Advanced Research + Invention Agency

ARIA

Precision Mitochondria

Call for proposals

Date: 03 October 2025

V1.0

Advanced Research + Invention Agency ARIA

Call for Proposals - Summary

What Is ARIA? ARIA is an R&D funding agency created to unlock technological breakthroughs that benefit the UK and beyond. Created by an Act of Parliament, and sponsored by the Department for Science, Innovation, and Technology, we fund teams of scientists and engineers to pursue research at the edge of what is scientifically and technologically possible.

The Precision Mitochondria Programme. Backed by at least £55m, the overarching goal of this programme is to make the mitochondrial genome programmable *in vivo*. This will be achieved through the creation of a toolkit that allows researchers to deliver nucleic acids into mitochondria, express functional proteins encoded in mtDNA, maintain engineered genomes in the face of heteroplasmy, and transfer engineered mitochondria or mitochondria-targeting engineering payloads into cells and tissues. Success will be measured by a single, **galvanising demonstration**: **the persistent, reproducible expression of a novel gene from engineered mtDNA in a vertebrate system**. Every project we fund must move us closer to achieving this galvanising demonstration.

Why this matters? Engineering mitochondrial DNA has resisted decades of effort. Programme success would provide a catalysing set of tools for future efforts to engineer mitochondria, opening the door to new medicines, new biology, and a new UK-led capability in organelle engineering.

What will we fund? To achieve the galvanising demonstration, we will fund projects across five Technical Areas (TAs):

- **TA1 - Deliver**: introducing nucleic acid payloads into the matrix through the double membranes of vertebrate mitochondria.
- **TA2 - Express**: stably expressing functional proteins or RNAs from introduced sequences within mitochondria.
- **TA3 - Maintain**: ensuring introduced mtDNA persists, replicates, and maintains functionality.
- **TA4 - Transfer**: achieving *in vivo* mitochondrial engineering via transplantation or direct toolkit delivery.
- **TA5 - Standardisation, translation, and reproducibility**: providing programme-wide replication, standardisation, and translation through shared models, methods, and metrology.

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Projects may focus on radical new methods or on steady enabling advances. Anything that helps achieve the galvanising demonstration. We encourage adapting and developing models and tools that can accelerate progress across the programme and improve reproducibility and comparability of results.

Who should apply? In short, whether you are a scientist at a university or research institute, work in biotech R&D, have a startup, or prefer to work independently in your garage, if you are driven to contribute to our mission, we want to hear from you.

We strongly encourage collaborative teams that span multiple TAs, but apply solo if you prefer or haven't identified a team yet — we can assist. We're interested in hearing from any combination of scientists and technologists – be it from Universities, research institutes, startups, established companies, individuals, or new spin-outs – who can meaningfully move the programme toward achieving its objective. Applicants can be based in the UK or abroad (see further information here).

How to apply? Concept papers, described in more detail here, are due 27 October. Submit one to get feedback from the programme team on your proposal, and opt-in to be introduced to potential collaborators ahead of full proposals.

Concept paper applications open	3 October 2025
Webinar	9 October 2025
Concept paper applications close	27 October 2025
Full proposals applications close *	15 January 2026
Successful/Unsuccessful applicants notified	6 March 2026

**Note: We recognise that the application period overlaps with the holiday period. We want to stress that the deadlines are not intended to interfere with holidays and to support this, we have extended the standard ARIA solicitation timeline by two weeks, giving applicants the space to take a break over the holiday period.*

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SECTION 1: Programme Thesis and Overview

This solicitation is derived from the programme thesis Precision Mitochondria – A platform for engineering the mitochondrial genome, in turn derived from the ARIA Opportunity Space: Bioenergetic Engineering. We strongly recommend reading both these documents.

The overarching goal of this programme is to make the mitochondrial genome programmable *in vivo*. This will be achieved through the creation of a foundational toolkit for mitochondrial engineering. The success of this toolkit – and the programme as a whole – will be validated by a single **galvanising demonstration**: **the persistent, reproducible expression of a novel gene from engineered mtDNA in a vertebrate system,** independently replicated across teams.

The ability to introduce, maintain, and express designed genetic material from mitochondria inside living vertebrate systems would transform mitochondria from passive targets into programmable engines of cell function, unlocking a new research and therapeutic modality of comparable significance to monoclonal antibodies or CRISPR-based editing.

A critical step towards achieving the programme goal is the creation of a toolkit that allows researchers to deliver nucleic acids into mitochondria, express functional proteins encoded in mtDNA, maintain engineered genomes in the face of heteroplasmy, and ultimately achieve functional mitochondrial engineering in a living animal. This programme aims to create a foundational, versatile toolkit for mitochondrial genome engineering that is as powerful and accessible as the tools available for bacterial and nuclear genomes today.

Programme success will be demonstrated by the achievement of a single **galvanising demonstration: the persistent, reproducible expression of a novel gene from engineered mtDNA in a vertebrate system**, independently replicated across teams. Successfully achieving this will equip a new generation of researchers with the practical tools needed to finally author, and not just repair, the mitochondrial genome and will pave the way to catalyse new classes of science, medicine, and biotechnology.

Background

Mitochondria are central to eukaryotic life, generating ATP and coordinating key processes including signalling, apoptosis, innate immunity, circadian rhythm, and epigenetic control. Evidence from biology, animal models, and epidemiology together make clear that they sit at the heart of health and healthspan. Defects in protein import, mitophagy, fusion–fission

dynamics, or oxidative phosphorylation compromise normal physiology. Manipulations that increase mitochondrial membrane potential extend lifespan and mobility in C. elegans, and engineered changes in dynamics affect sleep, resilience, and neuroprotection in flies and mice. Epidemiology consistently links mitochondrial dysfunction with type 2 diabetes, cardiovascular disease, neurodegeneration, and many cancers. Yet our ability to investigate the precise nature of that link is severely limited, largely because the tools to manipulate mitochondrial DNA remain rudimentary. Despite their importance, mitochondria remain the last major genome in biology that cannot be programmed, hindering both fundamental science and therapeutic possibility.

