Call for Application for PhD Scholarships at the East African Community Regional Centre of Excellence for Vaccines, Immunization, and Health Supply Chain Management (EAC RCE-VIHSCM)

I. Background

East African Community Regional Centre of Excellence for Vaccines, Immunization, and Health Supply Chain Management (EAC RCE-VIHSCM), at the College of Medicine and Health Sciences (CMHS), the University of Rwanda is funded by German Federal Ministry for Economic Cooperation and Development (BMZ) through Kreditanstalt für Wiederaufbau (KfW). As an anticipated solution to the problem of shortage in teaching staff workforce, EAC RCE-VIHSCM intends to offer PhD scholarships to candidates from the EAC Partner States, to pursue PhD studies in the EAC RCE-VIHSCM thematic areas listed in the following section.

II. Description of PhD Scholarships programme

This call is for ten (10) PhD Candidates and will be primarily funded by the EAC RCE-VIHSCM. The aim of this Scholarships programme is to develop faculty capacity in thematic areas as listed below to sustain training programs and produce evidence-based research outputs. The scholarships programme is expected to start in FY 2023-2024. The scholarships will be offered to candidates from EAC Partner States to study in selected partner institutions offering training and research in the identified EAC RCE-VIHSCM thematic areas. This involves either **working on the preidentified research synopses listed in the section below or other innovative research projects developed and submitted by potential PhD candidates around four priority areas below.**

1. **Health Supply Chain Management**

a. **Pooled Procurement:** Implementing an inter-country pooled procurement mechanism strongly relies on demonstrated willingness and commitment from stakeholders in the participating countries. This commitment and (political) will from stakeholders are required both at national (i.e., from stakeholders within EAC Partner States), as well as the inter-country (i.e., EAC) level. Pooled Procurement provide opportunities to increase market efficiencies through regional approaches to procurement. With these economies of scale, more funds will become available for procurement of health commodities and lead to increased availability of and access to health commodities. Therefore, the Pooled Procurement strategy is considered as the first step in the process of developing a large market in the region, which will attract investments in local production and market integration. However, implementation of pooled procurement has been noted to be a challenge despite the efforts deployed. Therefore, a PhD research project in this area of pooled procurement conducted in the EAC Region is highly encouraged.

b. **Addressing antimicrobial resistance with a One Health approach:** the intense use of fertilizers and antibiotics in food production, intensive animal domestication, and penetration of natural habitats through human settlements is contributing to the emergence of antimicrobial resistances and zoonotic diseases. Globally, the health of the population is increasingly under threat of pandemics as well as antimicrobial resistance (AMR). Resilient supply chains are essential to pandemic preparedness, in order to ensure access to medicines, vaccines, and health products. Consequently, a PhD Study addressing the issues of AMR with One Health approach is encouraged.

c. **Developing the 'next-generation' vaccine cold-chain for future resilience and sustainability in Africa:** The vaccine cold-chain (VCC) is critical national infrastructure that underpins public health protection to many infectious diseases in infancy and childhood. Recent disease outbreaks of SARS-CoV-2 virus, Ebola virus, circulating vaccine-derived polio virus type 2 (cVDPV2) and others have demonstrated the added need for a responsive vaccine cold-chain to safely contain and protect from new threats. Despite the development of many highly effective vaccines, in resource-limited settings an estimated 25-50% of vaccine doses are compromised by failures of adequate cold-chain custody (freezing or excess heat exposure) or incomplete vial usage (partially used vials), and this represents a huge inefficiency in the system and potential for missed opportunities for vaccination and/or ineffective immunisation programmes. This clearly indicates that African communities need a 'next-generation' vaccine cold-chain equipment management and remote temperature monitoring (CCEM and RTM) system for future resilience and sustainability. This next generation vaccine cold chain and RTM need also to be efficient and responsive. Like many other African countries, Rwanda has a multi-level network of vaccine distribution. Rwanda has different levels of health facilities which handle and manage vaccines and cold chain equipment and RTM . Using the existing VCC datasets, a research project with the following aims is important. Aims: (1) to understand the key determinants that underpin vaccine security, potency and development of a data analysis pipeline to generate detailed analyses of the VCC Vaccine by multiple key performance indices to inform and support strategic making; and (2) de-risking of key strategic investment and deployment decisions through the creation and use of 'digital twins' to undergo (a) virtual stress-testing of VCC readiness for loss of capacity from scenarios such as the effects of future global warming, energy failures, new disease outbreaks etc, as well as (b) real-world impact assessment for future innovation/intervention to support VCC resilience/sustainability such as the utility of digital tracking technologies for vaccine waste assessment, cost/value assessments of drone delivery systems, and sero-epidemiology data for better vaccine needs forecasting and potency across the supply chain system.

