African Union
Scientific Technical Research Commission

RESEARCH TRANSLATION FROM BENCH TO BEDSIDE

Bench

Understanding Disease Mechanism

Bedside

Everyday Clinical Procedures

Community

Improved Health

African Union Scientific, Technical and Research Commission

RESEARCH TRANSLATION FROM THE BENCH TO THE BEDSIDE

Ahmed Hamdy, Harriet Yayra Adzofu, Mohammed Kyari,
Gilbert Byatuhaire, Marie Johnson, Adaeze Akaduchieme

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This study was commissioned by the African Union Scientific, Technical and Research Commission and it reflects the views and opinions expressed therein, which are not necessary those of the AU and its Commission. This study was developed with the aim to improve and strengthen science, technology and innovation capacities at the national, regional and continental levels through building and upgrading research infrastructures, enhancing professional and technical competencies, promoting innovation and entrepreneurship development and creating an enabling environment for STI and ultimately to assist Member States and Regional Economic Communities (REC) to adopt /domesticate STISA-2024.

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RESEARCH TRANSLATION FROM THE BENCH TO THE BESIDE

PREFACE

This book was developed by the African Union, Scientific, Technical and Research Commission owing to the realization that much of Africa's health/clinical research works conducted in laboratories in continent which, would lead to better understanding of diseases as well as the introduction of novel interventions to be used in clinical settings were largely ignored and left on the shelves.

Now more than ever before clinical trials, new research and methods would presents new interventions. The value of these ideas and actions delivered should be assessed to determine whether it improves lives and wellbeing of Africans.

The most distinctive feature of the book is that it provides a roadmap of the ethical considerations towards a sustainable health system and defines the standards procedures for good clinical research practice in African Union Member States. This was based on the learning from imperatives and fundamental needs for knowledge based economy that is being propagated by the Science, Technology and Innovation Strategy for Africa 2014 – 2024.

Generally, the authors are of the view that this book will help Member States to build robust mechanisms that will respond to health research challenges in their countries and that this book will be used as a tool for taking research to the next level on the intra-Africa level and with all the concerned stakeholders and partners.

FORWARD

The health of Africa's population is at the centre stage of Agenda 2063 and shows a renewed approach to make Africa free of disease. The Agenda's aspiration number one, goal number three is 'healthy and well-nourished citizen'. In addition, the Science, Technology and Innovation Strategy for Africa 2014 – 2024 highlights the 'prevention and control of diseases' as a priority and the Africa Health Strategy 2016 – 2030 provides strategic direction to African Union (AU) Member States in their efforts to improve health sector performance.

The health research translation protocol is an indispensable part for health care development in Africa, especially that most of the research publication in the continent is in health and related fields. However, there is dearth of taking the research output from the "bench to the bedside" and this has been a significant challenge to Scientists, Entrepreneurs, Enterprise and the Governments.

With this document, the AU-STRC aims to add value to the scope of translational research to interpret laboratory, clinical, and public health research, and to aid in expediting the translation of health discoveries into new or improved standards of care.

This publication presents scientists and researchers a roadmap to the creation of mechanisms to support research translation from "bench to the bedside"; and among others, guidelines for improved clinical research practice for AU Member States. The publication provides useful direction on the necessary impetus on research translation.

The "home grown" successes recorded in the fight against the Ebola Viral Disease outbreak in West Africa demonstrated our capability, commitment and solidarity, and served as testimony that Africa can speaks for itself and translate our research to our benefit.

I am pleased to note that this will be outlet for many research studies that were shelved in Africa, to now reach the public, and also for scientists to be recognised for their contribution to the continent and to mankind, as well as to attract much needed funding for the development of Africa.

Dr. E. Osagie Ehanire MD, FWACS
Honourable Minister of Health
Federal Republic of Nigeria

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Secondly we are profoundly grateful to Dr. Ahmed Fahmi of UNESCO for the invaluable technical support and from the Summit the study groups collected views and suggestions into the problem "Weak Research Translation and Pathways in Africa and formed the bases of formation of this study. We also appreciate all participants who contributed to the research study from the study groups and participants who took part on the e-survey and who facilitated engagement on the publication of this book. We thank Dr. Baba Bukar Alhaji of Nigerian Defence Academy who examined and provided the statistical analysis from the e-survey.

We offer special thanks to the reviewers who reviewed the draft document and proposed useful ideas for further improvement: Professor Dominic Osaghae, Professor of General Paediatrics/Emergency Care at the University of Benin, Nigeria and from the South Africa Medical Research Council: Professor Charles Wiysonge, Director: South African Cochrane Centre, Dr. Thabi Maitin, Division Manager: Research Capacity Development and Mr. Seeiso Koali, Research Integrity Officer. Their valuable feedback and support inspired us to pull it all together here.

Finally we want to thank the entire team at the AU-STRC for the inestimable encouragement as we wrote this book.

OVERVIEW

The book is organised into ten thematic sections packaged within three parts. The book focuses on the common concepts used to describe varieties of research translation from the bench to the bedside including research translation, clinical research practice, and clinical ethics.

Part one of this book is addressing the research translation in Africa where its ***1st Section*** is devoted to the **understanding of research translation and clinical research**. It also highlights the translation models; the clinical trial phases; the stakeholders and the level of their involvement/interest. In ***Section two of Part one***, the authors give a **history and evolution of Science and Technology in the continent**. It is a retrospective on the African Union Commission Science, Technology and Innovation milestones and achievements realised.

Section three of Part one mentions the **health challenges that Africa faces** and their linkages to poverty, food insecurity and malnutrition. And ***Section four*** addresses the methodology that was used for the study of the problem **"Weak Research Translation and Pathways in Africa"** based two main approaches by conducting a wider consultation "face to face consultation and e-survey" with health participants and health research professionals.

Part two was focused on **strategic analysis to achieve effective research translation from bench to bedside**. ***Section One of Part Two*** addresses the **strategies to achieve effective research translation from bench to bedside**. These strategies are identified interventions to be considered "four individual pillars and three cross cutting pillars" to enhance stakeholder interventions. Each intervention identified is interlinked with the other and has some commonalities that aim at achieving a comprehensive system for research translation in Africa, through proposed solutions to obtain desirable and achievable outcomes for each pillar to attain to the ultimate goal. ***Section Two of Part Two*** focuses on the creation of **mechanisms to support research translation**.