Engineering mitochondria at scale would not only unlock research, but enable direct therapeutic routes—as CRISPR did for nuclear editing—with multi-trillion-pound implications for health and beyond:

- Near term – better science, drug development, and clinical translation. A programmable mitochondrial genome would immediately transform research and development. It would allow definitive experiments that move the field from documenting correlation to establishing causation, furthering our understanding and elucidating promising targets for conventional drugs. Robust and precise mtDNA editing enables creation of isogenic controls and rapid disease models that can accelerate and derisk drug development. This is the foundation on which all future therapeutic and industrial applications rest.
- Medium term – a new therapeutic modality. The toolkit would open a domain of intervention where today's drugs and gene therapies cannot reach. It would extend the scope of mitochondrial medicine from rare monogenic disorders to ageing and the common, chronic diseases of metabolism and neurodegeneration.
- Long term – platform industries in health. Programmable mitochondria would enable a new class of subcellular medicines that build on genetic circuits that sense local metabolic or stress states and actuate protective or restorative responses from within the organelle.
- Beyond health - the platform is not confined to medicine. Programmable organelles could underpin innovation in bioenergy, bioremediation, agriculture, and bio-hybrid devices, embedding mitochondria as a designable component in multiple industries.

Making the mitochondrial genome programmable requires solving a cascade of deep biological challenges that have long kept it beyond our reach.

- The first is a challenge of **delivery**: breaching the fortress of the double mitochondrial membrane, a barrier that has historically shielded the organelle's

genome from intervention and has optimized away an innate requirement for nucleic acid transport.

- The second is a challenge of **integration**: ensuring any new genetic code can be expressed and maintained by the organelle's unique and ancient machinery, persisting through replication and avoiding the cell's aggressive quality control systems.
- The final challenge is one of **impact**: moving beyond the single cell to achieve functional mitochondrial engineering *in vivo*, delivering these new capabilities to target tissues within a living animal.

This programme seeks to overcome these long-standing barriers and unite a new, interdisciplinary community, integrating expertise from mitochondrial and cellular biology with pioneers in fields like synthetic biology, virology, nanotechnology, and high-throughput screening. Recent advances in mitochondrial biology, gene delivery, and synthetic biology indicate that the time is ripe for a concerted effort across disciplines. Protein-based mtDNA base editors prove precise changes are possible and impactful. mRNA vaccine platforms have matured lipid nanoparticles and viral vectors into credible delivery systems. High-resolution metrology now allows barcoded tracking of heteroplasmy at single-cell resolution. Mitochondrial transplantation has shown survival and transient functional impact of exogenous organelles in animals.

These do not themselves deliver programmability, but together they create the conditions where a deliberate, integrated push could succeed, ultimately marking the end of mitochondria as the last unprogrammable genome and catalyse a new era of science, medicine, and biotechnology.

SECTION 2: Programme Objectives

Technical Areas

This solicitation seeks Creators, which are individuals and teams that ARIA will fund, from across the R&D ecosystem to undertake projects across five Technical Areas (TAs) in order to achieve the programme's **galvanising demonstration: the persistent, reproducible expression of a novel gene from engineered mtDNA in a vertebrate system**, independently replicated across teams.

+ **TA1 - Deliver:** Focused on the delivery of nucleic acid payloads across the mitochondrial double membrane, into the matrix
+ **TA2 - Express:** Focused on mitochondrial genome engineering and expression

+ **TA3 - Maintain:** Focused on persistence and maintenance of engineered mtDNA
+ **TA4 - Transfer:** Focused on *in vivo* enablement via systemic delivery and organelle transplantation.
+ **TA5 - Standardisation, translation, and reproducibility:** Focused on providing replication, standardisation, and translation capacity — models, methods, and metrology.

TA1: Deliver

Delivery of Nucleic Acid Payloads to the Mitochondrial Matrix

The primary goal of this TA is to achieve reliable and quantifiable delivery of genetic payloads (minimally, 1000bp DNA or 25 bp RNA) into the mitochondrial matrix of vertebrate cells. This TA confronts the fundamental challenge of traversing the mitochondrial double membrane, a primary barrier that has long isolated the mitochondrial genome from modern engineering techniques. We are seeking novel systems with a clear path to *in vivo* relevance.

Potential approaches are broad and we encourage any approaches, including those we haven't considered. Some examples of approaches we have considered include:

- Adapting viral vectors (e.g., bacteriophages) or engineering non-viral nanoparticles to target and penetrate mitochondria.
- Developing peptide-mediated transport systems that creatively exploit native mitochondrial import machinery.
- Designing microbe-inspired mechanisms for vesicle fusion or gene transfer directly into the mitochondrial matrix.
- Developing cell-free model systems for rapid screening of delivery vectors.
- Developing robust and quantitative measures of introduced nucleic acid localisation in the matrix.

TA2: Express

Mitochondrial Genome Engineering and Expression

The primary goal of this TA is to enable the stable expression of functional proteins from engineered genetic constructs maintained within mitochondria. Once a genetic payload is delivered, it must be transcribed and translated into a functional protein within the unique mitochondrial environment. This TA focuses on designing and building the necessary genetic hardware, which could range from minimal synthetic plasmids to entirely new mitochondrial genomes to novel CRISPR-Cas-based template insertion. Proposals should account for the distinct features of mitochondrial gene expression, such as its unique genetic code, compact architecture, and specific transcriptional machinery. This may require

developing auxiliary systems, like orthogonal RNA polymerases or novel transcription factors, to ensure compatibility.

Creative approaches may include:

- Synthesising and assembling minimal, synthetic mitochondrial plasmids or entire genomes from scratch.
- Engineering bespoke gene expression systems—including promoters, terminators, and regulatory elements—that are fully compatible with the mitochondrial environment.
- Developing next-generation mitochondrial-specific genome editing tools (e.g. base/prime editors or CRISPR variants) capable of targeted recombination or precise gene insertion.
- Developing "mitochondria-free" expression models for high throughput screening and experimentation.

TA3: Maintain

Control and Maintenance of Engineered mtDNA

The primary goal of this TA is to ensure that engineered mitochondrial genomes are stably maintained, replicated, and functionally propagated over time. Introducing an engineered mitochondrial genome is only the first step; ensuring it persists and functions across cell divisions and through quality control is a profound challenge. Cells contain many copies of mtDNA, and this TA seeks strategies to manage this population, a concept known as heteroplasmy. The goal is to develop methods that allow an engineered mtDNA variant to be durably maintained, such as by directly biasing its replication over wild-type versions or improving its competitive fitness. A significant advance would be the ability to predictably 'dial' the level of heteroplasmy to a desired percentage and hold it there indefinitely in a proliferating cell line.

