





REQUEST FOR APPLICATIONS

Joint Call for Research Projects on Tuberculosis

July 24, 2024

APPLICATION DEADLINE: 11:59pm CET (10:59pm UTC) October 31st, 2024

Proposals will not be accepted after this date and time

1. Introduction

Tuberculosis (TB) remains a major global health priority and, until the Covid-19 outbreak, has been the world's leading cause of death from a single infectious disease. According to the World Health Organization (WHO), worldwide, an estimated 10.6 million people fell ill with TB and a total of 1.3 million people died from TB in 2022.

The ANRS Emerging Infectious Diseases (ANRS MIE) and the South African Medical Research Council (SAMRC) have identified the acceleration of global TB control as a common strategic priority.

By jointly funding this call, the ANRS MIE and the SAMRC aim to promote and accelerate research geared towards improving the prevention, treatment and care of TB.

With this call, the ANRS MIE and the SAMRC also aim to encourage and support cross-country collaborations between stakeholders of South Africa and France in order to promote cooperation and alignment in scientific research between our two countries, their research teams and institutions, and wish to provide a general framework which would allow for the optimal development of strategic collaborations between said research teams and institutions.

Overall, this call aims to foster a better understanding, control and ultimately, elimination of TB through innovative strategies and develop scientific collaboration between researchers from South Africa and France over the long term.







2. Scope

2.1. Scientific priorities

The joint call aims to support research and innovation projects covering the whole spectrum of TB disease, including subclinical and drug-resistant TB.

Research proposals may address the following major topics in adults and children:

- (I) Epidemiology, pathogenesis, transmission and management of sub-clinical TB;
- (II) Identification of biomarkers for disease progression and the development of novel diagnostics based thereon;
- (III) Development of rapid diagnostic tools for evaluating drug resistance and for precision medicine in the management of TB;
- (IV) Development of new vaccine strategies, including new candidates to fill the vaccine development pipeline and strategies for feasibility and implementation of new vaccines that come onto the market;
- (V) Evaluation of new drugs or shortened regimens, especially for pediatric populations.

(I) Epidemiology, pathogenesis, transmission and management of sub-clinical TB

Subclinical TB is described as the stage when TB infected individuals show minimal or no symptoms yet may still be able to transmit infection to others, making them a reservoir nearly invisible to passive surveillance. Intensive research on subclinical TB seeks to provide primarily a better control of disease transmission by improved understanding, identification and management of such cases. The South African TB Prevalence Survey of 2018 showed that 58% of bacteriologically confirmed TB was asymptomatic or subclinical.

This objective involves expanding research efforts to better understand the epidemiology, pathogenesis, transmission and clinical implications of subclinical TB, as well as improved options for rapid identification and treatment in selected populations. Researchers may explore the epidemiology of subclinical TB, risk factors for progression to active disease, the impact of subclinical TB on TB transmission dynamics, biomarkers and other mechanisms for case finding and treatment options.

(II) Identification of biomarkers for disease progression and the development of novel diagnostics

This topic includes the identification and/or application of immune or other biomarkers associated with progression of clinical and subclinical TB, which can contribute to better diagnosis, risk stratification, and monitoring of treatment response.

(III) Development of rapid diagnostic tools for evaluating drug resistance and for precision medicine in the management of TB

Whilst there is a plethora of new diagnostic tools using nucleic acid amplification techniques and sequencing, there is currently a shift in the management of mono- and multidrug resistant TB and a rising risk of resistance to new agents. Thus, there is a need for better diagnostics and especially tools







for the rapid diagnosis of drug resistance across all classes of drugs especially those positioned for use in the new WHO and South Africa guidelines. Improved diagnostics are also needed for diagnosis in HIV co-infected individuals, paediatric populations and for extra-pulmonary TB.

Current diagnostic methods for TB, such as sputum smear microscopy and culture, have limitations in sensitivity, particularly for detecting latent TB, TB in its early stages, extrapulmonary TB, and resistant TB. There is a need for more sensitive, rapid, and affordable diagnostic tests, especially in resource-limited settings where the price of currently available TB-NAAT tests makes its use in widespread screening limited. These new diagnostics tools need to address current diagnostic gaps, including at various stages of TB disease and in co-infected individuals and other target groups listed above. Preference will be given to proposals that build on already identified markers.

