COLLABORATIVE RESEARCH AGREEMENT

For the implementation of the project

"Active surveillance of Dolutegravir (DTG) based antiretroviral regimens in Rwanda"

BETWEEN

RWANDA BIOMEDICAL CENTRE (RBC)

AND

MEDICINES TECHNOLOGIES AND PHARMACEUTICAL SERVICES(MTaPS)/MANAGEMENT SCIENCES FOR HEALTH (MSH)

Date: April 2021

This agreement is entered into by and between the **Rwanda Biomedical Centre** (here in after referred to as "**RBC**"), Rwandan Public Institution established by the Law № 54/2010 of 25/01/2011 repealed, except article one by the Law № 013/2019 of 30/06/2019 governing Rwanda Biomedical Centre (RBC) and determining its mission, organization and functioning; having its principal place of business at Rukiri II Cell, Remera Sector, Gasabo District, P.O. Box 7162 Kigali-Rwanda, Email: Info@rbc.gov.rw, represented by its Director General, Dr. Sabin NSANZIMANA; and **Medicines, Technologies, and Pharmaceutical Services (MTaPS) Rwanda Program** led by **Management Sciences for Health under** (here in after referred to as "MSH-MTaPS"), a Rwanda Non-Governmental Organization, having its address in Niboyi Sector, Kicukiro District, P.O. Box 371 Kigali-Rwanda, represented by its Country Project Director, John Patrick MWESIGYE, Email: jmwesigye@mtapsprogram.org .

WHEREAS, RWANDA BIOMEDICAL CENTRE ("RBC"), envisions to become a Center of Excellence for the prosperity of the country, ensuring quality health service delivery, education and research, with a specific mission to promote high quality, affordable, and sustainable health care services to the population through evidence-based interventions and practices guided by ethics and professionalism;

WHEREAS, RBC has developed expertise in health sector research, project and policy development, healthcare interventions and projects implementation and is interested in developing partnerships with academic and research and development institutions for the purpose of research, education and training and;

WHEREAS, the MTaPS, is implemented by Management Sciences for Health (MSH) and partners, to provide technical assistance to the Ministry of Health's (MoH) directorate of clinical & public health, RBC the Division of Maternal Child and Community Health (MCCH), and Rwanda Biomedical Center/HIV and STI division, Rwanda Food and Drug Authority (FDA) including other relevant implementing agencies to strengthen pharmaceutical systems including pharmaceutical sector governance, regulatory systems, pharmaceutical management information systems, and improve patient-centered pharmaceutical services; and to ensure sustainable access to and appropriate use of safe, effective, quality-assured, and affordable essential medicines and pharmaceutical services

Pursuant to the existing Memorandum of Understanding between MSH-MTaPS Program and The Government of Rwanda represented by the Ministry of Health endorsed on 18th November 2019 with a period of 2 years.

This Research Collaboration Agreement (RCA) will establish a mechanism for the Parties, RBC and MSH-MTaPS, to plan and execute cooperative research, educational and training activities related to the implementation of the study project "**Active surveillance of Dolutegravir (DTG) based antiretroviral regimens in Rwanda**", funded by USAID.

WHEREAS, the parties desire to engage in a collaborative research that will advance scientific knowledge and patient care and believe that the results of such research will produce information with potential to improve clinical outcomes and patient safety.

WHEREAS, each Party to this RCA recognizes the unique expertise of the other; and

The Parties represent that they are each authorized under the laws of the Government of Rwanda to enter into this Research Collaboration Agreement;

The administration of this RCA will be the responsibility of the Office of Director General through HIV/AIDS, STIs Diseases Division at Rwanda Biomedical Centre and the Office of the Country Project Director at MSH-MTaPS.

NOW THEREFORE, THIS AGREEMENT WITNESSES that in consideration of the mutual covenants and agreements herein and subject to the terms and conditions set out in this Research Collaboration Agreement, the undersigned Parties agree as follows:

I. DEFINITIONS

Whenever the words and expressions which follow appear in this Research Collaboration Agreement, they shall be interpreted according to the definitions given hereafter unless implicitly or explicitly expressed otherwise in the text:

- **"Intellectual Property"** means any new and useful art, invention, discovery, innovation, process, product, formulae, software, manufacture or composition of matter, or any new and useful improvement in any art, invention, discovery, innovation, process, product, formulae, software, manufacture or composition of matter, and any industrial and/or intellectual property rights and all such other rights whether or not statutorily protected or capable of being protected under statute.
- **"Arising Intellectual Property"** means, individually and collectively, all Intellectual Property made, conceived or developed during the term of this Agreement and directly resulting from the Research Project carried out hereunder.