We encourage the exploitation of existing approaches as well as the exploration of novel strategies, for example:

- Designing systems to selectively and controllably degrade wild-type mtDNA, clearing the way for the engineered variant to dominate.
- Developing controllable molecular tools that inhibit transcription/replication factors for competing genomes or otherwise bias replication towards the engineered variant.
- Optimizing D-loop design of engineered mtDNA to enhance affinity of its promoter sequences for the native replication machinery.

- Studying and adapting natural examples of heteroplasmy regulation from non-model organisms, such as those with multi-uniparental inheritance, for application in vertebrate systems.

TA4: Transfer

Delivery of Engineered Mitochondria to Cells

The primary goal of this TA is to enable functional mitochondrial engineering in a vertebrate system, either by developing robust methods to deliver whole, engineered (possibly autologous) mitochondria to target cells or via direct *in vivo* modification. This TA addresses the 'first mile' challenge: getting our tools to the right cells and tissues in a living animal to achieve the programme's galvanising demonstration. It provides two complementary pathways:

- Pathway A (Organelle Transplantation): This pathway involves transplanting mitochondria as fully functional organelles into target cells or tissues. This strategy must overcome any cellular defences that lead to degradation of transplanted mitochondria and ensure the preservation of organellar and genomic integrity post-uptake.
- Pathway B (Systemic *in vivo* Delivery): While we are open to any approach, a clear example would be packaging the molecular machinery developed in TAs 1, 2, and 3 into a single, cohesive vector (e.g., LNP, engineered AAV, exosome) for systemic delivery. Potential challenges include creating a vehicle that can protect its complex cargo, deliver it to a target tissue, and release it into the cell's cytoplasm, where the TA1-3 mechanisms can do their work.

Some examples approaches include:

- (Pathway A) Using exosomes or induced intercellular transfer as natural vehicles for whole-organelle delivery.
- (Pathway A) Engineering or pre-conditioning recipient cells to enhance their uptake and retention of transplanted mitochondria.
- (Pathway B) Developing tissue-specific LNPs or polymer-based nanoparticles that can carry a multi-component payload (e.g., a TA1 delivery vehicle plus a TA2 expression cassette).
- (Pathway B) Engineering viral vectors (e.g., AAVs) that can evade nuclear targeting and deliver their payload to the cytoplasm for subsequent mitochondrial entry.
- (Shared) Developing scalable platforms that use genetically barcoded mitochondria to track and quantify the fate and function of delivered organelles *in vivo*.

TA5: Standardisation, translation, and reproducibility (ST&R)

A persistent obstacle in mitochondrial biology has been the lack of shared tools and standardised methods. This fragmentation has made it difficult to compare results across different studies, leading to progress that has been sporadic and often irreproducible. To overcome this barrier we plan to fund a Standardisation, Translation, and Reproducibility (ST&R) project to ensure that the programme's results are robust, comparable, and rapidly accelerated. The ST&R project also serves to mitigate integration risk in the programme: that the breakthrough discoveries required to build a complete solution remain isolated within individual teams.

The ST&R project will serve as a central resource for the programme, responsible for refining and distributing unified measurement tools and assays, standardising experimental models, independently replicating key findings from other Creators, and adapting successful methods for use by the entire programme community.

By establishing shared benchmarks from the outset for key variables — such as mtDNA haplotype, cell type, and cell age — the ST&R project will help ensure that progress across the programme is verifiable, reproducible, and directly comparable across all projects.

Budget

We expect this programme to initially allocate £55m across all TAs. We aim to fund a diverse portfolio of projects covering a wide range of approaches and collaborations across the ecosystem We anticipate that the final programme will consist of:

TAs 1-4:

+ 3-5 large, multi-disciplinary projects that have the capacity to go from TA1 through to a successful *in vivo* demonstration. We expect Creators undertaking these projects to integrate within their team deep mitochondrial biology expertise with novel tools from adjacent fields (such as synthetic biology, virology, or nanotechnology).
+ Up to 5 smaller, technology-focused projects. These projects are expected to be more targeted, perhaps pursuing an approach to one of the TAs or to a specific technical or platform challenge within a narrower set of TAs.

TA5:

+ A single ST&R project to serve as a central programme resource for translation, standardisation, and reproducibility. We may decide to fund TA5 via a Creator working on all TAs or we may fund a standalone Creator to work on TA5 only.

SECTIONS 3: Technical Metrics

Each TA has the following metrics as indicative goals; we encourage applicants to propose ambitious and creative approaches to meet them. We remain open to other potential metrics of success suggested by applicants so long as they drive repeatable success of our galvanising demonstration.

TA	**Indicative Metrics of Success**
TA1: Deliver	• Quantifiable delivery of payloads (≥1000bp DNA or ≥25bp RNA) to the mitochondrial matrix. • Demonstrable efficiency, matrix-specific localisation, and integrity of delivered payloads. • Development of scalable, quantitative assays to confirm matrix-localised delivery, shareable across the programme.
TA2: Express	• Stable expression of a functional protein from an introduced genetic construct. • Quantitative validation of protein expression levels (e.g., via reporter fluorescence). • Confirmed evidence of proper protein localisation, folding, and function within the mitochondrial matrix.
TA3: Maintain	• Demonstration of stable maintenance of a target mtDNA variant at a detectable level in a proliferating cell line. • Ability to predictably 'dial' the level of heteroplasmy to a desired percentage and maintain it. • Robustness of the method demonstrated across multiple cell types and mtDNA haplotypes.
TA4: Transfer	• (Pathway A): Quantitative evidence of delivery and subsequent cellular uptake of transplanted mitochondria in a tissue within a vertebrate system. • (Pathway B): Quantitative evidence of targeted delivery of the vector and release of its payload into the cytoplasm of cells in a specific tissue within a vertebrate system. • (Pathway A): Demonstration that transplanted mitochondria successfully evade immediate cellular clearance mechanisms

	(e.g., mitophagy) and remain structurally intact, retaining their specific mtDNA, after entering the target cell. • (Pathway B): Demonstration that the systemically delivered molecular toolkit is functional and bioavailable within the cytoplasm. • Creation and validation of scalable methods to track and quantify the biodistribution, rate of cellular uptake, and post-delivery integrity of the payload (*in vivo*) for the chosen pathway.
TA5: Standardisation, translation, and reproducibility (ST&R)	• Number of performer technologies successfully replicated and validated. • Number of "programme-grade" components (methods with full SOPs) developed and available. • Number of standardized cell lines (or or other models) and assay kits developed and distributed. • The frequency with which other programme Creators utilize validated components and models in their own work.
Programme's galvanising demonstration	Persistent, reproducible expression of a functional reporter protein from an engineered construct within the mitochondria of a vertebrate model, independently replicated.