(IV) Development of new vaccines strategies

There is still no highly effective vaccine for preventing adult pulmonary TB, which is the most common form of the disease worldwide. New vaccine generation should focus on controlling and preventing TB infection, including drug-resistant and latent TB. Understanding of immune responses to new vaccines, both in animal models and in different populations and age groups, and identification of correlates of protection as well as development of preventative vaccines and therapeutic vaccines to treat drug resistant TB or shorten treatments are necessary. There is an urgent need for the discovery of new vaccine candidates to fill the vaccine R&D pipeline over the next five years. With only one promising candidate in Phase III vaccine trials in the pipeline, the need for new candidates and strategies is crucial both for adult and adolescent populations, as well as other target populations.

(V) Evaluation of new drugs or shortened regimens, especially for paediatric populations

Low-cost proposals for the evaluation of new drugs or shortened regimens are needed, especially for pediatric populations, as are prognostic biomarkers for early treatment cessation.

2.2. Available Funding

Total available funding for this call is up to 3 million euros, with successful proposals to be awarded for an expected maximum duration of 3 years.

Assuming that a sufficient number of proposals of merit are received and taking into account legislative frameworks and funding terms and conditions of each funder, the number of projects selected, and total award will depend on the alignment of individual project budgets with the proportional contributions from the ANRS MIE and SAMRC.

2.3. Partnership & Co-Funding

The SAMRC mission is to advance the nation's health and quality of life and address inequity by conducting and funding relevant and responsive health research, capacity development, innovation and research translation.

The ANRS MIE aims to support research to provide scientific responses to infectious diseases in times of crisis and over the long term, with a specific focus on research into emerging infectious diseases, HIV/AIDS, viral hepatitis, sexually transmitted infections and TB.





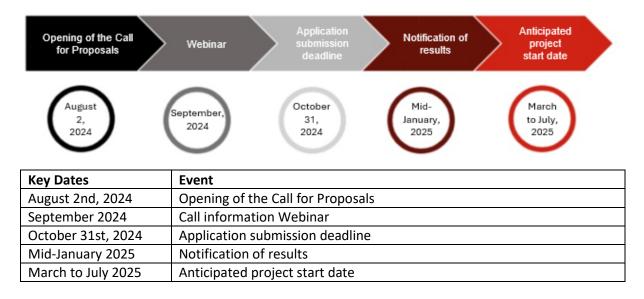
Recognizing the acceleration of global TB control as a common strategic priority, the ANRS MIE and SAMRC are launching this joint call to promote collaboration between researchers based in South Africa and France and accelerate progress towards this goal.

Following the criteria and review process laid out in this Request for Applications, only collaborative projects led by researchers from both French and South African institutions can be funded. Successful applications will be subject to separate funding agreements, with ANRS MIE on one side and SAMRC on the other side, which may contain different terms and conditions, such as, and without limitation: applicable policies, eligible expenses, intellectual property terms, and reporting obligations.

3. Application and Review Process

3.1. Application & Review Timeline

All proposals go through a multi-step review process before ANRS MIE and SAMRC together make a final funding decision.



3.2. Instructions for Application

Applications must be submitted in English on the ANRS MIE <u>APOGEE platform</u>, also available from ANRS MIE website (<u>https://anrs.fr/en/</u>), between August 2nd, 2024 and October 31st, 2024, and must include all the elements required for the scientific and technical evaluation of the project.

Prior registration on the APOGEE submission platform is required to submit an application.

The complete submission file consists of the following elements:

• Administrative section: administrative and scientific information on the project partners, including the list of the most significant scientific publications of the last five years, publications related to the Call thematic areas, and patents of the applicants;







- Scientific section: scientific presentation of the project, maximum 10 pages in length, and which must follow the template available on the APOGEE platform and on the page dedicated this Call on the ANRS MIE website.;
- Budget section: each proposal will include a comprehensive budget detailing the projected costs in HR, operating expenses and equipment for the entire duration of the project, broken down by individual teams as well as aggregated for the whole project (see eligible costs in section 5.1). Please note that all costs must be in euros. The rand/euro exchange rate at the date of the budget construction must be specified in order to ensure proper management of funding disbursements.
- **Appendices** to be uploaded separately from the scientific proposal: appendices must only be used for supporting material, such as figures, tables, raw data and other information supporting the research project. The main text of the research project must be sufficiently precise and detailed to be clearly understood without consulting the appendices.
- Letter of engagement: all proposals submitted for funding must include a letter of engagement signed off by each partner as well as an authorized representative of their respective institutions. It is the responsibility of host institutions to verify and certify the appropriateness, completeness and correctness of all information submitted by their researchers as part of their applications for funding. By co-signing applications, institutions commit themselves to administering the funding, if awarded, according to the relevant Terms and Conditions of Funding.