Part Three addresses **Guidelines for improved harmonized good clinical research practice for AU Member States.** ***Section One of Part Three*** underlines the **guidelines for improved harmonized good clinical research practice**. ***Section Two of Part Three*** describes the constitution and composition of the **Independent Ethics Committee**. It also describes the terms of reference and educational requirements of the IEC's members.

Section Three of Part Three explains the **Standard Operating Procedures** (SOPs) that are important to ensure standardised best practices for health research, compliance with national and international ethical and regulatory requirements. ***Section Four of Part Three*** is **addressing data handling protocols** and focuses on the procedures for sampling, handling and record keeping as well as the why and how these should be in compliance with regulatory standards.

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LIST OF ABBREVIATIONS

AAU	Association of African Universities
AfDB	African Development Bank
AJOL	Africa Journal Online
ARIPO	Africa Regional Intellectual Property Organization
AU	African Union
AUC	African Union Commission
AUNS	African Union Network of Sciences
AU-STRC	African Union Scientific, Technical and Research Commission
ASRIC	Africa Scientific, Research and innovation Council
CDC	Center for Disease Control
CIOMS	Council for International Organization of Medical Sciences
DEA	Department of Economic Affairs
DHRST	Department of Human Resource, Science and Technology
DSA	Department of Social Affairs
DTI	Department of Trade and Industry
ICMR	Indian Council of Medical Research
IEC	Independent Ethics Committee
IMF	International Monitory Fund
IP	Intellectual Property
IRB	Institutional Review Board
MSc	Master of Science
NEPAD	New Partnership for Africa's Development
NGO	Non-Governmental Organization
OAPI	Organization Africaine de la Propriété Intellectuelle
PAIPO	Pan African Intellectual Property Organization
PAU	Pan African University
PhD	Doctor of Philosophy
R&D	Research and Development
REC	Regional Economic Community
SMEs	Small and Medium Enterprise
UNAIDS	United Nations Program on HIV/AIDS
UNDP	United Nations Development Programme
UNESCO	United Nations Educational, Scientific and Cultural Organization
UNFPA	United Nations Population Fund
UNICEF	United Nations Children's Emergency Fund
WHO	World Health Organization
WIPO	World Intellectual Property organization

Part 1: RESEARCH TRANSLATION IN AFRICA

SECTION I: INTRODUCTION TO RESEARCH TRANSLATION

This chapter is devoted to aid the understanding of research translation and clinical research. It also highlights the translation models; the clinical trial phases; the stakeholders and the level of their involvement/interest.

1.0 Introduction to Research Translation

It is widely accepted that research is a systematic investigation, study of materials and sources in order to establish facts and reach new conclusions. The term 'research' covers a broad range of activities and can be defined as, 'the systematic search or inquiry for knowledge'. In other words, research is a process of arriving at a dependable solution for a problem through planned systematic collocations, analysis and interpretation of data. It is also defined as a systematic investigation designed to develop or contribute to the development of knowledge, where people will be in a better position to understand their environment and to address their daily challenges and ambitions. Several studies have shown that research according to its purpose can be classified generally to basic research, applied research and research and development.

Basic Research is experimental or theoretical work undertaken primarily to acquire new knowledge of the underlying foundations of phenomena and observable facts, without any particular application or use in view [1]. In simple words, it is research that is directed towards a fuller understanding of nature and discovery of new fields of investigation, with no practical purpose in mind.

Applied Research is original investigation undertaken in order to acquire new knowledge. It is, however, directed primarily towards a specific practical aim or objective [1]. In other words, it is research directed towards a specific practical aim, to serve man's need.

Research and Development (R&D) comprise creative and systematic work undertaken in order to increase the stock of knowledge – including knowledge of humankind, culture and society – and to devise new applications of available knowledge. The term R&D covers three types of activity: basic research, applied research and experimental development. For an activity to be an R&D activity, it must satisfy five core criteria, where the activity must be:

- Novel (to be aimed at new findings);
- Creative (to be based on original, not obvious, concepts and hypotheses);
- Uncertain (to be uncertain about the final outcome);
- Systematic (to be planned and budgeted); and
- Transferable and/or reproducible (to lead to results that could be possibly reproduced) [1].

That is to say, R&D simply is investigative activities to improve existing products and procedures that lead to the development of new products and procedures. It is also a systematic use of results of research and empirical knowledge directed towards the production and use of new materials, devices, systems and methods.

Health Research: The term "health research," sometimes also called "medical research" or "clinical research," refers to research that is done to learn more about human health. Health

research also aims to find better ways to prevent and treat disease. Health research is an important way to help improve care and treatment of people worldwide [2]. A more detailed understanding of health research and of a research project may be obtained from the description provided by the US National Commission for the Protection of Human Participants: "A research project generally is described in a protocol that sets forth explicit objectives and formal procedures designed to reach those objectives. The protocol may include therapeutic and other activities intended to benefit the participants, as well as procedures to evaluate such activities. Research objectives range from understanding normal and abnormal physiological or psychological functions or social phenomena, to evaluating diagnostic, therapeutic or preventive interventions and variations in services or practices. The activities or procedures involved in research may be invasive or non-invasive and include surgical interventions; removal of body tissues or fluids; administration of chemical substances or forms of energy; modifications of diet; daily routine or service delivery; alteration of environment; observation; administration of questions or tests; randomisation; review of records etc." [3].

On the other hand, and for the benefit of this guidance document, health research system is to be defined as the people, institutions, and activities whose primary purpose is to generate relevant knowledge adhering to high ethical standards, which can be used to improve the health status of populations in an equitable way [4,5].

There are different types of Health Research which are: Behavioural Studies; Clinical Trials; Community-Based Participatory Research (CBPR); Genetic Studies; Observational Studies; Physiological Studies; Prevention Studies; Public Health Research [6] Table (1) gives a brief definition to each of them.

Types of Health Research	**Definitions**
Behavioural	These are studies that test how people act in different ways.
Clinical Trials	These are studies of a drug, surgery, or medical device in healthy volunteers or people who have a specific disease. See below for more information.
Community-Based Participatory Research (CBPR)	This is research that engages community partners as equal participants in the research.
Genetic Studies	These are studies to find the role of genes in different diseases.
Observational Studies	These are studies in which a group of people is observed for many years.
Physiological Studies	These are studies to better understand how the human body functions.
Prevention Studies	These are studies that test ways to prevent specific conditions or diseases.
Public Health Research	This type of research can be one or a combination of the types of research mentioned above. Public health research tries to improve the health and well-being of people from a *population-level* perspective.