2. **<u>Quality Assurance and Quality Control</u>**

a. **Bioequivalence studies for Macrolides**: Macrolides have poor aqueous and pH-dependent solubility with dissolution rate-limited absorption corresponding to Biopharmaceutics Classification System BCS Class II (low solubility and high permeability). The most commonly used macrolides, namely azithromycin and clarithromycin belong to BCS Class II

which necessitate comparative bioequivalence studies to establish the pharmaceutical equivalence of generic formulations with their innovator products. Currently, there are no reports of comparative bioequivalence studies on the generic azithromycin and clarithromycin oral formulations in the EAC member states. Therefore, a study in this area in EAC Partner States is of paramount importance.

b) **Quality Control of antihypertensive medicines circulating on EAC Partner States market**: Counterfeit, falsified and substandard medicines pose a considerable threat to health security. They can fail to cure, cause injury, morbidity and death. The threat from them is growing, particularly in poor countries with weak regulatory mechanisms and poorly monitored distribution. Producers of counterfeit medicines are increasingly using complex and sophisticated channels. No area of the world is unaffected, but mounting evidence shows that the problem is disproportionately severe in poor, developing and emerging market countries. Almost all kinds of medicines are subject to counterfeit, falsification or substandard. However, many studies conducted in EAC Partner States have mostly investigated the quality of antimalarial and antibiotics and antihypertensive medicines were not fully investigated. The US Pharmacopoeia (USP) drug quality and information programme listed antihypertensive medicines among medicines subjected to counterfeit and falsification in the African region. Importantly, given that people with high blood pressure often require lifelong adherence to indicated medicines, the problem of substandard, counterfeit or falsified antihypertensive medicines is potentially a serious public health concern. Therefore, a study investigating the quality of these medicines is highly important.

c) **Efficacy and safety of Imidazole used for the treatment of Soil transmitted helminths (STH):** Soil-transmitted helminths (STHs) also known as intestinal worms are a group of intestinal parasites (Ascaris lumbricoides, Trichuris trichiura and the hookworms (Ancylostoma duodenale and Necator americanus)) that lead the global disease burden attributable to neglected tropical diseases (NTDs). STHs are the most common infections of Neglected Tropical Diseases (NTDs), primarily affecting the poorest and most deprived communities. To control STH-attributable morbidity, anthelmintic drugs are frequently distributed to children in endemic areas. Recently, the WHO has set new targets for 2030, namely reducing the proportion of moderate-to-heavy intensity (MHI) infections below 2%. This represents a shift from a mere program coverage target towards a disease-based target. Endemic countries aspire to achieve this WHO target but are facing important challenges. The World Health Assembly endorsed a resolution for regular treatment of high-risk groups, particularly school-age children, through mass drug administration (MDA). Preventive chemotherapy is a WHO-recommended strategy to control and eliminate STHs. The prevalence of STHs among school children in 2020 was at 77% in endemic areas and 31% country wide. In addition, low efficacy of some imidazole used in the control of STH species was reported with cure rate of only 31% and egg reduction rate of 50%. Therefore, a study examining the efficacy and safety of Imidazole is likely to improve the treatment of STHs.

d) **Quality by Design:** As part of current Good Manufacturing Practice, many pharmaceutical manufacturing are adopting Chemistry manufacturing and Controls (CMC) and Process Analytical Technology (PAT) to provide continuous process verification and analysis to

ensure that products quality attributes are met by predicting the design space for raw materials, process parameters, manufacturing, as well as environmental and other conditions. A study using mass spectrometry and chromatography is important to analyse the quality of pharmaceutical products during manufacturing processes.