Only the electronic version of documents submitted through APOGEE by the Call closing date will be considered for evaluation.

The contact person submitting the application will receive an electronic confirmation when the proposal is submitted.

It is strongly recommended:

- to open an account on the APOGEE platform as soon as possible;
- not to wait until the project submission deadline to enter data online and upload files (note: it is imperative to respect the submission deadline);
- to check that the documents submitted are complete and correspond to the expected information and templates;
- to regularly consult the APOGEE platform and the ANRS MIE website, which provide up-todate information on the process;
- to contact, if necessary, the ANRS MIE or SAMRC using the email addresses provided page 13.

3.3. Eligibility criteria

Applications must be submitted **in English**, before the closing date of this call, and must include all required information and documents.

The Call is open to projects led by researchers affiliated with public universities and/or public research institutions in France and South Africa. Proposals must include research teams from both countries and demonstrate equitable and effective collaboration. Each project submitted must have two







Principal Investigators (PIs), one being a South African (citizen or permanent resident) researcher and the other one affiliated to a French academic institution (regardless of nationality). French private not-for-profit research organizations can be considered eligible as leading institutions if they contribute to the public service missions of higher education and research, governed by article L. 732-1 of the French Education Code. South African research institutions eligible as leading institutions include universities, science councils and other legally constituted institutions or organisations wherein research is one of the primary purposes for its existence, including training postgraduate students. Other NGOs might be eligible for funding, but they are not eligible as leading institution.

Participation of additional international partner teams is also possible. In such cases, only LMIC, as defined by the World Bank, partners may receive funding. Additional international partners will not be eligible to serve as Principal Investigators. The list of countries eligible for funding is available in the following link:

https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups

Please note that due to the current geopolitical context, teams based in countries where cooperation with France or South Africa is currently suspended will not be eligible for funding under this Call. This criterion may change depending on ministerial directives.

Private companies (entities registered as private, for-profit companies) are not eligible to apply for funding through this Call for Proposals, but may be included as sub-contractors, in compliance with the institution's procurement policies, if they provide a service or capability that is not available among the project partners but is essential for the completion of project deliverables. Alternatively, private entities can join the project as non-beneficiary partners.

Any individual involved either directly or indirectly in any of the SAMRC or the ANRS MIE granting processes may not apply for funding.

Duplication of application to concomitant ANRS MIE calls is not permitted, and in case of such situation, the proposal will only be considered within the first call it has been submitted to.

Applications that do not meet the admissibility criteria will not be submitted to the Peer Review Panel and will not be considered for funding under any circumstances.

3.4. Review and Selection Process

Following verification of administrative and scientific eligibility of the applications, proposals will move forward to the external peer review stage. At this stage, an independent Peer Review Panel of international scientific experts will review the applications using the criteria described in 3.5.

The Peer review panel experts undertake to respect the rules of ethics and scientific integrity established by ANRS MIE and SAMRC. The ANRS MIE and SAMRC ensure strict compliance with confidentiality rules and the absence of conflicts of interest.

The peer review panel will put forward a ranked list of applications. Based on these results, ANRS MIE and SAMRC will make a final decision regarding funding through their respective Executive Management Committees and inform their relevant Boards.







Projects selected for funding may be required to make refinements to the proposed project plan, structure, and/or budget to address reviewer comments and funder requirements before an award and funding agreement are finalized.

