

National Centre for the Replacement Refinement & Reduction of Animals in Research



Technologies to Tools

Applicant guidance

Pioneering Better Science



National Centre for the Replacement Refinement & Reduction of Animals in Research

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1. Overview

The National Centre for the Replacement, Refinement and Reduction of Animals in Research (<u>NC3Rs</u>) and the Milner Therapeutics Institute (<u>MTI</u>) have established a strategic collaboration to accelerate the translation of non-animal, human relevant cell models, developed with NC3Rs grant funding into research tools that can be applied confidently in the pharmaceutical industry.

Researchers that have previously developed cell-based disease models with NC3Rs funding will be able to collaborate on a project with the MTI. Funding for the project will be provided by the NC3Rs with MTI contributing in-kind services (access to industrial expertise, facilities and equipment) equivalent in value to NC3Rs funding. Projects can be up to 12 months in duration.

This document provides a guidance to prospective applicants applying to the Technologies to Tools with Milner competition.

1.1. Competition objectives

The overall aim of the competition is to support the translation of NC3Rs-funded cell-based disease models into research tools that can be applied to identify potential new drug targets with increased confidence and at scale. Working collaboratively with MTI scientists, successful applicants will apply MTI's cutting-edge CRISPR screening technology to their models to identify and validate disease targets and support improved drug discovery using fewer animals. These awards cannot be used to support R&D work that was not completed during the lifetime of a previous NC3Rs grant, and any proposal requesting funding for this purpose through this competition will be deemed ineligible.

The objectives of the awards are to:

- Accelerate and maximise the scientific, commercial and 3Rs impact of project outputs arising from NC3Rs response mode grants.
- Foster collaborative working to support the wider uptake and impact of promising 3Rs technologies.
- Build confidence in 3Rs technologies and accelerate their path to market as tools that can be used in CRISPR screens to support the robust identification of clinically relevant drug targets.
- Increase knowledge exchange and co-creation between NC3Rs-funded researchers and the MTI.
- Nurture talent and skills development of NC3Rs-funded researchers.

Table 1: Overview of application and review process

Eligibility				
•	All applications submitted to the T2T with Milner competition must focus on the further development of a non-animal, human relevant cell model system originally created with grant funding from the NC3Rs.			
•	All applications will be lead by a researcher from the MTI in collaboration with an NC3Rs grant holder as the academic co-applicant.			
•	Academic co-applicants must be a UK-based recipient of a grant awarded through NC3Rs response mode schemes that have developed a non-animal, human relevant cell model system.			
	The original NC3Rs funded project on which the application to the T2T with Milner competition is based should ideally be in the last year of funding or be completed.			
-	Only one application per eligible NC3Rs grant will be accepted.			
Applica	tion and review process			
•	MTI lead applicants are required to discuss the outcomes of the NC3Rs grant, upon which the application will be based, with the academic researchers that developed the model to assess its suitability for genomic screening.			
•	The MTI will select projects that fall within their remit and to which they can add value and work with the academic researchers / NC3Rs grant holders to develop a collaborative application for submission to the competition.			
•	Completed application forms must be submitted prior to the deadline.			
•	Applications are reviewed by an expert Panel convened by the NC3Rs.			
green	ents and awards			
•	The lead MTI applicant is informed by email of the decision of the Panel approximately one weel after the Panel meeting.			
•	As the lead applicant organisation, the MTI will sign an agreement with the NC3Rs outlining the terms and conditions of the award. The document must be signed and returned to the NC3Rs before work on the award can commence.			
•	Co-applicants on successful applications will enter into a separate agreement with the MTI.			
Post-av	/ard			
	Regular Project Management Team meetings will ensure the project is on schedule and any risk are managed accordingly. The project management team will be formed of NC3Rs and MTI staff and researchers from the partnering academic team.			
•	The lead MTI applicant will be responsible for ensuring key deliverables of the funded project are met within agreed timeframes.			
•	A final report and a final expenditure statement (FES) are required by the NC3Rs within three months of the completion/termination date.			