Table 1: Types of Health Research and their brief definitions [6]

1.1 Research Translation

Research translation is the process whereby knowledge is passed anywhere along the translational pathway i.e. research findings are translated into practice, policy or further research, while Translational research is research that looks at how best to translate research into practice and/or policy e.g. research that addresses particular gaps in translation [7].

The terms 'research translation' and 'translational research' appeared in the literature of the 1990's in response to significant increases in basic or clinical science discoveries with little improvement in the provision of health care and health outcomes [7,8]. These concepts initially tried to address this gap by focusing on moving research from the bench-to-bedside. However, it is generally acknowledged that moving research from the bedside to population-wide health must also be considered [9, 10, and 11]. In other terms, research translation conceptually is the translation of new clinical knowledge into improved health [12].

There are different models/pathways for research translation that mainly divide the transition process into different number of phases (steps), for example the two (2) phase model [13]:

T1: Transfer of new understandings of disease mechanisms gained in the laboratory into the development of new methods for diagnosis, therapy, and prevention and their first testing in humans.

T2: Translation of results from clinical studies into everyday clinical practice and health decision making.

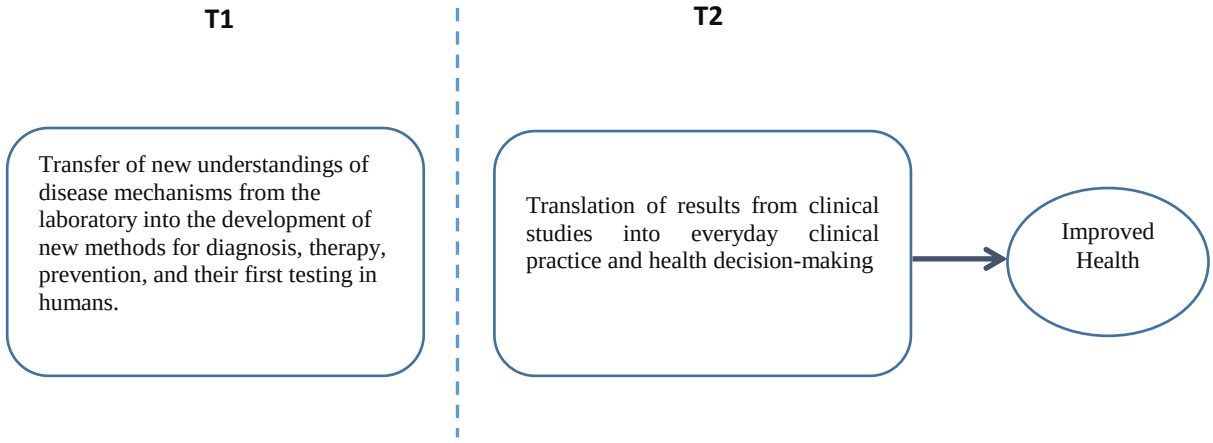

Figure 1: Research Translation 2-Phase Model [13]

In general terms, T1 research refers to the translation of basic biomedical research into clinical science and knowledge, while T2 research refers to the translation of this new clinical science and knowledge into improved health.

Another pathway (4- phase model) spans four phases [8 & 9]:

T1: Refers to the translation of basic research into a potential clinical application.

T2: Refers to efficacy studies, in which new interventions are tested under optimal conditions.

T3: Refers to effectiveness studies, where promising interventions are tested in 'real world' settings;

T4: Refers to impact studies, which examine the impact of a new intervention/ guideline at a population level [14].

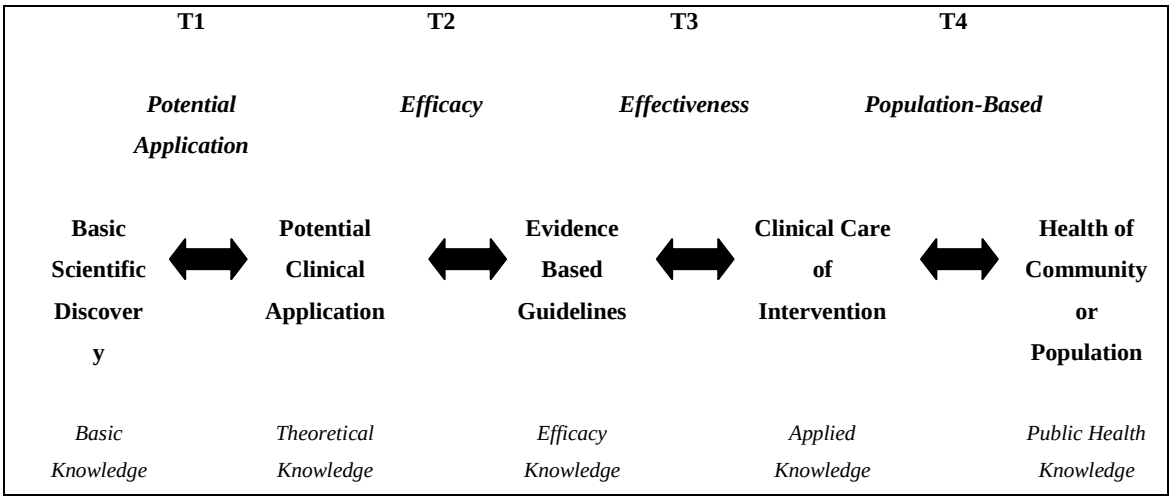

Figure 2: Research Translation 4-Phase Model, after [14]

The direction of flow along the translational pathway is often two-way. That is, findings from basic research or clinical observations can inform a clinical intervention or development of a product (T1) and then the testing of that intervention or product (T2) can feed back to the T1 stage and help improve on the intervention or product.

Observations made in the laboratory may lead to better understanding of disease and novel interventions to be used in clinical settings. Equally, clinical research, sometimes involving these novel interventions, will provide insight and information which can feed back to the laboratory and inform future laboratory studies.