3.5. Evaluation Criteria

Review Panel experts will review the full applications according to the following criteria, grouped into three main categories:

- 1. Scientific excellence and impact
 - Clarity of research objectives and hypotheses;
 - Level of innovation, impact, originality, methodological or conceptual break from the state of the art;
 - Relevance of methodology and feasibility of approach;
 - If relevant, the project's ability to address research issues from an interdisciplinary approach;
 - Relevance of project plan, management of scientific risks and alternative solutions, appropriateness of proposed milestones;
 - If relevant, the project's ability to incorporate co-production with all stakeholders, including decision-makers and the communities concerned, to foster community involvement and private-sector participation from the outset of the project.
- 2. Consortium quality, resources and governance
 - Competence, expertise, complementarity and involvement of the project co-leaders: ability to coordinate ambitious international collaborative projects, academic background, international recognition;
 - Quality, relevance and complementarity of the scientific consortium in relation to the project's objectives;
 - Adequacy of the human and financial resources mobilized (including those requested within the framework of the project), as well as the capacities available within the teams (including regulatory capacities), in relation to the targeted objectives;
 - Relevance and effectiveness of project governance (steering, organization, coordination, setting up of advisory committees, involvement of stakeholders if necessary, etc.).
- 3. Project impact
 - Contribution of the project to the objectives of the call, towards improving the prevention, treatment and care of TB;
 - Impact of the consortium on building international scientific collaboration for the long term;
 - Impact on the health of populations and implementation in public policies. Aspects of co-production of public policies with all stakeholders will be taken into account;
 - Economic, social and societal impacts, contribution to the development of solutions to the challenges of TB;





• Dissemination strategy (*in itinere* and *ex post*) and valorization of results. Ability of the project to meet the challenges of open science, dissemination to the public and transparency in the field of tuberculosis.

4. Activities and Deliverables

4.1. Progress report

Research consortia funded under this call will be expected to provide the specific deliverables listed below in order to demonstrate project progress:

- 1) Organization of a kick-off meeting to launch the project.
- 2) Conclude a research collaboration agreement between the project partners, preferably within 6 months of the award being made.
- 3) Annual written reporting (technical and financial) providing details on the progress in terms of completion of deliverables, utilization of funds, learnings and planning for the next period.
- 4) A final report accounting for financial expenditures, that captures a clear assessment of project impact.
- 5) Continued post-grant updates on scientific publications and impact.

Instructions for reporting will be provided to successful recipients.

Funds must be used for the purpose and research activities for which they were intended and approved by the SAMRC and ANRS MIE. Any significant deviations from the approved project objectives, methodology, milestones and/or deliverables must be approved by both the SAMRC and ANRS MIE in writing prior to implementation.

4.2. Dissemination

Recipients of this Call are expected to maximize the impact and utility of their work, including through timeous dissemination of their findings through, for example:

- Social media
- Open access publications
- Depositing of research data into publicly accessible repositories (in compliance with applicable regulations)
- Press releases
- Conferences
- Stakeholder engagement

The ANRS MIE and SAMRC acknowledge that recipients may reasonably delay the publication of data and results generated from the projects with the aim of first protecting any potential intellectual property therein.

All publications, press releases and other documents which include results obtained in projects funded through this Call must acknowledge both the SAMRC and ANRS MIE in the form indicated in the relevant Funding Agreement or Letter of Acceptance of Grant Conditions. If no statement is stipulated, then the following general statement should be used: *"Research reported in this [publication/press*





release] was supported by the South African Medical Research Council and the ANRS MIE, under the grant numbers XXX and XXX".

5. FINANCIAL POLICIES

The specific financial conditions applied by SAMRC and ANRS MIE can be found in Appendix A and B.

5.1. Allowable Costs

The following costs are allowable for this Call (all direct line items must be auditable):

- Personnel: Soft-funded posts for individuals working on the project (e.g. post-docs, PhD students up to one per associated team, students, technicians, project managers) will be funded, provided an accurate estimation of time allocation is provided and they are not already funded from other means.
- Equipment: Partial or full support for the cost of equipment may, in some instances, be requested, provided that it is directly required for the project. A budget limitation of 10% of total budget may apply.
- Supplies, consumables and other direct laboratory or research costs.
- Sub-contracts: These may be to any local or international private organization or individual engaged as consultant providing a service or capability that is not available among the project partners but is essential for the completion of project deliverables. These should not exceed 20% of the total project budget.
- Travel and accommodation that is directly related to the execution of the project.
- Institutional overhead: An indirect cost rate up to 8% is allowed.

Non-allowable costs include the following:

- Salaries of permanent or fixed term staff, e.g. tenured staff, professors etc., that are fully covered by the host institutions or other grants.
- Purchase or construction of a building.
- Rental costs for space that is owned by the institutions participating in the project.
- Recruitment or retrenchment costs for staff.
- Purchase of office furniture.