1.2. Competition remit

Applications to the competition are expected to accelerate towards industry application a technology/model that, through NC3Rs funding, has already completed the majority of R&D work required to produce a functional cell-based model. Using the modified technology readiness levels (mTRL) defined by Phadke & Vyakarnam¹ as guidance, a mTRL level of 2-4 is expected to be the minimum starting point for applying to the competition. The aim of the competition is to support activities towards mTRL 5-7 (Table 2).

mTRL 0	0 Research in progress				
	Fundamental research activity before any potentially useful and validated science or technology has been established				
mTRL 1	Validated research: Start concept definition				
	At the point at which the conceptual application of the technology has been defined in outline terms				
mTRL 2	2 Initial concept defined				
	The conceptual application has now been converted to a definition of the product or service which can potentially be offered using the technology				
mTRL 3	3 Working prototype or demonstrator				
	A working prototype or demonstrator has been built				
mTRL 4	Product or service testing and concept refinement				
	The new product, service or technology has been refined/modified following feedback from the initial customer				
mTRL 5	Proven product or service				
	The product or service is ready at a functional level, without the collateral around the product including the method of deployment and the proposed business model				
mTRL 6	Deployment with early customers in real commercial environment				
	The product or service is now ready for use with early Customers, and so includes all the associated collateral, including a service infrastructure where relevant.				

¹ Taken from Phadke & Vyakarnam, Camels, Tigers and Unicorns: Rethinking Science and Technology-enabled Innovation, World Scientific Publications, 2017

mTRL 7	Product or service ready for testing in real user environment	
	Early customer feedback has been used to define the modified product or service functionality, its required performance and critically, the chosen business model.	
mTRL 8	BTechno-commercial refinement of product or serviceThe refined product or service is now ready for deployment with mainstream customers.	
mTRL 9	Ready for commercial deployment with real customers The final product or service is now ready for commercial launch, including go-to-market collateral and proven business model. The challenge now is growing the mainstream custor base.	

Activities in remit for this competition include:

- Developing cell-based models of disease for functional genomics screens to a point where they can be deployed with academic/industry end-users (mTRL5 and 6).
- Demonstrating the cell-based disease model(s) is fit for purpose, to minimise risk and increase enduser confidence (mTRL7).
- Developing new applications of the cell-based model(s) to create novel means of impact generation (mTRL5-7).
- Establishing confidence (scientifically and commercially) to operate in the market (mTRL6 and 7).

Activities not in scope for this competition include:

- Consultancy, for example, advice on business/commercialisation strategy, business development, pitching for investment and market analysis.
- Marketing to attract potential investors and customers including website design, travel, academic publications, conference and exhibition fees.
- Research and development work not completed during the original funding period.
- Merchandising and advertising activities and materials.
- Export activities.

1.3. Eligibility criteria

 All applications submitted to the T2T with Milner competition will be led by a researcher from the MTI and must focus on the further development of a non-animal, human relevant cell model system originally created with grant funding from the NC3Rs.

- Any UK-based recipient of an NC3Rs response mode grant that has developed a non-animal, human relevant cell-based model system and who has completed, or is ideally within the last year, of their NC3Rs grant is eligible to be a co-applicant on an application submitted to the T2T with Milner competition.
- Prospective applicants must have a contract of employment that will outlast the duration of the proposed project and be based at either a Higher Education Institution (HEIs), Independent Research Organisation (IROs or Research Council (RC) Institute.
- MTI lead applicants are required to discuss the outcomes of the NC3Rs grant, upon which the application will be based, with the academic researchers that developed the model to assess its suitability for genomic screening.
- Following these discussions, MTI staff will select projects that fall within their remit and to which their expertise can add value and work with the NC3Rs grant holder to compile a collaborative application for submission to the T2T competition.