For example, at the Murdoch Children's Research Institute (MCRI) "Lab to Bedside Example; using 4-phase model" [14]:

- The Surgical Research Group developed a medical device to treat constipation (T1).
- They originally tested a physiotherapy method to provide electrical stimulation across the abdomen to make the bowel push more and to empty stool out (T2).
- They found that existing stimulation devices were hard for patients to set up and use at home. The Surgical Research team patented the method and then applied for funding to support commercial development of a device specifically for constipation (findings in T2 inform T1 improvement of the device).
- An unmet needs analysis showed a large patient group worldwide and a business plan was developed. Key opinion leaders were contacted in the UK and USA to determine if they would use the device. A start-up company was formed and design and regulatory requirements are underway.
- A prototype would be ready for trials in definite time/date (T2 to T3), with sales expectation date (T4).

As of the translation pathways above described, Clinical research and Clinical trials are main factors that impact tremendously in the success of any research translation system. So, what are clinical research and clinical trials?

Generally clinical research is a branch of medical science that determines the safety and effectiveness of medications, devices, diagnostic products, and treatments intended for human use. These may be used for prevention, treatment, diagnosis or for relief of symptoms of a disease [15]. In other words, clinical research is a branch of medical science dealing with any research or study in living humans and does not necessarily aim at commercialization i.e. clinical research is meant for academic and pharmacovigilance. While clinical trials are a kind of clinical research designed to evaluate and test new interventions such as psychotherapy or medications [16].

A clinical trial is the term interchangeably used with the term clinical research or clinical study. Although there are many definitions of clinical trials, they are generally considered to be biomedical or health-related research studies in human beings that follow a pre-defined and designed protocol. Clinical trial is defined as "a systematic study of new drug(s) in human participant(s) to generate data for discovering and/ or verifying the clinical, pharmacological (including pharmacodynamics and pharmacokinetics) and/ or adverse effects with the objective of determining the safety and/ or efficacy of the new drug". Clinical trial is meant for a new drug or device and carried out for a specific new use of an intervention [17]. Clinical trials are often conducted in four phases. The trials at each phase have a different purpose and help scientists answer different questions [15, 16, and 17]:

Phase I- Human / Clinical Pharmacology trial: This phase aims to obtain the precise information on initial safety in terms of safe dosage range and biological effects including adverse effects; metabolism and kinetics; and drug interactions. The trial is carried out on healthy human volunteers (20-80 in number).

Phase II- Exploratory trial: This phase is meant to find whether or not the drug possesses the actual therapeutic potential. It identifies the therapeutic efficacy of the drug with dose range, kinetics as well as metabolism. It is carried out at one or few clinical centres only on small but sufficient number of patients (100-300 in numbers) to reach clinical significance in outcomes. It also aims to find out the therapeutic index of the drug being studied. It is required to be carried out in patients meeting selection criteria of age group, sex, presence of particular disease with pre-defined and diagnosed severity etc. It also reports the adverse effects of the drug.

Phase III- Confirmatory trial: This phase applies the same study protocol designed for phase II to evaluate safety and efficacy at large. It is to confirm the effectiveness of the drug or treatment, to monitor side effects, to compare it to commonly used treatments and to collect information that will allow the drug or treatment to be used safely. It is simultaneously performed at a large number of clinical centres that include patients of various geographic origins with difference in responsiveness of the disease towards the drug treatment. Furthermore, it covers large number of patients (mostly above 1,000 in number) allowing the outcome to reach not only clinical significance, but also statistical significance. Once the drug passes this phase successfully, it is licensed for commercial use. Thus, phase III of the

trial is a key study forming the primary basis for regulatory approval of an intervention and is often referred as pivotal trial.

Phase IV- Post-Marketing Surveillance: This phase is so named because it is carried out after the drug is released in the market for therapeutic use. It is mainly to detect uncommon but significant adverse effects. Once the drug enters the market, it will be utilized by many more patients having other co-morbidity and co-existing diseases in addition to the disease for which the drug is indicated and licensed. This is also conducted to provide critical information on drug-drug interactions or iatrogenic diseases.

Phase	Description	Aim
Human/ Clinical Pharmacology Trial	Researchers test an experimental drug or treatment in a small group of people (20-80)	The researchers evaluate the treatment's safety, determine a safe dosage range, and identify side effects.
Exploratory Trial	Studies are done in more people (about 100-300)	These increase our understanding of the study drug's safety and effectiveness in a controlled setting.
Confirmatory Trial	The experimental study drug or treatment is given to large groups of people	To confirm the effectiveness of the drug or treatment, to monitor side effects, to compare it to commonly used treatments and to collect information that will allow the drug or treatment to be used safely.
Post-Marketing Surveillance	Post-marketing studies, which are conducted after a treatment is approved for use.	Provide additional information including the treatment or drug's risks, benefits, and best use.

Table 2: Clinical Trial Four Phases, after [15, 16, and 17]

Clinical trials are conducted either on healthy volunteers as in phase I above mentioned or on volunteer patients as in Phase III. This will lead to the need for human participant protection which resulted in the existence of several guidelines on conducting clinical trials such as the World Health Organization Guidelines for good clinical practice for trials on pharmaceutical products. The WHO guideline gives provisions and prerequisites for a clinical trial, protocol and protection of trial participants, responsibilities of the investigator, responsibilities of the sponsor, responsibilities of the monitor, monitoring of safety, record-keeping and handling of data, statistics and calculations, handling of and accountability for pharmaceutical products, role of the drug regulatory authority, quality assurance for the conduct of a clinical trial and considerations for multicentre trials [18].

Guidelines on conducting clinical trials should include the following [17]:

1) Ethical justification and scientific validity of biomedical research involving humans;
2) Ethics review board;
3) Informed consent process;
4) Choice of control in clinical trials; and
5) Research involving special group of research participants.

1.2 Systematic Review

Health policy-makers, programme managers, and implementers have limited time and resources to access research when it is needed and may resort to selective use of research, such as relying on the results of one primary study rather than a more comprehensive and reliable body of evidence. Systematic reviews attempt to answer important health questions by identifying and evaluating all relevant research studies and synthesising their results. A systematic review is characterised by a well-defined and focused question; pre-defined eligibility criteria for selecting studies; a comprehensive search strategy for identifying all potentially eligible studies; duplicate assessment of the risk of bias and extraction of data from included studies; an appropriate synthesis of data; and a complete presentation of the findings. Well-conducted systematic reviews provide the most authoritative source of evidence on the efficacy of preventive, therapeutic, and rehabilitative interventions. Without systematic reviews of previous research, ineffective or even harmful interventions may be used because they are thought to be effective and, conversely, effective interventions may be considered ineffective and withheld. A systematic review should be the first step when defining questions for new research and when taking decisions about health care. When taking decisions about health care, there should be clear documentation of how relevant systematic reviews were identified and assessed for their quality, local applicability, potential impacts on equity, cost implications, and scaling-up considerations. When systematic reviews are ignored, it is very likely that limited healthcare resources would be squandered on ill-conceived research and policies, and avoidable confusion would result from failure to set new research in the context of relevant existing research [19].