SECTION 4: What are we looking for/what are we not looking for

What we are looking for:

- **Interdisciplinary teams and radical collaboration**: We strongly encourage proposals from teams that bridge traditionally disconnected fields, including – but not limited to – mitochondrial biology, synthetic biology, virology, parasitology, nanotechnology, systems biology, biophysics, imaging, computational biology, and high-throughput automation.
- **Novel approaches**: We are interested in ideas that address the challenges of the TAs in novel ways.
- **Incorporation of deep mitochondrial expertise**: We expect each team to evidence deep mitochondrial biology expertise.

What we are not looking for:

- **Incremental advances**: Proposals that offer minor improvements to existing technologies (e.g., slight increases in the efficiency of existing base editors) without addressing the fundamental challenges within our TAs or moving us towards the galvanising demonstration.
- **Solely nuclear-based approaches**: Research that relies exclusively on allotopic expression without proposing novel solutions to its fundamental limitations in protein import, folding, and localised control.
- **Targeting non-vertebrate systems**: Proposals that lack a clear and credible path to application in vertebrate systems.
- **Siloed research**: Projects that do not demonstrate a commitment to the programme's collaborative ethos.
- **Research focused only on mitochondrial diseases**: the programme seeks platform technologies with the potential for broad impact across the full spectrum of mitochondria-associated conditions, including chronic diseases and ageing.
- Research that fits within the broader Bioenergetic Engineering opportunity space but not within this programme. Rather than submitting to this programme, applicants may consider applying for opportunity seed funding, which we anticipate accepting applications for in 2026.

SECTION 5: Programme Duration and Project Management

Programme structure

The programme will consist of a singular phase, in which all projects will start as soon as the funding agreement is in place.

The maximum term of the programme is 5 years, though applicants are strongly encouraged to propose plans which may reach success (or failure) on faster timelines.

Project milestones

Each project's progress will be monitored using clearly defined milestones. Milestones will be defined by the applicant prior to the start of a project, be agreed upon by ARIA during the contracting phase, and should be designed to easily convey progress to a third party. In order to do this, milestones should:

- Be specific, measurable, and signify a meaningful step towards reaching the overall programme goals.
- Be synergistic with those of other Creators across the programme.

- Include details on anticipated methods used for measurement and evaluation. If superior methods are developed during the course of the programme, evaluation methods may shift to best reflect the intended technical outcomes.
- Be defined on a quarterly cadence for all phases of the programme.
- Include major "Go / No-Go" decision points.

Success/pivot/closure criteria for each project will be determined by the applicant's ability to meet these agreed-upon milestones and the Programme Director will work with Creators throughout their project to refine and pivot as required.

Programme & Project Management

The programme team aims to operate as an active technical partner, and Creators should expect a high degree of engagement, including frequent, in-depth technical conversations. The programme team's role is to manage the programme portfolio to accelerate progress towards the programme's galvanising demonstration by identifying synergies, anticipating risks, and dynamically adjusting focus to capitalise on the most promising breakthroughs. This means funding may be redirected, project scopes pivoted, and new collaborations encouraged based on performance and emerging results. We view this process as a collaborative partnership focused on collective success.

Quarterly reviews will be held between Creators and the programme team to discuss progress against each Creator's milestones, as well as further details of the project. As part of that discussion, Creators will be encouraged to think through the following questions:

- What is/are the target deliverable(s) for each phase of the programme?
- What are the top three risks identified at this stage of the project?
- What are the highest leverage experiments required to overcome each risk?
- What are the expected outcomes/learnings from these experiments?
- How long will these experiments take and how much will they cost?
- What are the dependencies from prior activities/phases of the Programme?

Upon completion of each experiment, questions we will look to answer are:

- What new information has been gleaned?
- What (if any) risks have been overcome? What new risks have emerged?
- Did we learn what we thought we would learn? If not, why not?
- Is there anything we can do to learn more or faster?
- Is there still a path towards the target? Are we heading towards any dead ends?

Community events

To foster a collaborative research environment, we will host regular community events, including a programme kick-off meeting and bi-annual Creator workshops. These events will be essential for teams to exchange updates, share data and tools, and work together to solve cross-cutting challenges. Attendance is strongly encouraged, and applicants should include estimated travel costs in their budget proposals.

SECTION 6: Eligibility & Application process

Eligibility

We welcome applications from across the R&D ecosystem, including individuals, universities, research institutions, small, medium and large companies, charities and public sector research organisations.

Collaboration

Due to the integrated nature of the programme, we are encouraging a highly collaborative approach amongst Creators.

Applications may therefore be made by:

+ Applicants that are proposing a cohesive proposal addressing all TAs.
+ Applicants who apply to a single or subset of TAs but plan to collaborate with other applicants in the programme in order to be able to address all TAs if both are funded. These applicants should tell us about their intended collaboration in their proposals.
+ Standalone applicants who have no current plans to collaborate with other applicants. For standalone applicants applying to a subset of TAs, if successful, we may try to facilitate collaborations with other applicants where it makes sense.

Applications may be made by a single organisation or by a consortium consisting of two or more organisations. In the case of a consortium, the application should be made by a single lead applicant to whom the funding will be awarded if successful and other members of the consortium will be subcontracted/granted by the lead applicant.

At the concept paper stage, we welcome applications that address single, multiple, or all TAs. A brilliant idea in one area is a critical contribution, and we do not want to discourage any potential applicants who can meaningfully advance the programme's goals. Following our review of concept papers, we may ask applicants if they are willing for us to share

contact information with other applicants where potential collaborations could be formed ahead of full proposals. Whilst we are flexible, at the full proposal stage we will encourage applications that address all TAs in one proposal.

Finding potential collaborators and teaming

To support the formation of Creator teams who are able to address multiple TAs, we offer two pathways for collaboration:

1. **Proactive teaming:** Before applying, you can use ARIA's teaming tool to find potential partners with complementary expertise.
2. **Facilitated teaming:** After the concept paper review, we may help facilitate connections between applicants, with the aim of forming stronger, synergistic teams before the full proposal deadline. You will have the option to opt-in to ARIA making introductions where we feel there are synergies between proposals. Please note that no information about the proposal itself will be shared.

By following the link to the sign up form here you will be able to register and submit details on your area(s) of expertises, and gain access to a list of other individuals seeking to find/share their expertise. All requests are screened via ARIA's internal team prior to access, after which connections will be made by individual users based on aligned expertise.