1.4. Selection criteria

MTI criteria for selecting projects to submit a collaborative application with include:

- Ability to add value with their available expertise and technologies and move the technology to the desired mTRL.
- Fit with MTI key therapeutic priority areas and cell model platforms of interest*.
- Alignment with MTIs goal of developing novel in vitro approaches for drug discovery.
- Potential for the project to impact industry processes and more widely across MTI programmes.
- Expertise of the team.
- Potential for the project to significantly improve current standards used for drug discovery.
- Feasibility, focusing on evidence of genetic tractability, health and safety requirements, scale, freedom to operate and development stage of model.
- Does the proposed work fit with the project budget?

* This could include, but is not limited to, the following research areas; oncology, cardiovascular, respiratory, immune, fibrosis, and model platforms; iPSC models, primary cell models, 3D assays, microphysiological systems.

Only one application per eligible NC3Rs grant will be permitted.

2. The application process

2.1. How to apply

All applicants are expected, before applying, to have discussed their proposal with their own organisation or any other body whose co-operation will be required in the conduct of the project. By applying, applicants are confirming that the information provided in the application is complete and true, that they are actively engaged in the project and will be responsible for its overall management.

2.1.1. General guidance

Applications must be made using the application form provided. Completed applications must be sent by email to <u>innovations@nc3rs.org.uk</u>. All applications are treated in confidence.

- Application forms and attachments must be submitted as PDF files.
- Failure to complete mandatory fields on the application form and to submit all required attachments may result in the application being rejected.
- The application form should be completed using a font size no smaller than 10pt (Arial) and text limits must not be exceeded.
- The use of acronyms should be kept to a minimum.

2.1.2. Attachments

Supporting information can be provided in the form of separate attachments as indicated within this guidance and the application form. Attachments must:

- Be submitted as separate PDF files and not added or pasted within the application form.
- Be named appropriately (i.e. document type lead MTI applicant's name, CVs Dr A.N. Other).
- Be completed using a font size no smaller than 10pt (Arial).

Only provide attachments as specified in the application form and in this guidance. Any additional materials or documentation submitted will not be considered and may result in your application being rejected or returned without review.

Questions about the application process should be addressed directly to the NC3Rs via email <u>innovations@nc3rs.org.uk</u>.

2.2 The application form

This section contains guidance on how to complete the application form. Sub-sections are numbered as they appear in the application form.

1. Application details

- **Project title**: Please provide your own title for the project. This should be both clearly descriptive and concise. It should contain keywords relevant to the project.
- **Project duration**: Applicants can request up to the maximum duration of 12 months.
- **Proposed start date**: Please specify the date upon which activities will commence.

- Total project cost: The total amount of funding that can be requested should be commensurate with the scale of research required to deliver the project objectives. Applicants should be mindful that the total available budget for this call is £200k and that value for money will be a key consideration of the assessment panel.
- **Contact details of lead MTI applicant**: Please include the name of the lead MTI applicant, current position and contact details. This individual will have ultimate responsibility for delivery of the project.
- Contact details of lead academic co-applicant: Please include the name of the lead academic coapplicant on the proposal, current position and contact details including the organisation's name and address. This should be a researcher who was either involved in the original NC3Rs-funded model development or who has sufficient scientific/technical knowledge of the model to support its translation to MTI.

2. Previous NC3Rs grant details

- **Grant reference and title**: Please provide the grant reference and title of the NC3Rs grant upon which the current proposal is based.
- Grant start date: Date on which the NC3Rs grant commenced.
- **Grant completion date**: Date on which the NC3Rs grant completed or if still in progress, the date on which the grant is due to complete.

Please also provide details of the previous NC3Rs grant holder and organisation if this is different from the 'lead academic co-applicant' described above.

3. Project summary

Please describe the proposed project in language to be understood by a non-specialist audience. Please include the potential 3Rs impacts of the project.

4. Scale of the opportunity

i. **Relevance to industry**: Please describe the unmet industry need and the size of the industry opportunity. The maximum word limit for this section is 300 words.