1.3 Knowledge Translation

Knowledge translation is a dynamic and iterative process that includes synthesis, dissemination, exchange and ethically-sound application of knowledge to improve the health of the populace, provide more effective health services and products and strengthen the health care system [20]. It is also described in some literature as ‘ensuring that stakeholders are aware of and use research evidence to inform their health and healthcare decision making [21]. This definition recognizes that there is a wide range of stakeholders or target audiences for knowledge translation, including policy makers, professionals (practitioners), consumers (i.e., patients, family members, and informal careers), researchers, and industry. In other words, clinical research and clinical trials are conducted with the involvement of scientists, health practitioners, government’s legislative bodies, and private sector; hence there is a need to identify the stakeholders in this process and their level of involvement.

Generally, a stakeholder is a person or organisation who has something to gain or lose as a result of the outcomes of a project, programme or process [22]. The table 3 below analyses the stakeholders and the level of their involvement/interest in the different types of Health-related research.

Potential stakeholder	Type of research			
	Basic	**Clinical**	**Health Services**	**Population Health**
Consumers	-	+++	+++	-
Professionals	-	+++	+++	-
Local Administrators	-	++	+++	+++
National Policy Makers	-	+++	+++	+++
Regulatory Bodies	+++	+++	+++	+++
Industry	+++	+++	++	+
Research Funder	+++	+++	+++	+++
Researchers	+++	+++	+++	+++

- Not Relevant;

+ Low Relevance to +++ High Relevance.

Table 3: Stakeholders for Different Types of Research, after [23]

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SECTION II: AFRICAN UNION SCIENCE AND TECHNOLOGY MILESTONES

This chapter gives a background history and evolution of Science and Technology in the continent. It is a retrospective on the African Union Commission Science, Technology and Innovation milestones, achievements, and the repositioning process for a paradigm shift in Africa through strategic initiatives and programmes. Finally, this chapter measures the capacity of Africa in research where a special focus will be given to health research.

Since the dawn of time and over many years, Africa has gone through different stages of development and glories era that were founded on a strong system of research and innovation. The undisputable fact is that most technologies today employed across the world emanated from Africa. This remarkable long scientific history/contribution portrays Africa as the ***"Nerve of the World"***, the centre point; the incubator of global enlightenment, civilization, scientific research and innovation.

The early African people astounded the world, when their findings on science, research, technology and innovation were revealed by recent descriptions of past discoveries in the continent. The contribution of African glorious grandfathers was encompassing all Science domains covering Maths, Astronomy, Architecture, Navigation, Medicine and more; [see 1, 2, and 3]. However, in-spite of the remarkable achievements of the African people of the early era, on the contrary, as of today, Africa is a continent faced with socio-economic instability; political anarchy, technological setback; weak economic systems among others.

It is true that People of African descent come from ancient, rich and elaborate cultures that created a wealth of technologies in many areas around the world. It was against this backdrop that the First speech by President Kwame Nkrumah, at the foundation summit of the Organization of Africa Unity (OAU) in Addis-Ababa, 24 May 1963; where he stated that "We shall accumulate machinery and establish steel works, iron foundries and factories; we shall link the various states of our continent with communications; we shall astound the world with our hydroelectric power; we shall drain marshes and swamps, clear infested areas, feed the undernourished, and rid our people of parasites and diseases. It is within the possibilities of Science and Technology to make even the Sahara bloom into a vast field with verdant vegetation for agricultural and industrial developments". Such statement is a testimony to the placement of Science and Technology at the top of the continental political agenda since the establishment of the OAU in 1963.

Since then, the OAU started its pathway to utilize science and technology for the continent's development. In 1964 "barely a year after the Organization of African Unity (OAU) Charter was signed", the founding fathers of the OAU unanimously resolved in Cairo, Egypt to assimilate the Commission for Technical Cooperation in Africa (CCTA) "which was established in 1950s together with the Scientific Council of Africa (CSA) by Belgium, France, Portugal, United Kingdom, Southern Rhodesia (Zimbabwe) and South Africa as an instrument for bilateral technical assistance" and gave it a new name: the Scientific, Technical and Research Commission (STRC) [4].

That is to say, the OAU-STRC was born out of recognition by the heads of States that real and sustainable social and economic development of the continent depended on innovative scientific and technological policies. At the national level, Member States developed their learning institutes and universities, setup fellowship programmes to send young talented nationals abroad for education and capacity building. This effort relatively achieved a measure of success, with increased agricultural production; and investment in industrialization as well as the creation of tens of thousands of jobs in the OAU Member States.

In 2002, the African Union Heads of States and Government launched the African Union (AU) as the new phase of the OAU whereas; the OAU was focused on political liberation the AU was established to focus on economic integration and development. Therefore, this development indicates that AU has new mandate and responsibilities.

Focusing on the advancement of Science, Technology and Innovation, the African Union has engaged in some strategic events/initiatives targeted towards moving the continent forward through science and technology. The African Science and Technology Consolidated Plan of Action (CPA) founded in 2005 and its implementation strategy that was developed 2007, was a remarkable shift in utilizing Science and Technology for the African Union and its Member States Economic prosperity.

At the level of the AU, several continental strategies/policies and projects/programmes were developed; and more investment targeting scientific infrastructure was mobilized from within and outside Africa. The following table presents an inventory on such activities (strategies/policies and projects/programmes) implemented under the CPA and its brief description.