Collaboration agreements

Applicants who apply as a consortium or indicate an intention to collaborate with other applicants in the programme will be expected to enter into a formal collaboration agreement. A signed term sheet between the different organisations in the consortium must be executed by the date of the funding agreement, and a full collaboration agreement must be executed between the collaborating organisations within the first quarter of the project. The agreements must at minimum cover roles and responsibilities, treatment of confidential information, intellectual property and ownership of results, and dispute resolution. If helpful, we can refer applicants to established collaboration agreement templates that can be helpful as a starting point.

Intellectual Property

This programme will use our standard approach to Intellectual Property (IP): Creators will own any new IP they generate as a result of the grant/contract.

To ensure collective success, Creators will be expected to share some level of tools and methods they have developed during their ARIA funded project with other Creators in the

programme. During the contracting phase, we will agree with each Creator what they are expected to share with other programme Creators.

Animal testing

You can find more information on ARIA's policy on animal testing here.

If you intend to carry out animal testing as part of the proposed project you will be required to answer some additional questions in your proposal submission. These questions can be found in the concept paper guidance here and full proposal guidance here.

Application Process

The application process consists of two stages:

Stage 1 - Concept paper

Concept Papers are designed to make the solicitation process as efficient as possible for applicants. By soliciting short concept papers (no more than three pages) ARIA reviewers are able to gauge the feasibility and relevance of the proposed project and give an initial indication of whether we think a full proposal would be competitive. Based on this feedback you can then decide whether you want to submit a full proposal. You can find out more about ARIAs review process here.

If you miss the deadline for submission of concept papers you can still submit a full proposal. However, we strongly encourage you to submit a concept paper. In past ARIA programmes an average of 64% of applicants awarded funding had submitted concept papers.

To ensure the process is quick and open we do not require your organisation's consent prior to submission of a concept paper.

You can find guidance on what to include in a concept paper here.

Following a review of concept papers, applicants will either be encouraged or discouraged from submitting a full proposal. For more details on the evaluation criteria we'll use, click here.

After the concept paper review is complete, it is highly likely that this Call for Proposals document will be updated. The concept paper stage will provide valuable insight into the landscape of emerging ideas and the composition of the applicant community. Any updates to the Call for Proposals will be made to provide applicants with greater clarity on the

programme's objectives, to refine technical descriptions, and to help applicants prepare the strongest possible full proposals. All updates will be made before the window for full proposals opens.

Stage 2 - Full proposals

This step requires you to submit a detailed proposal including:

- **Project & Technical information** to help us gain a detailed understanding of your proposal
- **Information about the team** to help us learn more about who will be doing the research, their expertise, and why you/the team are motivated to solve the problem
- **Administrative questions** to help ensure we are responsibly funding R&D. Questions relate to budgets, IP, potential COIs etc

You can find more detailed guidance on what to include in a full proposal here. Please note this guidance may be updated when the Stage 2 call is launched.

You can submit a full proposal even if you did not submit a concept paper. For more details on the evaluation criteria we'll use, click here.

Non-UK funding

Our primary focus is on funding those who are based in the UK. For the vast majority of applicants, we therefore require the majority of the project work to be conducted in the UK (i.e. >50% of project costs and personnel time). However, funding will be awarded to organisations outside the UK if we believe it can boost the net impact of the programme in the UK. In these instances, you must outline your proposed plans or commitments that will contribute to the programme in the UK within the project's duration (note the maximum project duration is 5 years).

If you are successfully selected for an award subject to negotiations this proposal will form part of those negotiations and any resultant contract/grant.

More information on the evaluation criteria we will use to assess your application, including Benefit to UK, can be found later in the document here.

We have provided some additional guidance on non-UK funding in our FAQs including available visa options.

SECTION 7: Timelines

This Call for Proposals will be open for applications as follows (we may update timelines

based on the volume of responses we receive):

Applications open	**03 October 2025**
Webinar	**09 October 2025**

We are hosting a webinar, to provide an overview of the programme's objectives, scope, and application process, and to give potential applicants an opportunity to ask questions to the ARIA team. Please register your interest and submit questions in advance for this event here.

Concept paper submission deadline	**27 October 2025 (14:00 GMT)**
Concept paper review & notification of encouraged/not encouraged to submit full proposal sent	**28 October 2025 - 28 November 2025**

At this stage and based on your concept paper, you will either be encouraged/ discouraged to submit a full proposal. If you receive feedback indicating that you are not encouraged to submit a full proposal you can still choose to submit a full proposal. You should note that this preliminary assessment/encouragement provides no guarantee of any full proposal being selected for award of funding.

Full proposal submission deadline*	**15 January 2026 (14:00 GMT)**
Full proposal review	**16 January 2026 - 5 March 2026**

As part of our review we may invite applicants to meet with the Programme Director to discuss any critical questions/concerns prior to final selection — this discussion can happen virtually or we may seek clarification on certain aspects of your proposal via email.

Successful/Unsuccessful applicants notified	**06 March 2026**

At this stage you will be notified if you have or have not been selected for an award subject to due diligence and negotiation. If you have been selected for an award (subject to negotiations) we expect a 1 hour initial call to take place between ARIA's Programme Director and your lead researcher within 10 working days of being notified.

We expect contract/grant signature to be no later than 8 weeks from successful notifications. During this period the following activity will take place:

- Due diligence will be carried out
- The programme team and the applicant will discuss, negotiate and agree on the project activities, milestones and budget details
- Agreement to the set Terms and Conditions of the Grant/Contract. Please note ARIA does not negotiate these terms. You can find a copy of our funding agreements here

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**Note: We recognise that the application period overlaps with the holiday period. We want to stress that the deadlines are not intended to interfere with holidays and to support this, we have extended the standard ARIA solicitation timeline by two weeks, giving applicants the space to take a break over the holiday period.*

SECTION 8: Evaluation Criteria

Concept Paper and Proposal Evaluation Principles

To build a programme at ARIA, each Programme Director directs the review, selection, and funding of a portfolio of projects, whose collective aim is to unlock breakthroughs that impact society. As such, we empower Programme Directors to make robust selection decisions in service of their programme's objectives ensuring they justify their selection recommendations internally for consistency of process and fairness prior to final selection.