Associated attachment (optional): Letters of support/intent from potential customers / end-users / MTI Innovation Board.

ii. **Disease biology relevance**: Please describe the clinical need and the relevance of the proposed model development to disease biology. The maximum word limit for this section is 300 words.

iii. **Intellectual property**: Please provide details of any existing patents or other forms of intellectual property (i.e. know how, trademark) that have arisen from the NC3Rs-funded grant upon which this application is

Associated attachment (optional): Summary of patent filings.

based. In addition, please indicate any anticipated IP, which may arise in delivering the T2T project and how this would be handled (i.e. the proposed arrangements for ownership). Please provide details of any freedom to operate searches conducted to date (or plans for the future) and any restrictions this may impose on the dissemination and exploitation of the technology/product. The maximum word limit for this section is 200 words.

iv. Potential for scale up: Please describe the potential and pathway for scale up of the model. Please include a description of additional steps and stakeholders that will be needed to achieve this. If there is potential to commercialise the model developed please describe how this will be achieved. Please include the barriers and key risks to scale up/commercialisation and how you plan to address them. You may include letters of support/intent from potential partners able to support these activities. The maximum word limit for this section is 300 words.

Associated attachment (optional): Letters of support/intent from potential partners able to support these activities.

5. Use of T2T funds

Please explain in detail the proposed use of T2T funds including milestones, timelines and costs. Describe how T2T funding and access to MTI expertise and capabilities will accelerate the translation of the NC3Rs-funded technology/model into research tools that can be applied in industry. Describe what modified technology readiness level (mTRL) the technology/approach is currently, and the mTRL to be achieved by the end of the project. Please include a description of (i) what contributions each applicant will provide and how these will support achievement of the intended mTRL and (ii) the potential risks and mitigation strategies. Please outline your future plans following successful completion of your T2T proposal to fully drive the model into application and maximise use of the data generated. The maximum word limit for this section is 600 words.

Associated attachment (compulsory): Project milestones/Gantt chart (maximum two sides of A4).

6. Team and expertise

Please provide a detailed description of the project team (skills, expertise and track record). Include any relevant commercial/management expertise in the team and identify any gaps in experience where additional support is anticipated in the future. Please include any previous experience of generating impact from academic research. The maximum word limit for this section is 600 words.

Associated attachment (compulsory): The CVs of up to five principal team members should be combined and included as a single attachment (maximum one side of A4 per team member).

7. Application finances

T2T awards are non-Full Economic Costing (FEC) and as such, applicants can apply for **100% directly incurred costs**. Please provide a summary of the overall costs requested to support research conducted at the MTI (7a) and the costed MTI contributions (7b). Costs requested should be inclusive of VAT, as appropriate².

Direct Costs

These are costs that are specific to the project, including:

- Labour costs for any non-MTI staff contributing to the project broken down by individual.
- Material costs, including consumables for research/validation work relevant to the project and conducted within the MTI.
- Travel and subsistence costs.
- Other costs specifically attributed to the project.

Itemisation of costs and methods of calculation may be requested to support the application at a later date.

In addition, please provide justification for the resources required to undertake the proposed project.

• Additional funding from external sources: Please provide details of additional funding from external sources that will support this project.

² It is the responsibility of the lead MTI applicant to determine whether VAT should be paid.

8. 3Rs impact

Please provide your own assessment of the 3Rs impact of the work, including qualitative assessment of the 3Rs benefits and quantitative estimates of the numbers of animals affected wherever possible. Please also consider the wider application of the technology/model beyond the current application and the 3Rs benefits of this. For guidance on writing effectively about the 3Rs visit the <u>NC3Rs website</u>. The maximum word limit for this section is 600 words.

9. Declaration

The lead MTI applicant is expected to have discussed the application within their own organisation and any other body whose co-operation will be required to deliver the project. By submitting an application, the applicants are confirming that the information provided within the application is complete, that they are actively engaged in this project and responsible for its overall management and agree to administer the award if made. They are also confirming that the guidance has been read and understood.

The completed application form must be submitted by email to <u>innovations@nc3rs.org.uk</u>.

