EMCG Guidance for Applicants

This EMCG guidance for applicants should be read in conjunction with the MRC applicant’s handbook.

The EMCG scheme will support a range of award scales, from smaller, focussed, more exploratory and highly innovative projects (based e.g. on an intellectually sound hypothesis but perhaps lacking extensive pilot data), to large programmatic awards based on a more substantial platform of data.

The following points are suggested as facets of good experimental medicine (EM) studies, and should form the core of proposals:

1. Focus on the Experiment

EM studies should be hypothesis led/defining/refining; EM is more than hypothesis-free characterisation, and is more exploratory than hypothesis-testing confirmatory work.

- EM is more than just data collection; emphasis on the Experimental. Proposals may include:
  - All proposals should include an experimental intervention/challenge in humans, perturbing the system to explore disease mechanism. The challenge may be pharmacological, immunological, physiological, psychological, infectious etc.
  - The use of novel readouts or technologies (with sufficient supporting evidence of feasibility).
  - The use of drugs, other interventions or measures with established safety profiles in new settings/conditions: e.g. repurposing drugs as tool compounds to probe disease mechanism.
    - Applicants are encouraged, where appropriate, to engage with the MRC-Industry Asset Sharing Initiative, where a pool of assets are available, many of which have sufficient clinical data to enable exploration to clinical hypotheses
- Proposals may include, but should not solely focus on, deep characterisation/phenotyping of subjects. Proposals which are predominantly descriptive are unlikely to be shortlisted; an experimental approach, and a clear plan for establishing causal relationships and mechanisms, is expected.
Projects do not need to develop/test therapeutic interventions – developmental clinical projects are usually supported through MRC’s translational schemes – but exploratory studies with potential to both advance understanding of disease mechanism and also provide initial evidence for a potential treatment are welcomed.

As part of previous EMCG rounds a webinar was held to articulate the remit and strategic intent of the EMCG scheme, and pose questions to the panel, which included: the Chair of the EMCG panel, an MRC Board Chair and EMCG Panel Member, an EMCG co-PI and the MRC Programme Manager for experimental medicine. The Panel addressed the aims of the scheme, what qualifies good experimental medicine, challenges identified from previous rounds and how successful applications were designed, reviewed and conducted.

2. Detailed Plans

Full applications must include detailed experimental plans, comparable to requirements for a programme grant application. Lack of detail was a very common reason for rejection in previous funding rounds (outline applications should have a defined plan for the experiments, with commensurate detail).

- Proposals need a structured rationale for the mechanistic hypothesis to be defined and tested, and for the readouts and measures which are proposed.
- Studies should be methodologically and statistically rigorous in design and should take appropriate steps to minimise bias, and we recommend that applications include appropriate support (e.g. a statistical co-applicant) for this aspect.
- Novel approaches, imaging, integrative models and computational approaches are encouraged where appropriate.

3. Partnership

Applicants are encouraged to explore collaboration with industry to facilitate the above experimental approach (however this is not mandatory). Opportunities also exist through the MRC-Industry Asset Sharing Initiative.

MRC is working with a number of industry partners (including AstraZeneca, GSK, J&J, Pfizer, Takeda and UCB) to provide researchers access to their deprioritised compounds. This virtual library of compounds is available to support experimental medicine studies, and for use in the Experimental Medicine Challenge Grants competition.
Partnership with charities is welcome, e.g. in access to established patient cohorts or use of infrastructure. Co-funding of proposals will be considered.

Collaborations between institutions, between scientific/clinical disciplines, with industry or with overseas expertise are encouraged but must add demonstrable value to the project, and include clear management plans. Partnerships may add value, for example, in terms of access to expertise, technologies, reagents, patient groups, data or funding. The MRC does not have the capacity to broker these arrangements.

Applicants are encouraged, where appropriate, to make use of existing infrastructure across the UK for experimental medicine, e.g. the NIHR Biomedical Research Centres (BRCs).

4. Scientific Risk and Adaptation

Projects that explore new areas will involve scientific risk that results are not as anticipated. For larger, longer-term programmes we expect to see risk mitigation plans addressing, for example:

- What alternate strategies will be employed if results at an early stage of the project are not as expected?
- What would need to be established before embarking on the higher-cost parts of the programme?

MRC is keen to provide researchers with committed support for longer term programmes, but may need to identify milestones and stage-gates – identified by the applicants in the proposal, or identified in review – along the pathway of the study.

