UK - Korea Multi-omics Based Research for Precision Medicine Research Initiative 2019

GUIDANCE ON PREPARING THE 'CASE FOR SUPPORT' AND 'GANTT CHART'

Important information

This document outlines the format and structure of the Case for Support.

As there will be a single Case for Support, it is vital that it provides full details of the work proposed for both the UK and Korean components.

Both partners must submit an identical joint Case for Support (including the optional one page methodology annex) and a separate one page Gantt chart written in English to the MRC and MSIT/NRF. The submission to MSIT/NRF will be via NRF's Integrated Research Support System https://ernd.nrf.re.kr). Failure to submit a valid application to both funding agencies will invalidate both submissions.

The optional one-page methodology reproducibility and statistical design **methodology annex** provides additional detail of the methodology and experimental design aspects of the proposal. This information must be provided as a clearly marked annex at the end of the main Case for Support entitled '**Methodology and experimental design annex'**. Please note that you are not required to duplicate information presented elsewhere in the application.

The use of this annex is strongly advised where the proposal includes the use of animals and/or human participants (in either country), or where the methodology/experimental design proposed is practically novel. Please see section 4.3 of the standard MRC Guidance for Applicants.

Format and page limit

The English version of the case for support must be:

- on A4 paper
- Arial font
- size 11pt or bigger
- have 2cm margins on all sides (the top and bottom as well as the left-hand and right-hand sides

Case for Support page limit:

- up to 12 pages for the main **Case for Support** (including illustrations and references) (compulsory)
- + up to 1 page for the reproducibility and statistical design **methodology annex** (optional but recommended)

These should be submitted as a single PDF.

The case for support must not exceed 10MB. Avoid the use of large colour figures as these will increase file size. There is no guarantee that documents will be reproduced in colour for the peer review process.

Please attach the Case for Support as a PDF document when you submit your proposal, especially if mathematical symbols are used in the content.

Gantt Chart page limit:

- Applicants should also submit as a separate document a **Gantt chart** (optional but recommended) which can be up to 1 page.

The Gantt chart must be converted to a .pdf file (max **1 x A4 page**) and submitted to both the MRC and NRF. Please note that the maximum file size for the Gantt Chart is 5MB. On the MRC's Je-S application system the 'Gantt Chart' should be attached using the attachment type 'Letter of Support'.

Structure

Applicants should use the structure outlined below when preparing their Case for Support and Gantt Chart

Consortium Details Overview

State the title of your project.

List the UK and Korean Consortium Principal Investigators
These are the individuals who will take responsibility for the leadership of the consortium. They will be the funders' main contacts for the proposal.

List all UK and Korean Co-Investigators and Work Strand Lead Facilitators
We would normally expect there to be one lead per work-strand and that each would also be co-investigators on the application.

Section 1: Consortium Vision, Outputs and Rationale

1.1 Please describe the Consortium's vision and the nature of the challenge(s) it seeks to address, to include how the vision meets the call's remit and why an initiative of the scale proposed is necessary to address the targeted challenges

1.2 Please describe the nature of the outputs that you hope the consortium will deliver both within the period of support (taking into consideration the different funding timelines in the UK and Korea) and beyond

1.3 How will these outputs potentially change patient care pathways? Please give specific examples where possible with timelines to delivery, including, for instance, utilisation of potential new diagnostic tests to help direct therapy selection

1.4 Please describe the potential health economic benefits of these outputs. We recognize that further work will likely be required in the course of the consortium to assess the economic realism of developing outputs

1.5 Please describe the rationale/hypothesis underpinning the proposed lines of research

Section 2: Patient/Public Involvement and Engagement

2.1 What are the plans for realistic patient involvement and engagement? What moves have already been made to ensure patient input into the consortium planning phase and how do you plan to involve/engage patients in the delivery of the consortium?

2.2 What are your plans for broader public engagement?

Section 3: Industry Needs and Partnership

3.1 What are the needs of industry in this field? Where appropriate, please demonstrate any intellectual input from industrial partners to shape this application

3.2 What is the potential industrial pipeline in this disease area? How will engagement with this consortium benefit development of this pipeline?

3.3 If appropriate, describe plans for engagement with industry partners e.g. pharmaceutical, diagnostics, devices, etc?

Section 4: Work Strand Durations, Costs and Plans

4.1 Work Strand Durations and Costs

4.2 Please provide an overview of the proposed lines (work strands) of research, explaining how these strands will form a dynamic research platform that will synergistically address the consortium's targeted challenge(s).