ACTIVITY	DESCRIPTION
THE AFRICAN INSTITUTE FOR MATHEMATICAL SCIENCES (AIMS)	The African Institute for Mathematical Sciences (AIMS) is a pan-African network of centers of excellence for postgraduate education, research, and outreach in mathematical sciences. [5]
AFRICAN UNION BIOSAFETY INITIATIVE	The African Union Commission in 2003 adopted The African Model Law on Safety in Biotechnology now renamed African Model Law on Biosafety, which was developed to guide the drafting of domestic biosafety frameworks and legislation at the country level in order to robustly regulate GMOs [6].
BIOSCIENCES NETWORKS ACROSS AFRICA	The African Biosciences Initiative (ABI) focuses on research and development (R&D) in the areas of biotechnology, biodiversity, indigenous knowledge systems and technology. Four biosciences regional networks have been established under ABI on the basis of geographical delineations. The **Southern Africa Network for Biosciences** (**SANBio**) covers the health biotechnology domain [7].
THE BOOK OF LIGHT HOUSE PROJECT	An Africa- EU Strategic Partnership Agreement; 8th Priority Action on "Science, Information Society and Space" endorsed at the AU-EU Summit of 9th December 2007. It illustrates projects and programmes according to the three (3) Priority Actions [8].
AFRICA LEADERSHIP ICT PROGRAMMES	Africa Leaders ICT Programme aims at building Leadership for a robust knowledge-based society in Africa and bringing Africa to a point of being led by people with a sound skill, and knowledge to create an inclusive knowledge society for the continent [9].
FRAMEWORK ON INFECTIOUS DISEASES IN HUMANS ANIMALS, AND PLANTS	This Framework centres on improving Africa's capability through science and technological solutions to detect identify and monitor infectious diseases under the concept of one health [10].

AFRICAN UNION PHARMACOPOEIA	African pharmacopoeia volume one second edition is revised - adopting measures to control and regulate herbal product quality in terms of identity, purity, safety, efficacy and sustainability. That will aid in the appropriate utilization of African medicinal plants to provide quality herbal drugs to African populations as well as boost international trade in African herbal products. In this edition the profiles are indicated in a consecutive manner for each plant: the name of the species and family, the synomyms and common names known in English and French; followed by the African names in principal local languages namely Arabic, Bambara, Hausa, Peuhl, Swahili and Yoruba; finally, brief botanical description and the geographical distribution which will permit the identification of the plant and the knowledge of its area of cultivation and subsequently exploitation in the different climatic zones of Africa. [11].
AFRICAN INTERNET EXCHANGE SYSTEMS	The African Union under the Internet Exchange Systems Project aims to keep the internet traffic in Africa local by providing capacity building and technical assistance that will facilitate the establishment of internet exchange points in various regions of the continent [12].
THE AFRICAN UNION RESEARCH GRANT (AURG)	The African Union Research Grant (AURG) is one of the programmes initiated to support Pan African research and development through grants and direct funding. The programme provides the needed opportunity to use Science and Technology (S&T) as a tool for sustainable development, building and strengthening Africa's S&T capacities [13].
GLOBAL MONITORING FOR ENVIRONMENT AND SECURITY AFRICA (GMES-AFRICA)	Global Monitoring for Environment and Security in Africa (GMES & Africa) is an Earth Observation system designed to respond to global needs to manage the environment, understand and mitigate the effects of climate change and ensure civil security [14].
KWAME NKRUMAH AWARDS	The Commission of the African Union is committed to support the use and development of science in Africa and has, the AUKNASE programme implemented at national level for young researchers, regional level for women scientists and continental level open to all scientists. The Continental level is the highest level of the programme. The objective is to give out scientific awards to top African scientists for their scientific achievements and valuable discoveries and findings [15].
AFRICAN OBSERVATORY OF SCIENCE TECHNOLOGY AND INNOVATION (AOSTI)	The AOSTI is to be a continental repository for Science, Technology and Innovation (STI) statistics and a source of policy analysis in support of evidence-based policy making in Africa. The AOSTI being a repository for STI is to champion evidence-based science, technology and innovation policy-making by backstopping African countries to manage and use statistical information in accordance with the African charter of statistics [16]
THE PAN AFRICAN UNIVERSITY	The Pan African University **(PAU)** project is the culmination of the efforts of the African Union to contribute to the revitalization of higher education and research in Africa, by nurturing quality and exemplifying excellence. This would usher in a new generation of African leaders with capacity to optimally harness available human and material resources towards a peaceful, prosperous and integrated Africa [17].
PAN AFRICAN INTELLECTUAL PROPERTY ORGANISATION (PAIPO)	PAIPO comes against the existing gap in revolutionary reforms from regional fragmentations and further underpinned by geographical limitations and lack of continental inclusiveness. PAIPO supports policy guidance with respect to innovation, inventions and commercialization processes [18].
THE AFRICAN SCIENTIFIC TECHNICAL AND RESEARCH INNOVATION COUNCIL (ASRIC)	The African Scientific Technical and Research Innovation Council (ASRIC) is a continental platform to mobilize African research excellence, innovation and provide a platform for dialogue and voice of the scientific community in building and sustaining continental research-policy nexus with the aim of addressing Africa's socio-economic development challenges [19].
SCIENCE, TECHNOLOGY, AND INNOVATION STRATEGY FOR AFRICA (STISA-2024)	The STISA-2024 recognizes Science, technology and Innovation as a tool/mechanism for Africa's transformation to an innovation lead economy. Science, Technology and innovation socio-economic impact is to be in the fore front in Africa's battle for existence [20].

Table 4: Activities (Strategies/Policies and Projects/Programmes) for CPA's Implementation [21]

STISA-2024: On the wings of Science, Technology and Innovation and towards a paradigm shift in the continent, in 2014, the Science, Technology, and Innovation Strategy for Africa (STISA-2024) was developed to bring about the expression of the AU Agenda 2063, a new dimension and determination of science, technology and innovation in Africa. The STISA-2024 recognizes Science, technology and Innovation as a tool/mechanism for Africa's transformation to an innovation-led economy. In this regard, Africa needs to work at all levels of Member States, Regional Economic Communities and the African Union to identify its Science Technology and Innovation comparative advantage and priority areas to build its success stories. Science, Technology and Innovation socio-economic impact is to be at the forefront in Africa's battle for relevant existence, and to claim its rightful position on the global arena. It is now compulsory to strengthen the capacities of African researchers and scientists by facilitating the integration of their efforts for the sustainable development of the Africa continent. The cooperation on specific scientific topics, sharing data and scientific knowledge, at national, continental and international level will create the conditions for better understanding and solving of African problems via the African scientists.