We take a criteria-led approach to evaluation, as such all proposals are evaluated against the criteria outlined below. We expect proposals to spike against our criteria and have different strengths and weaknesses. Expert technical reviewers (both internal and external to ARIA) evaluate proposals to provide independent views, stimulate discussion and inform decision-making. Final selection will be based on an assessment of the programme portfolio as a whole, its alignment with the overall programme goals and objectives and the diversity of applicants across the programme.

Further information on our proposal review process can be found here.

Proposal evaluation process and criteria

Proposals will pass through an initial screening and compliance review to ensure proposals conform to the format guidance and they are within the scope of the solicitation. At this

stage we will also carry out some checks to verify your identity, review any national security risks and check for any conflicts of interest. Prior to review of applications, Programme Directors and all other reviewers are required to recuse themselves from decision making related to any party that represents a real or perceived conflict.

Where it is clear that a proposal is not compliant, outside the scope and/or does not pass a quality assurance review, these proposals will be rejected prior to a full review on the basis they are not compliant or non-eligible.

Proposals that pass through the initial screening and compliance review will then proceed to full review by the Programme Director and expert technical reviewers.

In conducting a full review of the proposal we'll consider the following criteria:

1. **Worth Shooting For:**
    a. The proposed project uniquely contributes to the overall portfolio of approaches needed to advance the programme goals and objectives.

    b. It has the potential to be (i) transformative i.e. it has the ability to unlock entirely new lines of scientific inquiry or therapeutic development and/or (ii) address critical challenges within and/or meaningfully contribute to the programme thesis, metrics or measures.

2. **Differentiated** – The proposed approach is innovative and differentiated from commercial or emerging technologies being funded or developed elsewhere. The proposed project focuses on approaches that are distinct from existing mtDNA editing tools e.g. TALENs or base editors. The proposed project uses novel modalities for the delivery and expression of large genetic payloads.

3. **Well defined** – The proposed project clearly identifies what R&D will be done to advance the programme thesis, metrics or measures, is feasible and supported by data and/or strong scientific rationale. The composition and planned coordination and management of the team is clearly defined and reasonable. Task descriptions and associated technical elements provided are complete and in a logical sequence with all proposed stage-gates and deliverables clearly defined. The proposal identifies major technical risks, and planned mitigation efforts are clearly defined and reasonable.

4. **Responsible** – The proposal identifies major ethical, legal or regulatory risks and that planned mitigation efforts are clearly defined and feasible. A

proposed project involving the use of animals provides a robust justification and demonstrates clear adherence with ARIA's Policy on Research and Innovation Involving Animals.

5. **Intrinsic motivation** – The individual or team proposed demonstrates deep problem knowledge, have advanced skills in the proposed area and shows intrinsic motivation to work on the project and key individuals are dedicating sufficient time to the project. The proposal brings together disciplines from diverse backgrounds.

6. **Benefit to the UK** – There is a clear case for how the project will benefit the UK. Strong cases for benefit to the UK include proposals that:
    a. are led by an applicant within the UK who will perform the majority (>50% of project costs spent in the UK) of the project within the UK
    b. are led by an applicant outside the UK who seeks to establish operations inside the UK and perform a majority (>50% of project costs spent in the UK) of the project inside the UK and present a credible plan for achieving this within the programme duration.

    For all other applicants we will evaluate the proposal based on its potential to boost the net impact of the programme in the UK. This could include:
    c. A commitment to providing a direct benefit to the UK economy, scientific innovation, invention, or quality of life, commensurate with the value of the award;
    d. The project's inclusion in the programme significantly boosts the probability of success and/or increases the net benefit of specific UK-based programme elements, for example, the project represents a small but essential component of the programme for which there is no reasonable, comparably capable UK alternative.

    When considering the benefit to the UK, the proposal will be considered on a portfolio basis and with regard to the next best alternative proposal from a UK organisation/individual.

Proposal Feedback

At the concept paper stage, applicants will be notified whether or not they are encouraged to submit a full proposal. If you are encouraged to submit a full proposal, we will provide

detailed feedback to help inform your full proposal. For those applicants not encouraged to submit full proposals we will not provide feedback.

At the full proposal stage, applicants will be notified whether or not they have been successfully selected for award. For those applicants not selected for award we are not able to provide feedback.

SECTION 9: How to apply

Before submitting an application we strongly encourage you to read this call in full, as well as the general ARIA funding FAQs.

If you have any questions relating to the call, please submit your question to clarifications@aria.org.uk

Clarification questions should be submitted no later than 4 days prior to the relevant deadline date. Clarification questions received after this date will not be reviewed. Any questions or responses containing information relevant to all applicants will be provided to everyone that has started a submission within the application portal. We'll also periodically publish questions and answers on our website, to keep up to date click here.

Please read the portal instructions below and create your account before the application deadline. In case of any technical issues with the portal please contact clarifications@aria.org.uk

If you are disabled or have a long-term health condition, we can offer support to help you engage with ARIA, navigate our funding application process, or carry out your project, you can find more information here.

Application Portal instructions

APPLY HERE

Advanced Research + Invention Agency ARIA

Concept Papers Guidelines

How to format your proposal

- Page count: a maximum of 3 pages, including diagrams but excluding references
- Format: single line spacing, standard character spacing (neither expanded nor condensed)
- Font: Arial. Colour: black. Size: 11-point font or larger
- Margins: At least 0.5" margins all around
- File Type: PDF only

Section 1: Technical concepts

Applicants are required to provide a concept paper no longer than 3 pages in length that outlines:

- Which Technical Area or Areas you seek to pursue (TA1, 2, 3, 4, 5)
- A description of the approaches and/or methodologies that will be employed to address the research objectives. Including:
    - A description of the ideas/solutions proposed, why you have not been able to realise them previously, and how they support the objectives of the TA(s) and the programme as a whole
    - Any data or scientific rationale to support your proposed concepts - supporting data, journal articles, blogs, code or other materials may be referenced or linked to in the submission if they directly support your paper, but do not necessarily have to be your own work.
    - Identification of the technical challenges or obstacles that must be overcome to achieve the research goals. This includes potential risks and mitigation strategies.
    - Any key models, measurement tools, or platforms that would benefit your approaches. Please specify if these are essential or "nice to have" and whether they are a) existing capabilities you will use, b) novel tools you propose to develop, or c) capabilities you would use if they were developed.
- An overview of the proposed activity of work, any key metrics and milestones and any dependencies and assumptions
- An overview of the proposed project team including information about the expertise of the research team, relevant experience, skills, and capabilities.