The proposal should clearly specify which tasks will be carried out during stage 1 in the UK and Korea, and which tasks will be carried out during stage 2 in Korea only. Please note that UK researchers will not be funded by the MRC for Stage 2.

You may wish to reference your GANTT chart, to show the relationships between work strands, and consider inclusion of a flow diagram, to highlight the logic of these relationships

4.3 Please describe, in turn, the detailed plans for each of the individual work strands

This should form the bulk of your case for support. The scientific quality must be excellent, and you should be very clear on how the science will translate to real world stratification in the clinic.

To include for each work strand:
- *Nature of question being addressed,*
- *Proof of concept data (if relevant).*
- *People and track record:*
    - o *Each applicant's CV will be provided separately in the electronic application form but elaborate here on why the group is well qualified to do this research.*
    - o *Explain how the applicants work together, and outline other major collaborations important for the research.*

- *Scientific and methodological approach:*
    - *Give details of the general experimental approaches, study designs, methodological approaches and techniques you will use. It is not necessary to describe each experiment, but you must give enough detail to show why your research is likely to be competitive in its field*

- *Highlight plans which are particularly original or unique.*
- *Explain in greater detail how new techniques, or particularly difficult or risky studies, will be tackled and alternative approaches should these fail.*

o *Contributions of project partners and how these are enabling for the proposed work*
o *Justification for use of animals, where appropriate*
o *Please clearly articulate how you will undertake a health economic assessment of the benefits of the stratification approach described.*

Section 5: Methodology

5.1 Please describe and justify your selection and prioritization of potential sources of differentiating markers of response to treatment, or risk, diagnosis and/or prognosis, and for your proposed search strategy for these markers

5.2 Please describe and justify the analysis strategy you will use to identify associations between markers and response to treatment, or risk, diagnosis and/or prognosis, and to aid mechanistic insight

5.3 Where appropriate, please describe and justify the design of proposed clinical trials to test your stratification hypothesis

5.4 Please explain why your proposed studies/trials will have sufficient statistical power to robustly answer your research questions

Section 6: Resources and Environment

6.1 What key resources (materials, methods, data, people, infrastructure, outsourced tasks etc) are needed to undertake the proposed research?

6.2 Are these resources in hand? If not, what gives you confidence that they will be available when required?

6.3 Please describe the scientific and clinical environment(s) in which the research will be done and how these will increase the chances of success

• *Explicitly highlight the contribution of clinical research infrastructure. For example, biomedical research centres, clinical research networks etc.*
• *Explain how the research will benefit from facilities provided by the host Research Organisation*

Section 7: Data and Samples

7.1 Please describe how samples and data will be collected, quality controlled, curated, pooled and shared across the consortium and beyond. **Please outline how any issues related to sharing data across borders would be approached.**

7.2 Please describe the arrangements for integrated health and biomedical informatics expertise and support across the consortium. This section should be highly detailed.

7.3 Explain how the research will benefit from interactions with existing health and biomedical informatics research infrastructures, for example (but not exclusively) MRC and MSIT/NRF major investments.

Section 8: Consortium Management

8.1 Please provide an overview of consortium governance and management plans. As the consortium develops, how will you ensure that new opportunities are seized upon and less fruitful activities are dropped? How will this process be managed in a complex consortium?

8.2 Please provide details of the track record of the consortium team in delivering consortia similar to that proposed

8.3 Who will the consortium project manager be? If already identified, please provide details of their experience in managing consortia similar to that proposed. If not yet identified, please provide a job specification for the project manager role and your recruitment strategy.

8.4 What are the consortium's key risks, how likely are these to occur and what would their impact be? How will these risks be managed?

Section 9: Downstream

9.1 What are the major downstream hurdles that will need to be overcome if the consortium is to deliver true patient benefit and how will these challenges be met?

9.2 How will the durability of the consortium be ensured beyond the period of MRC/MSIT/NRF support?

Section 10: Consideration of ethical, governance and Intellectual Property (IP) issues

• Explore the ethical considerations associated with the research programme and describe, in full, the ethical approvals which will be sought if successful for funding.

  o For further information on research involving procedures on animals, please see the scheme-specific call guidance on the MRC call website[1].

• Describe the governance structure of the Consortium and describe clearly how the decision-making process will be managed.

• Where applicable, describe any expected Intellectual Property that will result from the proposed research and outline how this will be managed.

Section 11. Data preservation, exploitation and dissemination

• Describe how the group will work together to maximise sharing of data and create a legacy of data available beyond the consortium's funding period.

