?

Will any of the staff involved require specific training for any of the procedures concerned?	

Please provide details of the training needed and where it will be undertaken.

Risks of research misuse

Please confirm that you have considered whether your proposed research could generate outcomes that could be misused for harmful purposes.

In preparing research proposals, Wellcome wishes to encourage applicants and their host organisations to consider

carefully any risks that the potential outcomes (information, products or technologies) of the research could be misused for harmful purposes. Such purposes would include actions that pose a significant threat to humans, animals, plants or the environment - including terrorist misuse.

Examples of possible research areas that are associated with dual-use risks of this type, include (but are not restricted to) research that aims to:

- *demonstrate how to render a vaccine ineffective*
- *confer resistance to a therapeutically useful antibiotic or antiviral agent*
- *enhance the virulence of a pathogen or renders a non-pathogen virulent*
- *increase the transmissibility or alter the host range of a pathogen*
- *enable the evasion of diagnostic and detection methods*
- *enable the weaponisation of a biological agent or toxin*
- *generate or reconstitute an eradicated or extinct agent or toxin*

*Where there are judged to be **tangible** (i.e. real and non-hypothetical) risks that the proposed research **will itself** generate outcomes that could be misused to cause harm, researchers and organisations should take appropriate steps to monitor the research as it proceeds and minimise these risks. Risk mitigation could include establishing a process to review dual use risks on an on-going basis through the project and to gain independent expert advice as appropriate. Researchers should also ensure that all members of their team are aware of these risks in progressing their research, and receive appropriate education and training on these issues.*

The identification of tangible risks in a research project should be clearly balanced against the benefits and value that is to be gained for health, science and society. We recognise that most research could conceivably generate results that might hypothetically be misused at some point in the future, and we are not asking applicants to appraise these kinds of remote and hypothetical risks.

Applicants should refer to the joint BBSRC, MRC and Wellcome policy and position statement on managing risks of research misuse (https://wellcome.ac.uk/funding/managing-grant/managing-risks-research-misuse), and our guidelines on good research practice (https://wellcome.ac.uk/funding/managing-grant/policy-good-research-practice).

Have you identified any tangible risks of this type?	

Please briefly describe these risks and the steps that you and your organisation will take to manage them (250 words max.)

Freedom to operate/conflicts of interest

Describe any freedom to operate issues or potential conflicts of interest that have been identified or that might arise and how these will be or have been addressed.

In particular, please consider the following:

- Do any of the individuals involved in the project hold any consultancies or equities in, or directorships of, companies or other organisations that might have an interest in the results of the proposed research?
- Will the proposed research use technology, materials or other inventions that are subject to any patents or other form of intellectual property protection?
- Will any element of the research be subject to agreements with commercial, academic or other organisations, including arrangements with collaborators named in the grant application, that might lead to intellectual property issues or restrictions?

(350 words max.)

Please describe any freedom to operate issues or potential conflicts of interest that may affect your ability to carry out the proposed research and/or to comply with the Trust's grant conditions.

Where the proposed research, in whole or in part, is subject to agreements with commercial, academic or other organisations, e.g. Materials Transfer Agreements, the Wellcome Trust will expect a written assurance from the administering organisation that the terms of any such agreement do not conflict with the Trust's grant conditions, particularly in relation to the publication of research and the granting of research rights.

Please refer to the Wellcome Trust's website for our policy on the relationship between Trust-funded researchers and commercial entities: www.wellcome.ac.uk/funding/managing-grant/policy-relationships-between-trust-funded-researchers-and-commercial-organisations.

Details of our policy on intellectual property can be found in our Grant Conditions www.wellcome.ac.uk/funding/managing-grant/grant-conditions.

Applicants should disclose all relevant information pertinent to their grant proposal, including proprietary information where appropriate, in order to provide the most comprehensive picture of their proposed research.

If no issues have been identified, please enter N/A.

Wellcome Trust supported facilities

Will the project be based in one of the following Wellcome Trust supported facilities: • the Wellcome Trust Sanger Institute • a Wellcome Trust Centre • an Africa and Asia Programme • the Francis Crick Institute?	

We are interested to find out about Trust-funded projects based in these facilities and wish to collect this data for information purposes.

Please specify