If research equipment is purchased through this Call, it becomes the property of the host institution. Under no circumstances may equipment become the property of the individual researcher to whom the funding was allocated. The equipment may not be removed from the host institution and/or transferred to another institution without the express written approval of the host institution and concurrence by the SAMRC and ANRS MIE. The institution must take responsibility for any necessary maintenance and insurance of the equipment.

5.2. Terms of Disbursement

Specific disbursement rules may apply depending on the funder (see Appendix A and B).

In general terms, successful applicants, depending on the respective funder, must enter into a Funding Agreement or sign a Letter of Acceptance of Grant Conditions with the SAMRC or ANRS MIE before any funds are disbursed. The Funding Agreements will usually be with the primary /lead institutions







(co-lead consortium members), which will also be responsible for managing all sub-contracts with and disbursements to project partners falling under the same Agreement. Exceptions can be made for project partners from countries other than France or South Africa. No administration fee may be charged by the institutions for disbursements to sub-contractors or other project partners.

The frequency of funding disbursements will be as stipulated in the approved budget. Funding disbursements are subject to the submission of ethics approvals and satisfactory progress and financial reports. Funding disbursements may be delayed or altered, at the discretion of the SAMRC and ANRS MIE, if insufficient spending has occurred on previous instalments.

5.3. Fund Management

The host institutions and Principal Co-Investigators are required to ensure that the procurement of any goods, equipment and/or services for the purposes of the project are in strict accordance with the provisions of the institutions' procurement and travel policies. Funds may be spent solely according to the approved project budget and proposal.

Additional specific fund management rules may apply depending on the funder (see Appendix A and B).

At the end of the contractual term and/or upon completion of the project deliverables, any surplus project funds are to be re-paid to the SAMRC or ANRS MIE unless an alternative use for the funds by the institution has been agreed in writing by the SAMRC and/or ANRS MIE.

The SAMRC and ANRS MIE are entitled, at any reasonable time during or after the project, to appoint an independent team of auditors to inspect and take copies of the project books of account, records and supporting documents of the institution to the extent necessary to verify any statement on reasonable notice and during office hours. The institution must for this purpose provide the auditors with reasonable access to the books of account, technical reports and all records relating to the management of the project together with any other information required by the auditors for this purpose.

The Institution is also required to inform the SAMRC and ANRS MIE in writing of any and all other funding for the project from third parties, which is used in the furtherance of the project. Additional funding should not be duplicative (i.e. double dipping) of funds received from the SAMRC and ANRS MIE.

6. GENERAL POLICIES AND TERMS

6.1. Submission Materials and Privacy Notice

The proposals submitted in response to this Call will be subject to external review by international subject-matter experts, in addition to analysis by staff from both SAMRC and ANRS MIE. Please be advised that a copy of the external review for each submitted proposal may be disclosed to ANRS MIE and SAMRC Executive Management Committees and Boards.

ANRS MIE and SAMRC will exercise all reasonable efforts to respect the confidentiality of information that is received in Submission Materials. ANRS MIE and SAMRC reserve the right to publicly disclose





the titles, public summary and names and institutions of co-investigators, as well as the amount of funding granted, for each successful application.

6.2. Open Science/Sharing and Access Policy

In agreement with the promotion and implementation of open science, beneficiaries of this Call are committed to guaranteeing immediate open access to peer-reviewed scientific publications, and to adopt a FAIR (Easy to Find, Accessible, Interoperable, Reusable) approach to manage research data in line with the principle of "as open as possible, as closed as necessary".

In particular, recipients agree:

- To make publications arising from the project immediately openly discoverable and accessible online under a Creative Commons Attribution (CC BY) or equivalent license, in one of the following three ways:
 - publication in a natively open access journal;
 - publication in a subscription journal that is part of a so-called transforming agreement or transforming journal;
 - publication in a subscription journal. The editor's version or the manuscript accepted for publication will be deposited in the French open archive HAL by the authors under a CC- BY license, in compliance with the rights retention strategy, as specified in the funding decision or contract.
- To deposit in the French national HAL open archive, the full text of these scientific publications at the latest at the time of publication, (version accepted for publication or publisher's version) and to mention the grant from which they originate.
- To employ best efforts and endeavour in good faith to deposit project data outputs into a relevant open access repository within 12 months of project completion.
- To employ best efforts and endeavour in good faith to openly and publicly disseminate results and conclusions of the project, whether positive, neutral, or negative, within 12 months of project completion.
- To provide ANRS MIE and SAMRC with a Data Management Plan (DMP) for the whole project. A first version of the DMP must be provided within 6 months of the start of the project. This plan should be updated as necessary, at least at the end of the project and at mid-term. The plan can be entered and updated on the <u>OPIDoR DMP portal</u>, using the so-called structured, machine-readable model.