During the development of STISA-2024, four prerequisite pillars were defined to ensure the achievement of its mission which is to **"Accelerate Africa's transition to an innovation-led, Knowledge-based Economy"** and the realization of its goals and objectives. These pillars are **Upgrading/Building Research Infrastructure**; **Enhancing Technical and Professional Competencies**; **Innovation and Entrepreneurship**; and **Providing an Enabling Environment for STI Development in the African Continent** [22]. These four pillars are being currently made implementable in different dimensions across AU Member States through the Policy Analysis on Science, Technology Innovation Strategy for Africa-2024 (STISA-2024) [22]. The STISA policy analysis was developed in consideration of STI for economic development in Africa with critical analysis of the past, present and future challenges. Against this backdrop, the policy analysis determined the needs and gaps hindering the advancement of STI in the continent; where pre-requisite and required systems and mechanisms including policies and institutions were identified. The analysis was made to ensure that Member States and RECs are informed on the systems needed for the domestication, integration of STISA-2024 in their regional and national development plans.

Summarily, STISA-2024 is the first decade incremental strategy that is designed to address Africa's challenges with the ultimate goal of contributing significantly to the realization of the AU Agenda 2063.

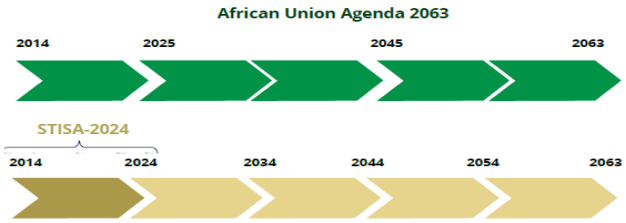

Figure 3: Timeline for STISA- 2024 [22]

Linked with the STISA-2024 and promotion of science and technology, several projects were developed and implemented – (See table 5):

Projects Developed Towards the Implementation of STISA 2024

ACTIVITY	DESCRIPTION
AFRICAN SPACE AGENCY (AFSA)	This initiative would ensure that Africa will benefit from space science and related technologies for its socio-economic developments; in one hand while on the other is responds to the STISA-2024 priority area on protecting our space for more details; see [23].
AFRICA DRIVEN BY INNOVATION: POLICY ANALYSIS ON STISA-2024	Africa Driven by Innovation: Policy analysis on STISA-2024 is a predecessor to CPA with 10 years incremental plan for Science, Technology and Innovation Strategy for Africa (STISA-2024) that was adopted by the African Union (AU) Assembly of Heads of State and Governments in June 2014, which implementation is integral to achieving the AU Agenda 2063. More details on this policy analysis and its output see [24].
AFRICAN UNION NETWORK OF SCIENCES (AUNS)	The African Union Network of Sciences is a virtual network that involves a wide range of individuals working together to address the African science and technology development challenges. It is a platform where African Scientists, Engineers, Technology Developers, Innovators and Inventors will be able to interact, cooperate, exchange information/knowledge and complement one another in research and academic work [25].
AFRICAN COMMISSION ON NUCLEAR ENERGY (AFCONE)	The African Commission on Nuclear Energy (AFCONE) was established by Article 12 of the Treaty of Pelindaba as the body responsible for, *inter alia*, ensuring States Parties compliance with their obligations under the Treaty and its Protocols and promoting regional and sub-regional programmes for cooperation in the peaceful uses of nuclear science and technology [26].
THE AFRICAN MEDICINES REGULATORY HARMONIZATION-CONTINENTAL RESULTS	THE African Medicines Regulatory Harmonisation-Continental Results is a result of The African Health Strategy (AHS) 2016-2030 which was developed in cooperation with the Department of Social Affairs at AUC. The Strategy spells out an operational approach for pursuing the aspirations and the associated goals and targets that related to health and well-being of the African population, as encapsulated in the First Ten Year Implementation Plan of Agenda 2063 [27]
ALLIANCE FOR ACCELERATING EXCELLENCE IN SCIENCE IN AFRICA	Alliance for Accelerating Excellence in Science in Africa (AESA) was established as a pan-African platform created by the African Academy of Sciences (AAS) and the NEPAD Agency. AESA is a platform for developing science strategies and funding health research in Africa that runs calls for proposals and proposal writing [28].

Table 5: Activities (Strategies/Policies and Projects/Programmes) for STISA-2024 Implementation [22]

The 2007 Addis Ababa Declaration on Science and Technology is a milestone on the commitment of the African Union and its Member States to invest in Science and Technology advancement in the continent, where the Union's Heads of State and Government committed themselves to allocate 1% GDP to Science and Technology; Assembly/AU/Decl.5 (VIII) [29]. This could be realized by reflecting on R&D expenditure, where in 2013, the Africa GERD[1] amounted to ppp$[2] 19.9 billion compared to ppp$ 12.9 billion in 2007 "that is to say an increase of 54% in investment in the said period" which resulted in R&D intensity to climb up from 0.36 to 0.45 in the reference years 2007 and 2013 respectively [30]. In furtherance to this, a remarkable increase in the GERD per researcher was observed where it was increased from 86.2 to 106.1 (ppp$) with reference years 2007 and 2016. Over the same period, the number of researcher/Million inhabitants increased from 156.8 to 168.8. However,

[1] Gross domestic expenditure on R&D (GERD) as a percentage of GDP is the total intramural expenditure on R&D performed in the national territory during a specific reference period expressed as a percentage of GDP of the national territory.

[2] Purchasing power parity in US dollars

this increment in the number of researcher/Million inhabitants is not satisfactory particularly when it to be compared to the world average which is 1083.3 researcher/ Million inhabitants.

A deeper look can show that Sub-Sahara Africa has 91.4 researcher/Million inhabitants which is about 90% less than the world average while North Africa have 456 researcher/Million inhabitants which is about 50% less than the world average. That is to say, Africa is not only suffering financial investment/instruments to support its research programmes, but also, there is a huge demand for African Researchers/Scientists.

According to the African Observatory of Science, Technology and Innovation studies (AOSTI), Africa scientific output has changed dramatically considering the fact that total number of papers published by the AU in 2005 was 21,237 while in 2010, the total number was 39,390 (Figure 4) [31]. On the other dimension, the study shows that if countries are to be ranked by the total number of their publications, the AU is to be ranked 19th in the World in 2005, when considered as a single country. Though some might find it discouraging that a whole continent published the same amount as some relatively small countries, there is a positive aspect to be noted, namely that considering the whole of the AU as one, and examining the growth in scientific production of only the 20 largest countries, the AU would have ranked fourth between 2005 and 2010, just behind India, China and Brazil and ahead of the Republic of Korea.