5. What not to do

Recurrent issues with unsuccessful applications in previous rounds included:

- Excessively broad and all-inclusive ‘omics’ approaches, without sufficient rationale for the variables to be measured.
- Unnecessarily high costs resulting from lack of focus – applicants should consider “what is the critical path?”.
- Under-powering and poor statistical consideration and study design, e.g. around effect size estimation.
- Weak case for the importance of the work in the context of other studies in the area, and the potential impact of the mechanistic knowledge that will be gained. How will the insight gained be exploitable or developed further in subsequent studies?
- A lack of innovation in the methods and measures employed (this may facilitate new avenues of investigation and new insight, but is not mandatory).

**Assessment criteria**

Full proposals will be assessed on the standard criteria for an MRC research grant, in addition to the following EMCG criteria:

- **Fit to the call remit**: Is the proposal within remit?
- **Rationale & potential impact**: Is there a strong scientific rationale for the project? Does the proposal address an important, clearly-articulated and tractable gap in understanding? Is the proposal likely to lead to major improvements in understanding of human disease mechanisms? Is there an appropriate level of evidence to support the proposed rationale? Is it sufficiently ambitious and/or innovative/challenging to warrant funding through this scheme rather than through standard research grant support?
- **Research strategy**: Is an appropriate experimental scientific strategy presented to address the research question? Have the investigators chosen a suitable range of approaches to deliver new insights, and do the individual strands of work reinforce each other? Do the initial phases of the work proposed give confidence in the project?
- **Quality and skills of the research team**: Are these appropriate to deliver the proposed research?
- **Research environment & infrastructure**: Is the required research and/or clinical infrastructure in place? Do the applicants plan to make use of NIHR’s Biomedical Research Centres (BRCs), patient cohorts or other established infrastructure across the UK?
- **Experimental design and statistical considerations**: Have the applicants described a clear experimental design with appropriate statistics for the conduct and analysis of the research? Are appropriate staff involved to support this?
- **Risk mitigation & management**: Projects that explore new areas will involve scientific risk that results are not as anticipated; EMCG can accommodate this. Are there appropriate plans in place for risk mitigation and management, including milestones or stage-gates if appropriate?

**Ethics and Regulatory Approval**

The MRC does not require ethics permissions and regulatory approvals to be in place when you submit an application (outline or full).

However, given that research involving human subjects or requiring the use of human tissue/organs may raise various ethical and regulatory
issues, applicants will be required to demonstrate that they have adequately considered these matters.

Early discussions with regulatory bodies are advised to ensure that all requirements can be met in a timely manner. Once an application is successful, it is the responsibility of the host institution to ensure that the appropriate ethics and regulatory approval has been obtained and that no research requiring such approval is initiated before it has been granted. (Please read the MRC terms and conditions for further details.)

Guidance

Prospective applicants are strongly encouraged to engage with their institution’s Research Governance Office who will be able to offer guidance and support.

Guidance is available on the MRC Regulatory Support Centre website, developed in collaboration with the Health Research Authority, for those conducting research with human participants, their tissues or data. Applicants are strongly encouraged to look at and make full use of The Experimental Medicine Tool Kit.

The vast majority of studies that involve human participants, their tissues or data should undergo a research ethics committee (REC) review and many research studies may require an NHS REC opinion. The HRA Decision Tool can be used to determine whether your study requires this type of approval.

The Integrated Research Application System (IRAS) should be used when applying for NHS REC approval and for other regulatory approvals. IRAS is a single system for applying for the permissions and approvals for health and social/community care research in the UK.

Industrial Collaborations

Applications involving collaboration with industry should adhere to the MRC Industry Collaboration Agreement (MICA) guidance. The lead applicant must be the academic partner, and MRC will meet the academic costs of the project only. MICA forms and Heads of Terms are not required at the outline application stage (but are required at full application stage), but letters of support confirming industrial partner engagement are expected.

The terms of collaboration, particularly in relation to industry, should be determined early in the study development and relevant agreements must be in place by the outset of the project. Partnership arrangements should ensure transparency in the project design and in the analysis and publication of results (including if these are negative).
Consideration should also be given to issues such as: relative responsibilities, governance arrangements, regulatory approvals, indemnity, intellectual property rights, reporting, and access to data and samples.

**Intellectual Property**

Note that the generation of intellectual property is not a requirement for this scheme.

Intellectual property generated in the course of a project will (subject to the conditions of the MICA system) be owned by the host institution, which will have the right to manage and exploit this intellectual property.

The costs of managing, protecting and exploiting the intellectual property are borne by the host institution and are not eligible costs for MRC support.

**Enquires**

You should contact the MRC Programme Manager for Experimental Medicine, Dr Rebecca Barlow, before submission:
rebecca.barlow@headoffice.mrc.ac.uk  Tel: 0207 395 2204

For other queries please contact:
Experimental.Medicine@headoffice.mrc.ac.uk