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Section 2: Timeline, Budget and Additional questions

In completing your application you must also provide answers to the following questions. Answers to these questions are not included in the 3 page cap. You should complete these questions in the application portal so there is no need to format these in a specific way.

Budget: How much funding do you need?

Please complete the table below providing an estimate in GBP (inclusive of VAT where applicable and all other costs) of what you consider a reasonable funding amount for your project. It's ok if you're not sure – give your best estimate.

Cost Type	Budget (£ Inc VAT)
Labour	
Materials	
Subcontract	
Equipment & Facilities	
Travel	
Other	
Subtotal	
Indirect Costs	
Total	

Timeline and additional questions:

Question	Guidance
Are you proposing to contribute funding?	*Where you or your organisation are proposing to contribute funding to the project please let us know. If yes, tell us how much funding you/your organisation plan to contribute.* *ARIA will fund 100% of project costs and contribution of funding is not essential however, we welcome proposals that contribute funding in cases when such funding will strengthen the*

	potential success. In these cases, this funding contribution will be considered as part of the overall strength of the project proposal.
How many months will you need to work on your proposed project?	*There is no minimum length for a proposed project. The maximum length is 60 months.*
Are you planning to give a portion of the work to external subcontractors?	*If yes, let us know what work you plan to give to a subcontractor. Subcontractors are any proposed third parties that you plan to enter into a contract or agreement with for services necessary for the delivery or management of the project.*
Do you consent to ARIA introducing you to other programme applicants to facilitate potential collaborations?	*The primary goal is to facilitate potential collaborations that can strengthen the applicants proposed projects.* *Please note that we will not share any information about your proposal.* *All personal data provided to ARIA will be processed in accordance with UK data protection legislation, including the Data Protection Act (2018) and the General Data Protection Regulation (GDPR). Further information on how we use personal data and how you can exercise your right as a data subject can be found in the ARIA Privacy Policy.*
Do you intend to use animals as part of your proposed project (even if you don't intend for us to cover the costs of such research)?	*(If yes, what type of animal do you foresee using and roughly how many?* *Why do you think there is a need to use animals as part of your proposal?)*

Are there any conflicts of interest?	*Please provide a short description of any potential conflicts of interest.*
Are there any other factors or restrictions that might impact your freedom to operate and deliver the project?	*Please provide a short description of any import/export restrictions; security, ethical, legal and regulatory restrictions that you are aware of.*
Are you proposing to perform the majority of the proposed project outside of the UK?	*Our primary focus is on funding those who are based in the UK. For the vast majority of applicants, we therefore require the majority of the project work to be conducted in the UK (i.e. >50% of project costs and personnel time).* *However, we can award funding to applicants whose projects will primarily take place outside of the UK, if we believe it can boost the net impact of a programme. In these instances, you must outline any proposed plans or commitments in the UK that will contribute to the programme within the project's duration (note the maximum project duration is 5 years).* *Please provide a brief summary of your proposed plans or commitments*
Additional questions about you/your organisation that can be found in the application portal.	

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Full Proposal Guidelines

How to format your proposal

- Page count: up to a maximum of 11 pages (including diagrams, excluding references)
- Format: single line spacing, standard character spacing (neither expanded nor condensed)
- Font: Arial. Colour: black. Size: 11-point font or larger
- Margins: At least 0.5" margins all around
- File Type: PDF

Applicants are required to provide a proposal no longer than 10 pages in length that outlines:

Section 1: Programme & Technical

The aim of this section is to gain in-depth, technical information about the project being proposed. This should include:

- A detailed explanation of the proposed idea/solution, how it supports the technical objectives of the chosen pathway.
    + This should be supported by visual aids, data and/or strong scientific rationale for why what you are proposing would work.
    + Please include any required technical information, as specified in sections 2 and 3 of the call for proposals document.
- A comprehensive list of the known technical risks/unknowns standing in the way of achieving the stated goals.
- How the proposed approach is differentiated, e.g. from commercial or emerging technologies being funded or developed elsewhere.
- A description of the proposed activity of work, key metrics and milestones and any dependencies and assumptions.
- Estimated timelines - applicants should provide a project plan for the lifecycle of the project, showing what you plan to achieve for each period of the project. This should be in the form of a gantt chart to show the proposed schedule where possible.

Section 2: The Team

This section includes information about the proposed individuals or teams that will conduct the research and management structures. This must include:

- Details of the project team - we want to know who will be doing the work (not just the principal investigator or project lead) and what portion of their time will be dedicated to this project. While we are open to any proposal that advances the programme's goals, we prefer any lead or key researchers to be spending 50% of their time on the project.
- You could include short bios about each team member (we discourage you from submitting CVs).
- If you intend to collaborate with or rely on any third parties, sub contractors/grantees, who they are and which elements of the project they will support/deliver.
- How you intend to coordinate and manage the teams including any collaborations with third parties.
- How you will manage resources, particularly personnel, in a dynamic environment where non-viable approaches are terminated so that project resources remain focused on the most promising avenues.
- Any potential gaps in your core competency which would be required in order to achieve the overall goals.
- What motivates you or the team to want to do this project and why you are the right person/team to work on this project.

In addition to the above, the following table should be completed and attached as an annex to your proposal.

Labour table to be completed for all individuals working on the proposed project (*filled here with hypothetical examples*)

Individual	Role / expertise	Already in place? If not, how long after project kickoff are they likely to start?	FTE	Total time on project (months, rounded)
Sophia Fleissig	*Synthetic biologist, project lead (TA2, 3)*	*Currently assigned to a different project but could transfer to this project with 6 weeks notice*	*80%*	*28*

Unknown	*Expert in tissue culture and transformation (TA1, 3)*	*To be recruited, aiming to start within 3 months*	*100%*	*33*
Magnus Formaggio	*Gene expression expert advising genome design (TA2)*	*Yes*	*40% during months 1-12, 20% during months 13-36*	*10*
Etc	*Etc*	*Etc*	*Etc*	*Etc*

Section 3: Administrative Response

This section includes information about the budget, intellectual property that you intend to rely on, any perceived conflicts of interest and for non-UK applicants how the proposed project may benefit the UK.

In completing your application you must also provide answers to the following questions. Answers to these questions are not included in the 11 page cap. You should complete these questions in the application portal so there is no need to format these in a specific way.