3. **Vaccines Manufacturing and/or Vaccinology**

a) **Mycobacterial Pathogenesis and Tuberculosis Research Program:** Members of the Mycobacterium tuberculosis-complex (e.g. M. bovis, M. tuberculosis) are bacterial pathogens that cause tuberculosis (TB) - a highly infectious disease that primarily affects the lungs in a variety of mammals including humans. According to the World Health Organization, TB is the biggest cause of human deaths due to a single infectious disease agent. The disease can be cured with a daily multi-drug treatment regime over at least 6 months. Unfortunately, due to the complexity of treatment and unpleasant side effects, many patients do not adhere to treatment. This has resulted in multi- and extensive drug-resistant TB. There is a live attenuated TB vaccine for humans called BCG that has been in use for almost 100 years. Although very safe and protective against TB in infants, efficacy decreases over time and does not provide protection against TB in adults. Bovine TB, caused by M. bovis, is endemic in many cattle-rearing and developing regions of the world. There are pockets of infection in wildlife in many countries that are reservoirs of the disease. Confirmed cases can lead to significant economic losses to the global cattle industry. M. bovis is also a major cause of zoonotic TB infections in humans in developing parts of the world. Thus, more effective drugs and vaccines, and diagnostics are needed to combat TB in humans and livestock.

b) **African Swine Fever vaccine development:** African Swine Fever is a devastating disease of pigs that leads to haemorrhagic fever and death of infected animals. Endemic in many parts of Africa, the disease represents a major threat to the North American and European Swine Industry. African Swine Fever is caused by infection with a large arthropod-borne DNA virus. Vaccines are currently not available. In collaboration with researchers at the University of Alberta, the Canadian Food Inspection Agency, and the South African Research Council. Studies evaluating a novel proprietary adenoviral vector vaccine for this important disease is desired.

c) **Adenovirus vectors for vaccine delivery:** Adenoviruses have proven to be highly effective viral vectors that offer a wide range of advantages. For example, they induce both humoral and cell-mediated immunity, they are highly cost effective, and they can be developed very rapidly, which allows their use for control of emerging diseases. This includes understanding of the basic mechanisms of viral replication and characterizing the role of bovine adenovirus-3 (BAdV-3) structural and non- structural proteins in virus-cell interaction leading to the production of infectious progeny virion, which will help in contributing to the advancement of knowledge on fundamental biology of not only bovine adenovirus -3 but adenoviruses in general. Moreover, the research findings of the proposed study will help in developing and evaluating improved bovine adenovirus-3 based vaccine delivery vehicle(s) for vaccination of animals and humans.

Similarly, porcine adenovirus offers a great potential to deliver foreign antigens and biotherapeutics to pigs. Therefore, studying in this area is highly important.

d) **Development of novel combination adjuvants:** Adjuvants are often used to modify or augment the effect of the antigen in vaccine formulations. Adjuvants function by stimulating the immune system to elicit better and more vigorous responses to the antigen and can be used to protect the antigen from untimely degradation, premature release or clearance. A limited number of adjuvants are licensed and available for use in vaccines. Research and discovery of novel adjuvants is targeted at screening new compounds, understanding mechanisms of action, and evaluating the use in human and animal vaccine candidates. Individual adjuvants may not effective in some types of vaccines. In this regard, a research focusing on developing new combinations of adjuvants is desired.

e) **Developing immunology tools to support better vaccine use in Africa:** Recent advances in biomedical technology (antibody detection) mean we can now achieve significant steps towards the next-generation vaccine cold-chain. The current situation indicates that there is a need to vaccinate everyone, which is expensive, logistically challenging, and may not be necessary for all individuals. A research project that aims to incorporate novel biomedical and technical capabilities into the vaccine cold-chain and generate real-world performance data on approaches at the individual-level in the field and at the population-level for whole communities is highly essential. In addition, this focuses on measles and an accelerated programme for the WHO target of measles eradication. Similarly, this should also focus on the detection and prevention of chronic hepatitis B virus.