- **"Background Intellectual Property"** means, individually and collectively, all Intellectual Property developed, produced or obtained by a Party outside the scope of the Research Project.

- "**Agreement Period"** means the period, beginning _____[Month] _____, 2021__ through _____[Mounth] _____, 2022__, renewable in accordance with the terms hereof, unless earlier terminated pursuant to this Agreement.

II. OBJECTIVES

The overall objective of this RCA is to strengthen the existing collaboration between RBC and MSH-MTaPS with a special emphasis on the implementation of focal research projects. Most important, under this RCA, while RBC will be mainly implementing the project, MSH-MTaPS will mainly provide technical and finicial support to facilitate the process.

RBC and MSH-MTaPS agree to establish a collaboration that covers a number of collaborative activities in the implementation of **surveillance of Dolutegravir (DTG) based antiretroviral regimens project.**

III. SCOPE OF COLLABORATION

1) Overall emphasis

In furtherance of the above objectives and subject to the availability of funds, resources and approval of the authorized representatives for the implementation of the collaborative on active **surveillance of Dolutegravir (DTG) based antiretroviral regimens project**, the Parties agree to the following:

(a) The execution of this Research Collaboration Agreement aligns with mutual interests and achieving targets related to the safety of DTG based regimens.

2) Responsibilities of RBC

1. Serve as the Principal investigator for the activity
2. Develop a research protocol and obtain RNEC approval for the program
3. Avail RBC staff required to be part of the study team
4. Support training of research team at the national and facility level
5. Ensure effective implementation of the active surveillance program at the national and facility-level including recruitment of participants and data collection
6. Support data collation, cleaning, analysis, and dissemination

7. Undertake continuous monitoring of study implementation
8. Organise together with MSH-MTaPS coordination meeting at each stage of the study project and assess progress, challenges and way forward
9. Provide required data to inform the project under implementation

3) Responsibilities of MSH

Under this research collaboration agreement, MSH-MTaPS shall:

1. Provide advisory and Technical support in the development of research protocol and other tools (SOPs and checklists) required for implementation
2. Support development of progress report and compliance with agreed timelines throughout study implementation
3. Support meetings for coordination of study implementation activities
4. Support training to the research team (data collectors) before starting study implementation
5. In collaboration with RBC, organize and coordinate actively the meeting in dissemination of research findings for inputs
6. Support coordination and implementation of the whole project
7. USAID through MSH-MTaPS will fund the agreed activities in this Active safety surveillance of DTG based regimens

   NOTE: Rwanda Food and Drug Authority will be part of the research project having a role of Co-Principle investigator.

IV. PROJECT'S SPECIAL PROVISIONS

1. Specific Objectives of the project

The specific objectives of this RCA reflect the main objectives of the project in the pipeline, including:

1. To characterize adverse event (AE) and adverse drug reaction (ADR) profile among patients using DTG-based regimens.
2. To determine the incidence rate for AEs, in patients using DTG-based regimens.

3. To assess causality between observed AEs and the use of DTG-based regimens.
4. To determine the effect of DTG-based regimens on weight gain as well as the blood glucose and lipid profiles.
5. To identify risk factors AE/ADR development and determine their effect on AE/ADR incidence and severity among patients using DTG-based regimens.
6. To propose possible interventions to prevent AEs and ADRs associated with the use of DTG-based regimens.

2. **Specific project's activities to be implemented by the Parties**

(a) The Parties shall support each other to achieve successful implementation of this project.

(b) The Parties shall jointly appoint study coordinator to liaise with the Principal Investigator and ensure the oversight of the administrative, financial and technical procedures of the project at each stage.

The following highlight details about the stages and activities under this Research Collaboration Agreement:

(a) Study protocol development and seeking for ethical approval

(b) Development and validation of research activities implementation plan

(c) Training of implementation teams (data collection and analysis)

The implemation team will ensure ;

(i) data capture at the health facility level

(ii) Mobilization of the participants

(iii) Regular contacts with participants to get relevant information

(d) Mobilization of study participants

(e) Organising coordination meetings for planning and monitoring of research activities implementation

(f) Field activities coordination and data collection

(g) Data analysis and findings reporting

(h) Finalization of collaboration research agreement between RBC and MSH-MTaPS:

(i) Develop, review and validate the Research Collaboration Agreement between RBC and MSH-MTaPS approval

(ii) MSH-MTaPS in collaboration with RBC will engage research team (data collectors and other technician) required for study implementation.