Application	Guidance
How much funding do you need?	*Please provide a cost breakdown by completing the spreadsheet here. In your proposal you may submit your budget using yearly, quarterly, or monthly phasing.* *Prior to completing this template you should review ARIA's Eligible cost guidance here.* *If your proposal is successful, prior to contract signature when the scope of work has been agreed, you will be required to provide a monthly cost breakdown.*

Are you proposing to contribute funding?	*If you or your organisation are proposing to contribute funding to the project please let us know how much funding you plan to contribute, who is contributing the funding, is the funding already secured and any other relevant details.* *ARIA will fund 100% of project costs and contribution of funding is not essential however, we welcome proposals that contribute funding in cases when such funding will strengthen the potential success. In these cases, this funding contribution will be considered as part of the overall strength of the project proposal.*
Does your proposal depend on background IP (pre existing)?	*If yes, give us an indication of: What background IP is required, Whether you currently have rights to that IP.*
Have you already secured funding for a similar project or are you currently in the process of seeking support from other funding sources for the same project?	*If yes, tell us more about the funding you already have or are applying for.*
Any other factors or restrictions that might impact your freedom to operate and deliver the project?	*Please provide a detailed description of any perceived conflicts of interest with the programme director, import/export or security restrictions that you are aware of*
How do you envision commercialisation of the proposed project?	*Please complete and upload a commercial hypothesis for your project using the guidelines here.*

Are you proposing to perform the majority of the proposed project outside of the UK?	*Our primary focus is on funding those who are based in the UK. For the vast majority of applicants, we therefore require the majority of the project work to be conducted in the UK (i.e. >50% of project costs and personnel time).* *However, we can award funding to applicants whose projects will primarily take place outside of the UK, if we believe it can boost the net impact of a programme.* *In these instances, you must outline any proposed plans or commitments in the UK that will contribute to the programme within the project's duration (note the maximum project duration is 5 years).* *Please provide a detailed description of any proposed plans (including a timeline) or commitments).*
Has a suitably authorised member of your Organisation approved the submission of this proposal?	*In the application portal, please select the option that best describes your situation and provide details where required.*
Do you intend to use animals as part of your proposed project (even if you don't intend for us to cover the costs of such research)?	*If yes, applicants will be required to answer the additional questions in the portal (also included in Annex 1 to this document).* *Please note we are not accepting proposals that intend to involve the use of non-human primates.*

Have you read and understood our funding terms?	*Our goal is to ensure your research can get going quickly, so we want to ensure a fast negotiation and award process. We aim to have agreements signed within 6 weeks, which we recognise can be much faster than standard at some organisations. Before proceeding, please confirm that you have read and understand our funding terms. If you are unsure which terms apply to you, you can find more guidance here.*
Additional questions about you/your organisation that can be found in the application portal.	

Annex 1 - Additional questions for projects that include animals

Note: You can find more information on ARIA's policy on funding animal testing here: ARIA's Policy on Research and Innovation Involving Animals.

Applicants should design their proposals in line with the above, the NC3Rs guidance and NC3Rs 'Experimental Design Assistant' for experimental design support.

1: Need - Describe (i) the need to use animals as part of your proposal, (ii) the use and current limitations of replacement technologies or non-animal methods in the research area, and (iii) how the proposed animal use is proportionate in light of your research objectives and the potential breakthrough that might be achieved.

2: Location - Specify the location of the proposed animal use (including details of the establishment where that information is available).

(Please note that the appropriate additional NC3Rs questionnaire must be provided alongside your application if (a) the location is outside of the UK and (b) the animals involved are one or more of the following: rodents; rabbits; sheep; goats; pigs; cattle; xenopus laevis and xenopus tropicalis; or zebrafish.)

3: Species - Indicate the choice of species to be used, the rationale for this choice, and the decision making process used.
(Please ensure that you address why the animal species and models being used can address the scientific objectives of your proposal and the relevance to human biology.)

4: Animal characteristics - Indicate the characteristics of the animal(s) to be used, for example, strain or substrain, sexes, age or developmental stage, weight range, genetic modification status, pathogen status, and the rationale for this choice and the decision-making process used.
(Both sexes should be used throughout the research pipeline unless appropriately justified. If the use of only one sex is proposed, please provide a scientific justification for this.)

5: Experimental procedures - Outline the planned experimental procedures, including the frequency, duration and timing of all procedures. Include details of the maximum prospective severity rating (and, for activity undertaken in the UK, with reference to the Home Office severity ratings). For moderate or severe procedures, detail the percentage of animals expected to reach this classification. Provide details of the refinements in place to reduce the pain, suffering and harms to the animals and give information on the expected clinical signs and humane endpoints that will be put in place.

6: Experimental design - Outline the total number of animals required and how this number was reached. Provide details of the (i) control and experimental groups, (ii) the experimental unit, (iii) sample size per group, including a justification for the chosen sample size, and (iv) the methods implemented to reduce confounders during the conduct of the studies (e.g randomisation and blinding strategies). If randomisation or

blinding is not used, provide rationale for this. For research generating inferential statistics, provide details of any power calculations used to determine the sample size.

7: Licences and ethical approval - Where the proposed research is to take place:

A. In the UK, please provide details of the Home Office licences in place in respect of the proposed research, researchers, and venue. If the necessary licences under the Animals (Scientific Procedures) Act 1986 are not yet in place, please outline your plans to ensure that such licences are acquired and estimated timelines; OR
B. Outside of the UK, please provide details of any relevant licences in place in respect of the proposed research, researchers, and venue to the extent applicable. If licences or other approvals are not yet in place but will be required, please outline your plans to ensure that such licences are acquired and estimated timelines.

(Please note that it is the responsibility of all applicants to ensure that the appropriate licences and approvals are obtained where this is required. This includes the approval by a local ethical review process (and, where UK based applicants are undertaking research outside of the UK, additional approval from any relevant UK institutional Animal Welfare and Ethical Review Board). Licences (or amendments to existing licences) do not have to be obtained before your application is submitted to us, but if your application is successful you must have the necessary licences in place before any animal experimentation begins.)

8: Outcomes and analysis - Outline primary outcomes to be assessed and describe the planned statistical analyses.

(Provide details of all the outcome measures taken during the conduct of each study and indicate the primary outcome measure, that is the outcome measure that is used to determine the sample sizes. Provide a description of the statistical analysis methods that will be used, explaining how they relate to the experimental design used and the experimental unit (that is, there is a difference between N samples from one animal, as distinct from one sample from each of N animals, or combining samples from multiple

animals), and showing that they are appropriate for the types of data that will be collected. Applicants should consider whether and how to access statistical support.)