



Developmental Pathway Funding Scheme

Supplementary Applicant Guidance: Clinical Test Development and Validation

To be read in conjunction with the MRC and DPFS Applicant Guidance
for outline and full applications

OFFICIAL

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Introduction

MRC is the leading UK funder for early-stage biomarker development and validation and plays a vital role in underpinning the development of in vitro tests in the UK. MRC, along with its sister organisations EPSRC, BBSRC and Innovate UK, has provided over half of all UK public and charity sector funding in 2018 that was committed for the development of biomarkers and in vitro tests.

In May 2022, MRC conducted a portfolio analysis of applications to the Developmental Pathway Funding Scheme (DPFS) and the associated Panel feedback to applicants following review of their proposals. The analysis identified opportunities for applicants to enhance the competitiveness of their DPFS applications across several common challenge areas. Following consultation with the DPFS Panel and other expert stakeholders, this supplementary guidance speaks to these challenge areas and provides additional guidance for applicants applying to DPFS for funding to develop and validate clinical tests.

1) Clinical Need

Applicants should have a detailed understanding of the existing diagnostic and care pathways in their intended target market. For clinical tests destined for the NHS for example, an understanding of (i) the current NHS diagnostic pathway for the proposed clinical indication, (ii) the accuracy, use case (including use population) and limitations of the current reference standard test and (iii) how the current reference standard is used to inform treatment or clinical outcome, should be clearly articulated in your DPFS application. An awareness of the test procurement landscape in the proposed market should be evidenced to ensure that uptake of the proposed test is feasible and economical. DPFS welcomes applications that are predominantly intended for LMIC countries.

Ensuring relevant clinical input to the development of your DPFS application, either through consultation or through involvement of clinical investigators / partners in your project team, is essential to ensuring that there is a clear clinical need for the proposed test.

Key questions to consider when completing your outline and full DPFS application:

- What is the target patient group, market, user and proposed site of use for the test?
- What is the current reference standard test? What are the proposed test's advantages and disadvantages in relation to accuracy, cost, time from test to result, scalability, feasibility in deploying to LMIC settings etc?
- Have you conducted any Patient and Public Involvement (PPI) - if this is feasible and the patient population is accessible - to initially assess the acceptability and potential utility of the proposed test?
- Is the proposed platform technology in which the test will operate on appropriate? Can it be economically scaled up and will it be used locally or centrally? For examples, tests utilising mass spectrometry will unlikely be appropriate for local testing in LMIC countries with limited resources and sample transportation infrastructure.
- What biological sample types will the test probe and how does this align with the clinical setting the test will be used in? Do primary care providers have the resources or funding to implement a rapid POC test in a primary care setting when there could instead be efficiencies of scale in sending patient samples to centralised testing centres?

Relevant sections of the application: Case for Support (Section 4&5); Supplementary Data attachment (insert TPP here).

2) Deliverability

Applicants should ensure that they have the appropriate expertise assembled during the development of the grant application and the delivery of the project. This is particularly relevant of clinical experts who understand the current diagnostic / care pathway (as described in Section 1 above) and statisticians with relevant expertise in studies design for test validation, head-to-head comparison studies etc. Human factor experts assessing health economics, barriers to adoption etc should also be considered.

Key questions to consider when completing your outline and full DPFS application:

- What patient groups / demographics are relevant for the development of the proposed test to ensure that it is fit for end use? Clarification of patient inclusion and exclusion criteria should be clearly articulated.
- Are the technical specifications for end use feasible? Can the target sensitivity, specificity, reproducibility etc be achieved and how have these targets been determined? Has a Target Product Profile¹ been developed with input from clinical end users and has it been included in the application's supporting data attachment? Has a national or international (e.g. [FIND](#), [WHO](#)) TTP already been described for the disease you aim to test for?
- Can a standardised protocol be used for the acquisition, processing and storage of clinical samples to ensure sample quality and data reproducibility? For later stage proposals, can the standardised protocol be aligned with common industry and ISO standards, considering aspects such as automation of sample processing etc? Can clinical samples undergo genomic / proteomic characterisation prior to storing, to provide information to underpin future evaluation studies?
- Have regulatory go / no go points been included within the project's milestones and has engagement within relevant regulators or regulatory consultants been embedded into the research plan?

Relevant sections of the application: Case for Support (Section 6); Supplementary Data attachment (provide TPP here).