Application form section	Attachment name	Page limit (sides of A4)	Optional / compulsory
Section 4 (i)	Letters of support	1 per letter	Optional
Section 4 (iii)	Summary of patents	Template provided in application form	Optional
Section 4 (iv)	Letters of support	1 per letter	Optional
Section 5	Additional milestones/ Gantt chart	2	Compulsory
Section 6	CVs (up to five)	1 per team member (5 in total)	Compulsory

Table 3: Summary of attachments

3. Assessment procedure

Following submission, applications will be checked for remit and eligibility before review by the T2T Assessment Panel.

Table 4: Panel assessment criteria

Assessment criteria

- Potential for T2T funding to progress technology to mTRLs 5-7 (as defined in Table 2)
- Potential 3Rs impact
- Scale of the market opportunity
- Value for money and justification for use of funds in achieving deliverables
- Expertise and track record of the team

Membership of the Panel is published on the NC3Rs website. All Panel members sign a confidentiality agreement upon appointment and are expected to abide by the principles set out in the '<u>UKRI Conflicts of</u> <u>Interest Policy</u>'. Panel members are required to declare any private, professional or commercial interests that might, or might not be perceived to, conflict with the NC3Rs interests. These declarations are published on the NC3Rs website.

The Panel's decision is final and is not open to appeal.

3.1. Award starting procedures

The lead MTI applicant is informed by email of the outcome of their application approximately one week after the Panel meeting. Awards are made to the MTI which then administers the award including return of signed documentation.

The lead MTI applicant must agree to manage the award on behalf of the co-applicants. Co-applicants negotiate their agreements with the MTI directly.

It is expected that work on successful projects should commence promptly.

The NC3Rs leads on award announcements. Award holders may be required to participate in media-related activities regarding the announcements.

4. Post award information

4.1. Intellectual property

The MTI and the academic co-applicant shall between themselves agree written terms setting out ownership and rights of use of intellectual property, including but not limited to any commercialisation income or revenue share arrangement. Although the NC3Rs is not a joint owner of any IP arising from a project, it is a condition of funding from the NC3Rs that work furthering the 3Rs must be made available to the rest of the bioscience sector. The protection of IP through filing of patents should therefore be pursued without unreasonable delay, and access by third parties to 3Rs benefits must be provided through publication and dissemination, or by appropriate licences, royalty-free or royalty-bearing on fair and reasonable terms.

4.2. Project management

The lead MTI applicant will be responsible for ensuring key deliverables of the project plan are met within agreed timeframes. A project management team consisting of the lead MTI applicant, relevant members of the project team and the NC3Rs will be established to oversee successful delivery of the project and to determine best next steps if it is decided that the model does not meet genetic tractability requirements or if project deliverables are not being met. Should this occur, possible next steps could include terminating the project or redirecting it to assess the utility of the model for compound screening or target validation purposes. The project management team will meet at quarterly intervals unless otherwise agreed.

4.3. Reporting

All competition awardees are required to submit a **final report** and a **final expenditure statement** (FES) within three months of the completion/termination date. The final report should describe the work undertaken, the achievements and outcomes of the project and details of how the project advanced the 3Rs. The report template, FES and additional guidance will be sent to awardees four weeks before the completion date.

Failure to provide the requested report and FES, within the specified timeframe, may result in funding being recouped. It is the responsibility of the lead MTI applicant to manage the funds awarded responsibly and any additional costs incurred above the total amount awarded will not be reimbursed.

4.3.1. Researchfish and publications

Award holders are expected to disseminate their results by publishing in appropriate scientific journals and at relevant conferences. The <u>UKRI policy</u> on open access should be adopted. Award holders are required to report research outputs and outcomes on a regular basis using <u>Researchfish</u>. There is a mandatory annual collection period for the submission of data.

The NC3Rs support for the project should be acknowledged on all publications and presentations where such support has been significant. The NC3Rs should be informed of any publications or other promotional material or events arising from the award.

It is the responsibility of the lead MTI applicant to keep the NC3Rs informed in a timely manner of outputs from the funded project.

Further information on reporting requirements can be found on the Researchfish website.