(iii) MSH-MTaPS in collaboration with RBC will provide detail of the criteria for needed research team.

(iv) MSH-MTaPS in collaboration with RBC will provide training to the research team.

(v) Data collection supervisor will come from research team with experience in supervision of the field activities

(i) Recruitment of the Study participants;

This study will involve a cohort of HIV patients treated with DTG-based regimens in selected sentinel sites across the country. This will include treatment naïve patients starting their treatment with a DTG-based regimen and those who may be initiated on this regimen after the failure of other regimens. To be able to detect an AE occurring with the rate of 1:1000, at least 3,000 people will need to be enrolled in this study. This number gives a 95% probability of identifying such an AE at 80% statistical power (45, 46). Among the study participants, 300 people will be randomly selected for the monitoring of glucose and lipid profiles in addition to the general follow-up.

Inclusion criteria:

- All HIV patients regardless of age and gender who commence antiretroviral treatment with any DTG-based regimen including treatment naïve patients and those switching from other ART regimens, will be included in our study.
- Pregnant women in the first, second, and third trimesters
- Patients with other co-morbidities who are initiating treatment with any of the monitored DTG-based regimens.

Exclusion criteria for enrollment:

- All patients irrespective of age and sex that commenced treatment with any DTG-based regimen prior to being enrolled into the active monitoring exercise.
- Patients who do not wish to be part of the active monitoring, or
- Patients for whom adequate medical history cannot be obtained.

(j) Field activities coordination and data collection

(k) Data Analysis and reporting

The study coordination team will ensure overall study data cleaning, analysis, discussion and reporting, specifically:

(i) The study coordination team will oversee data management, processing and analysis plans and activities
(ii) The study coordination team will facilitate timely reporting, dissemination, manuscripts writing and publication

V. Confidentiality

(a) The Parties agree that each of them may receive confidential or proprietary information from the other in connection with a specific collaborative research project. Each Party agrees, therefore, that such information received from the other, and marked as confidential, (the "Confidential Information") will not be disclosed to any third party or used for its own purposes other than in connection with activities contemplated by this agreement without the written consent of the disclosing Party, and that reasonable and prudent practices shall be followed to maintain the Confidential Information in confidence.

(b) This prohibition includes but is not limited to, press releases, educational and scientific conferences, training and promotional materials, government filings, and discussions with lenders, investment bankers, public officials and the media and shall also be subject to Article V regarding Publication.

(c) The obligations of confidentiality set forth in V (a) hereof, shall not apply to any information which:
(i) is already known to the receiving Party before receipt from the disclosing Party as evidenced by written records;

(ii) is generally available to the public or becomes publicly known through no fault of the receiving Party;

(iii) is received by the receiving Party from a third Party who had a legal right to disclose without restriction; or

(iv) is developed by the receiving Party independently of and without reference to Confidential Information received from the disclosing Party as evidenced by written records.

(v) must necessarily be disclosed by either Party to financial institutions or other funding sources to obtain financial assistance, provided that such entities agree to keep the information confidential; and/or

(vi) must necessarily be disclosed by either party to file patent applications with respect to inventions that are part of the Arising Intellectual Property.

(d) Not with standing any other provision of this Agreement, disclosure of Confidential Information shall not be precluded if such disclosure is in response to a valid order of any governmental agency, court or other quasi-judicial or regulatory body of competent jurisdiction, provided however, that the responding Party shall, as promptly and as reasonably possible, give notice to the other Party of the requirement so that the other Party may contest the requirement to provide such Confidential Information.

(e) Any Party shall have the right to release any non-confidential information or to publish any non-confidential material resulting from the research project. However, the other Party shall first be advised in writing of the substance of any proposed disclosure related to this sub-agreement at least sixty (60) days in advance of presentation or publication and; be provided with the proposed disclosure for their own review.

(f) Disclosure includes articles, seminars, and other oral and written presentations, but does not include these or other communications submitted for the purpose of academic evaluation.

VI. **Publications**

(a) Rights to all outputs and outcomes, including data and derivatives thereof, resulting from activities conducted under this Research Collaboration Agreement will be primarily owned by Government of Rwanda and shared based on the confidentiality clauses set in part V.

(b) RBC, MSH-MTaPS, and the Principal Investigator each acknowledges the importance of public disclosure/publication of information collected or generated as a result of or related to the Research, under the condition that public disclosure/publication takes place under the provisions of this clause.

(c) If the results of the collaborative research project will be jointly published, authorship and proper acknowledgment will be made for the contributions of each Party to the research results being published.