Recipients are encouraged to deposit publication's initial versions, or "pre-prints", in open platforms or open archives, and to give preference to perennial or unique identifiers (DOI, HAL Id or ORCID, for example).

Publication costs or "Article Processing Charges" (APC) are eligible for partial ANRS MIE funding and partial SAMRC funding, with the exception of those hybrid journals (subscription journals with no current agreement).

6.3. Intellectual Property

Successful applicants may retain ownership of intellectual property rights in supported innovations, including innovations that arise from the funded projects. ANRS MIE and SAMRC aim, however, to







ensure that any such intellectual property rights are utilized and managed in a manner that is consistent with achieving the goal of this Call.

In particular, successful applicants agree to employ best efforts and endeavour in good faith to provide widespread, affordable and equitable access to the supported innovations to achieve the greatest possible impact for those most in need.

ANRS MIE and SAMRC recognize the value of intellectual property and commercialization, and the benefits of first and continuing use of data, but not prolonged or exclusive use. In some cases, intellectual property protection, laws or regulations may delay or preclude access to data. In cases where an adequate justification has been provided, ANRS MIE may grant a partial or complete waiver of the data access requirement.

Specific intellectual property terms and conditions of SAMRC and ANRS MIE respectively are detailed in Appendix A and B.

6.4. Regulatory and Ethical Compliance

The ANRS MIE and SAMRC are committed to ensure that research involving human subjects, research with animals, and research subject to additional regulatory requirements is conducted in accordance with the highest internationally recognized ethical standards.

Recipients of this Call are required to obtain approval for any research involving human or animal subjects or samples therefrom from the appropriate institutional review board or ethics committee and provide the SAMRC with a copy of such approval prior to embarkation on the research. This requirement extends to all sites participating in the research.

Any such research must, in addition to ethical approval compliance, be conducted in accordance with the generally accepted principles of "Good Clinical Practices", which shall include but not be limited to, requiring prior informed consent from the human subjects and shall be conducted in accordance with all applicable national and international regulations and guidelines pertaining to research involving human subjects, management of data confidentiality, research involving animals, use or release of genetically modified organisms, research use of recombinant DNA, and/or use of any organism, substance or material considered to be a biohazard, including adherence to all applicable standards for transport of specimens, both locally and internationally, as appropriate.

6.5. Other Commitments

Environmental sustainability

ANRS MIE and SAMRC require that applicants commit to ensuring that their research project will not have significant adverse environmental effects including, but not limited to, long-term and cumulative effects.

Investigators are invited to include in their projects an assessment of its environmental impact, in particular an estimate of the carbon footprint of travel and other activities required to carry out the project, as well as the justification for these activities and/or the means proposed to limit their impact on the environment.







Useful resources (principles and tools) for this assessment can be found here: <u>https://labos1point5.org; www.basecarbone.fr</u>.

Gender equality

ANRS MIE and SAMRC are committed to furthering principles of gender equality in the research projects funded under this Call.

As such, several actions have been implemented by ANRS MIE to avoid potential gender bias in project evaluation, to contribute to the evolution of scientific culture towards a systematic consideration of the sex and/or gender dimension in research work and evaluation, and to enhance the place and role of women in science.

Human rights

ANRS MIE and SAMRC are committed to furthering a Human Rights Based Approach. This particularly includes the promotion of principles of participation, inclusion, equity, transparency, and accountability in an applicant's project.

7. CONTACTS

Each project funded through this Call is managed by specific SAMRC and ANRS MIE Project Managers who will be the primary contact for all queries and communications thereon.

Any general queries in relation to these Funding Terms and Conditions may be addressed to:

aap@anrs.fr and gipd.rfa@mrc.ac.za

For technical assistance with registration or online application through APOGEE, please contact:

apogee@anrs.fr







Appendix A: South African Medical Research Council – Terms and Conditions of Funding (2024) Appendix B: ANRS MIE – Terms and Conditions (MOASF, Charte éthique)