3) Development Pathway

It is essential for applicants to have carefully considered their test's developmental plan through to clinical impact before submitting a DPFS application, with support from their Translational Research Office or equivalent. Depending on the development stage of the proposed test, the applicants should set out how the biomarker(s) or platform technology will be further developed, undergo retrospective validation (including blinded validation and validation in independent retrospective cohorts etc) or early prospective validation. Prospective evaluation of a test in large numbers of patients is out of remit of DPFS and may be better suited to NIHR's [Efficacy and Mechanistic Evaluation](#) (EME) scheme or [Health Technology Assessment](#) (HTA) scheme. Applicants may find referral to the Technology Readiness Level (TRL) scale helpful in orientating themselves with the technical development pathway of their test. Guidance is available to help you navigate scheme remit between [DPFS and EME](#), and between [EME and HTA](#).

¹ Further information relating to the information typically considered in a Target Product Profile is provided at <https://www.vaccinedevelopment.org.uk/target-product-profile.html>. Although this resource focuses on vaccine development, the framework and listed categories of consideration will likely be useful in TPP development for *in vitro* tests.

Applicants should have a clear understanding of the competitive market landscape - especially if there is a current reference standard test used in the target market – and be able to clearly articulate how the proposed test presents a competitive advantage. A high-level overview of the costs associated with (i) the current reference standard, (ii) the proposed test and (iii) savings possible through the deployment of the proposed test should be included in a DPFS proposal. Depending on the development stage of the proposed test, it may be useful to include a more detailed health economic study within your proposal’s research plan (which MRC will consider funding).

Applicants are encouraged to consider the Commercial Readiness Level (CRL) of their test in parallel to the TRL scale.

Applicants should ensure that they have Freedom to Operate during and after the proposed project, considering any required access to background Intellectual Property Rights (IP) and how arising IP will be managed.

Industry partners

Applicants should ensure that they have assembled the relevant expert organisations to deliver the project research plan and to take forward project outputs.

Industry organisations may be able to offer specialist resources, expertise and insight into the test development pathway and provide a commercialisation route following the end of the proposed project. **MRC data has shown that early-stage engagement between applicants and industry organisations sees an improvement in the competitiveness of MRC translational funding applications.**

Industry engagement may take the form of:

- A project industry partnership, supported by MRC’s [Industry Collaboration Framework \(ICF\)](#), which provides which provides a framework to assist the development of collaborations with industry organisations;
- Industry advisors providing input on market opportunities, commercialisation routes and regulatory pathways across different jurisdictions - either during the development of a proposal or during a project’s delivery; or
- Initial dialogue with an industry organisation, evidenced appropriately within your DPFS application, that is supportive of the proposed research or potentially has interest in future partnering to commercialise the project outputs.

Regulatory Pathways

Once the initial target market(s) have been identified, applicants should consult with their Translational Research Office (or equivalent), the [MHRA Innovation Office](#) or other regulatory consultants to gain a clear understanding of the relevant regulatory pathway for their proposed test and its regulatory classification.

Different regulatory jurisdictions have varying legal definitions of IVDs and medical devices, in addition to different conformity marks and conformity mark acquisition routes, such as for Great Britain’s UKCA, Northern Ireland’s UKNI mark and the EU’s CE mark. Regulators in each jurisdiction will require the test developer to assess their test against specified risk classifications, which will dictate the performance assessment requirements before the test can be made available for end use.

For a test which is to be launched in the GB market, the UK regulatory body, MHRA, requires researchers to demonstrate the analytical performance of a test to obtain an analytical UKCA mark, which then enables the test to be used to inform clinical care. This is relevant for DPFS applicants

who intend to or have already conducted retrospective test validation and wish to conduct prospective validation which could impact subsequent clinical decision-making around patient care. A study that validates an IVD for medical use is termed a 'performance evaluation'; MHRA must be notified prior to any test performance evaluation, therefore DPFS applicants should ensure this is reflected in the proposed research plan as relevant.

Although many DPFS applications may focus on early-stage test development, it is important for applicants to evidence their understanding of what data packages will be required for downstream regulatory assessment and to include plans for the acquisition of the required data packages in the proposal's research plan.

MRC's regulatory guidance for applicants developing medical devices and IVDs may be found on our [website](#). Please reach out to MRC's Regulatory Support Centre for additional information:

rsc@mrc.ukri.org

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| Relevant sections of the application: Case for Support (Section 7); Letters of Support; MRC Industry Collaboration Framework (ICF). |
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