(d) If a proposed publication is not a joint publication, the Party wishing to make the publication shall provide a copy of the manuscript or abstract to the other Party at least thirty (30) days prior to publication to allow the other Party an opportunity to protect its Intellectual Property that might be disclosed by the manuscript or abstract. In addition, a Party will not publish Confidential Information received from the other Party without the other party's written consent, which shall not be unreasonably withheld or denied. Once the research results of the Research Project have been published, the confidentiality restrictions of this Agreement shall no longer apply to such information.

(e) Neither Party will use the name of the other in any publication, promotion or advertisement with respect to the Research Project or its results, without the prior written consent of the other except that both Parties may publish the title of the Research Project, the name of the other Party, the value of the Agreement, and the name(s) of the Principal Investigator(s) in its internal records and reports regarding research funding. The Parties agree in advance that each may also use the name of the other in announcing this Research Collaboration Agreement.

(f) Upon completion of the Research (whether prematurely or otherwise), the Principal Investigators, RBC and MSH-MTaPS shall co-operate in producing a report of the Research detailing the methodology, results and containing an analysis of the results and drawing appropriate conclusions and recommendations.

(g) The Principal Investigator shall have the right to publish or present the methods and results of the Research in accordance with the provisions of this clause. The foregoing provided however, that any such publication will take in account the rights and interests of all investigators involved in the Research and authorship will be determined in accordance with the participation and agreed by the two parts.

(h) The material for public dissemination shall be submitted to the RBC leadership for review at least thirty (30) days prior to submission for publication, public dissemination, or review by a publication committee. If RBC leadership does not respond within this period, the Principal Investigator(s) is/are free to proceed with the intended publication or presentation without further delay.

VII. **Miscellaneous**

(a) For the purpose of this agreement and all services to be provided hereunder, each party shall be deemed to be an independent contractor and not an agent or employee of the other party. Neither party shall have the authority to make any statement, representations or commitments of any kind, or to take any action which shall be binding on the other party, except as may be explicitly provided for herein or authorized by the other party in writing.

(b) This Partnership agreement and the attached appendices constitute the entire agreement between the parties with respect to the subject matter hereof and supersedes all prior agreements, understandings, negotiations and discussions, whether written or oral related to this matter. There are no conditions, covenants, agreements, representations, warranties or other provisions, expressed or implied, collateral, statutory or otherwise, relating to the subject matter hereof except as herein provided. This partnership agreement cannot contradict the existing agreement between parties rather complement it.

(c) No amendments or waiver of any provision of this partnership agreement shall be binding on any of the parties here to unless consented to in writing by all parties to this agreement. No waiver of any provision of this agreement shall constitute a waiver of any other provision, nor shall any waiver constitute a continuing waiver so as to impair such party's rights to future enforcement of its rights unless otherwise expressly provided in writing.

VIII. **Governing law**

This agreement shall be construed, interpreted, enforced in the respective rights and obligations of the parties in accordance with the laws of the Republic of Rwanda, as applicable.

IX. **Dispute settlement**

Any questions arising from interpretation of this Agreement will be settled amicably through discussions between the parties in good faith. If such questions are not settled between the parties within 30 days following commencement of discussions, this Agreement will be subject to termination.

X. Term, Renewal, amendment and Termination

This agreement shall be effective upon signature by both parties and shall remain in force for two (2) years that can be renewed.

Either party may initiate the amendment of this agreement by a written notice to the other party for that effect. No amendment can be made to this agreement unless approved by both parties in writing.

This Collaboration Agreement may, at any time during its period of validity, be terminated by either party upon giving a written notice signed by the presiding officer of the notifying party provided that such termination shall not affect the completion of any program or activity underway at the time the notice of termination is given.

In the event of any unforeseen incident during collaborative activities in either Party both Parties agree to negotiate a mutually acceptable solution.

XI. Non-Discrimination

Both Parties subscribe to the policy of equal opportunity and will not discriminate on the basis of gender, age, disability, race, color, religion, and marital status, national or ethnic origin.

XII. Final provisions

This agreement shall enter into force on the date it is signed by both parties. It shall expire after two (2) years unless terminated earlier in accordance with the relevant provisions in this collaboration research agreement.

IN WITNESS WHEREOF, the undersigned, duly authorized by the respective Parties, have signed this agreement.

RWANDA BIOMEDICAL CENTRE (RBC)	**MANAGEMENT SCIENCES FOR HEALTH /MTaPS**
Signature: _____	Signature: _____
Names: **Dr. Sabin NSANZIMANA**	Names: **John Patrick Mwesigye**
Director General	Country Project Director
Date: _____	Date: _____