Section 12: References

References

[1] https://mrc.ukri.org/funding/browse/uk-korea2/multi-omics-based-research-for-precision-medicine-research-initiative-2019

Annex 1 to Case for Support: Reproducibility and statistical design methodology annex (optional but recommended) (maximum 1 page)

The purpose of this annex is to provide important additional information on reproducibility, and to explain the steps taken to ensure the reliability and robustness of the chosen methodology and experimental design. Please note in this context, methodology refers to the rationale for choosing which method to use and not the provision of detailed descriptions of the methods to be used.

It is **strongly advised** that a one-page annex to the case for support is included (this is in addition to the page limits for the main case for support) to provide additional information specifically relating to the statistical analyses, methodology and experimental design aspects of the proposal (beyond that contained in the main case for support). Please note that you should not duplicate information presented elsewhere in the application.

This information must be provided as a clearly marked 'Annex 1' at the end of the main case for support, entitled 'Reproducibility and statistical design annex' and should not be added as a separate attachment. Standard formatting guidance applies. Applications not adhering to these conditions will be returned unprocessed.

Applications that do not provide sufficient detail to convince peer reviewers and panels that the proposed experiments will be carried out appropriately to produce robust and reproducible research will be rejected for funding on these grounds and subject to the usual limits on resubmission.

The UK's National Centre for the Replacement, Refinement & Reduction of Animals in Research (NC3Rs) have developed a free online tool to guide researchers through the design of their experiments, helping to ensure that they use the minimum number of animals consistent with their scientific objectives, methods to reduce subjective bias, and appropriate statistical analysis. The NC3R's *Experimental Design Assistant* can be found on the NC3R's website.

What to include in the annex
It is expected that professional statistical (or other relevant) advice would be sought in putting this section together. Each experiment does not need to be described in detail, but sufficient information must be included that reviewers are readily able to understand the experimental plan. Where appropriate, the use of figures, tables and/or diagrams is encouraged.

The following table highlights the key points you should include in the annex.

Experimental approach to address objectives. **This information may be provided in diagrammatic or tabular form if appropriate.**	• Primary and secondary experimental outcomes to be assessed (e.g. cell death, molecular markers, behaviour change) and how these relate to experimental objectives • Number of experimental and control groups • A clear definition of the 'experimental unit' in the analysis and the implications thereof (i.e. 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) • Number of 'experimental units' in each experimental group. • Total number of 'experimental units' to be measured • Number of times each 'experimental unit' will be measured • Number of independent replications of each experiment. • Steps taken to minimise the effects of bias (e.g. blinding, randomisation) or an explanation of why this would not be appropriate • Breeding strategies may be included here, if applicable.
Justification of model(s) chosen (e.g. animal model, cell line etc.	• How and why the models and/or methods are appropriate to address the scientific objectives
Sample sizes	• Show clearly how effect sizes have been calculated and justify how they are biologically relevant • Demonstrate that statistical power calculations are grounded in justifiable and explicit assumptions about both anticipated effect size and variability of the experimental effects • If statistical power calculations cannot reasonably be applied, applicants should provide a principled explanation of the choice of numbers • Explanations based solely in terms of 'usual practice' or with reference solely to previously published data will not be considered adequate.
Planned statistical analyses and their relation to the choice of sample size	• Overview of the planned statistical analyses in relation to the sample size • Details of any statistical/methodological design advice sought (you may cost a relevant expert, e.g. statistician, into your proposal if necessary and justified). A letter of support from the expert involved is permitted, but not mandatory

If your proposal includes the use of animals, please also refer to the UK scheme-specific Guidance for Applicants (available on the MRC Call website) in addition to the guidance above, for more information on the key points you may wish to include in the annex.

What not to include in the annex
The annex should not to be used as a simple continuation of the methods set out in the case for support; please do not include detailed descriptions of the methods. Applications misusing the annex in this way will be returned. The case for support should be a self-contained description of the proposed work with relevant background, and should not depend on additional information.

For proposals involving animal use, information on the rationale for using animals, choice of species, information about the animals used (e.g. weight, sex), animal costs and procedure severity information should be provided elsewhere in the application.

Consortium Gantt Chart annex (optional but recommended) (maximum 1 page)

Applicants should provide a separate PDF with a Gantt chart of the proposed consortium plan.

The Gantt chart must be converted to a .pdf file (max **1 x A4 page**) and submitted to both the MRC and NRF. Please note that the maximum file size for the Gantt Chart is 5MB. On the MRC's Je-S application system the 'Gantt Chart' should be attached using the attachment type 'Letter of Support'.