4. **<u>Vaccine and Medicines Regulatory</u>**

a) **Vaccine regulatory capacities, supply chain, and safety monitoring system in EAC member states:** Immunization is a global health and development success story, saving millions of lives every year. Vaccines reduce risks of getting a disease by working with your body's natural defenses to build protection. As of now, there are vaccines to prevent more than 20 life-threatening diseases, helping people of all ages live longer and healthier lives. The UN Sustainable Development Goals (SDGs) set out ambitious targets for the global community over the period 2015–2030. SDG3 focuses on good health and well-being, aiming to 'support the research and development of vaccines and medicines for the communicable and non-communicable diseases that primarily affect developing countries (and) provide access to affordable essential medicines and vaccines. Some studies on vaccinology in sub-Saharan Africa reported that Africa's limited capacity to design, manufacture and regulate vaccines is an important barrier to advancing priority vaccines through the research and development (R&D) pipeline. The need to strengthen vaccine manufacturing capacity in low-income and middle-income countries was underlined in the Global Vaccine Action Plan and reiterated in the Addis Ababa Declaration on Immunization endorsed by African Heads of State in 2016. Therefore, a study assessing the vaccine regulatory capacities is highly important.

III. Hosting institutions

The selected candidates will do their PhD studies in selected Universities from Belgium, Canada, Germany, Netherlands, and UK, among others which have collaboration with the UR EAC RCE-VIHSCM.

IV. Application requirements

1. General eligibility criteria

The applicant must be:

i. A citizen of one of the EAC Partner States
ii. Holding a relevant MSc degree related to the above thematic areas;
iii. A full-time employee of an academic institution, regulatory authorities and/or a pharmaceutical industry;
iv. Prepared to work full time on the PhD project;
v. Ready to travel abroad and spend a maximum of 5 years for the PhD programs;
vi. Ready to contribute to teaching at EAC RCE-VIHSCM after completion of the PhD studies;
vii. Aged 45 years or less at the time of application;
viii. Prepared to return home and serve for the home institution immediately after receiving a letter confirming satisfactory completion of the PhD degree;
ix. Not in possession of another fellowship for PhD studies;
x. English proficient.

V. Application file

Interested candidates shall submit the following documents:

1. An application letter addressed to the University of Rwanda Director of Centre for Postgraduate Studies (UR-CPGS) indicating for which thematic area the application is being made.
2. A personal motivation statement for the scholarship programme. This statement should demonstrate commitment, motivation, and reasons for interest in the scholarship programme (max. 2 pages).
3. Updated Curriculum Vitae (maximum of 3 pages).
4. Notarized Masters and Bachelor's degrees and transcripts.
5. Recommendation letters from at least two academic or professional referees. One of the recommendation letters should be issued by a previous academic supervisor, preferably the Master's degree supervisor.
6. Copies of valid identification card or passport;
7. A statement of not having another active scholarship;

8. A recommendation letter from the current employer stating past and current positions occupied by the candidate in the institution; and ensuring the candidate gets study leave for the entire period if chosen for the scholarship.
9. Copy of publication(s) (if any);
10. Master's Dissertation abstract;
11. PhD research concept note (Max. 5 pages) clearly indicating a working title of your proposed PhD project, the research gap, the research problem and research objectives; the methodological approach; and a description of the expected scientific significance and development impact of the research you propose.

VI. Selection process

Shortlisted candidates will be invited to the interview on dates that will be communicated through emails.

VII. How to apply:

Interested applicants shall send the above mentioned (scanned and saved as one document or as a zipped folder) to the following email: ur-cpgscholarship@ur.ac.rw with a copy to director.rcevihscm@ur.ac.rw please name the application folder as "your names – Application for EAC RCE-VIHSCM PhD Scholarship" **no later than 15th September 2023**. At the same time, you should also submit your application via the following link: https://www.surveymonkey.com/r/KGZNLG2.

Note: A candidate should submit only one application.

Done at Kigali, on 14/08/2023

Dr KAYIHURA Muganga Didas, PhD
Ag. Vice Chancellor