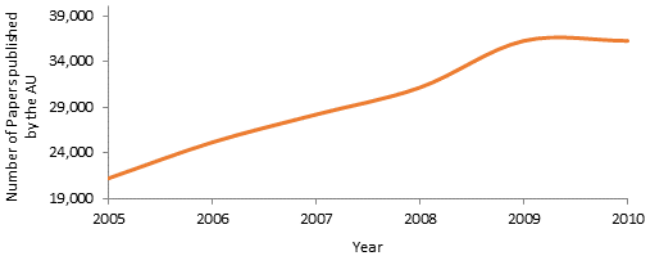

Figure 4: Total Number of Papers Published by the AU [31]

At the Member States level, six (6) member states are leading others in scientific productions which are Republic of South Africa, Egypt, Nigeria, Tunisia, Algeria and Kenya; where they contribute in total 81% of the total papers in 2005 and almost 90% in 2010 – (see Figure 5 and Table 6). Furthermore, the production of each of these countries grew faster than that observed at the world level. On the other hand, the growth index for those lagging behind is promising for countries such as Mozambique, Gambia, Togo and Swaziland as the number grew from 97 to 198, with respect to the same reference period.

It is also noted that small populated countries are moving forward in their scientific output/contribution which is evident when production is normalized per capita (papers per year per one million inhabitants), South Africa, Egypt and Nigeria shift to the third, fifth and seventeenth positions respectively, and the top three countries for per capita production are Tunisia (1st), Seychelles (2nd) and South Africa (3rd).

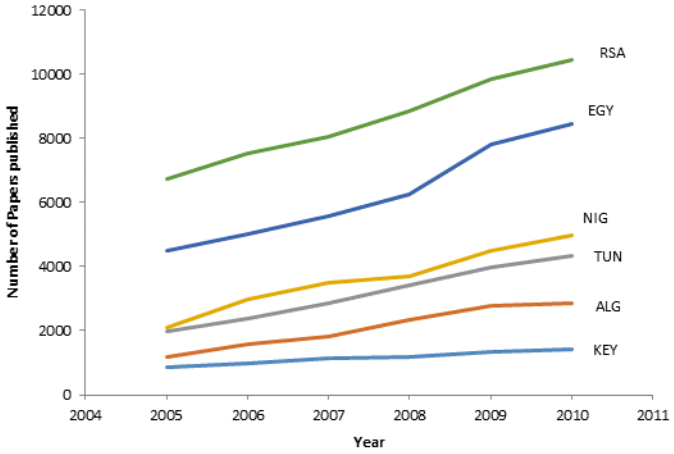

Figure 5: Number of Papers Published by the 6 High Ranked MS [31]

Year	South Africa	Egypt	Nigeria	Tunisia	Algeria	Kenya	Total for top the 6 ranked MS	Other MS	AU	Percentage of the top 6 contribution
2005	6,748	4,485	2,090	1,994	1,170	848	17,335	3,902	21,237	81.63
2006	7,544	5,003	2,971	2,390	1,597	961	20,466	4,709	25,175	81.29
2007	8,039	5,562	3,487	2,876	1,831	1,122	22,917	5,300	28,217	81.22
2008	8,852	6,247	3,714	3,400	2,323	1,190	25,726	5,439	31,165	82.55
2009	9,840	7,816	4,498	3,994	2,789	1,326	30,263	6,007	36,270	83.44
2010	10,477	8,469	4,977	4,328	2,874	1,430	32,555	3,715	36,270	89.76

Table 6: Contribution of the 6 High Ranked MS on Papers Publications [31]

The growth in the output of the AU has been accompanied by an increased ability to publish in highly cited journals. This can be seen by calculating an impact factor for every journal (an indicator of how frequently the papers in a journal are cited on average) taking into consideration differences in citation patterns between scientific disciplines. This normalized measure of journal impact "the average of relative impact factors (ARIF)" is presented in (Figure 6). It shows that, year on year, AU papers are on average increasingly being published in higher-quality journals. The situation is not as clear-cut with the level of citations received, as indicated by the average of relative citations (ARC). In this area, the AU's output is relatively stable, although progressively greater impact (and thus ARC values) could be expected in the future, as there is usually a correlation between the ability to publish in highly cited journals and the capacity of the papers to receive many citations (namely, papers published in journals with a high impact factor can be expected to receive more citations) [31].

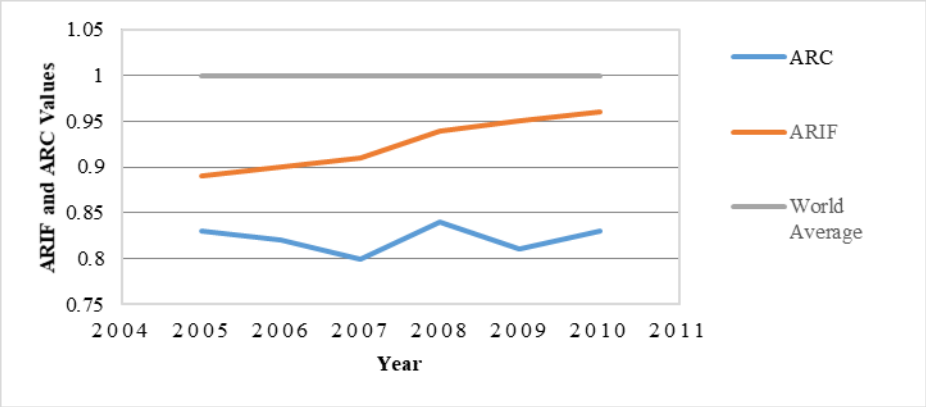

Figure 6: Evolution of the Ability to Publish in High Cited Journals (ARIF) & Level of Scientific Impact of the AU, 2005-2010 [31]

Another indication is that the quality of the scientific output produced in African countries is increasing as well as the number of AU member states that obtained an ARIF value above the world average (ARIF > 1). The number increased from 12 countries in 2005 to 19 countries in 2010. Likewise, there were 10 AU members with an ARC score above 1 in 2005, and 17 in 2010 [31].

The AOSTI study also shows that some fields of engineering, and public health and health services are achieving levels similar to or higher than the world average of 1.00 in terms of research quality, impact and intensity (effort), which is certainly positive, as these areas are important development stepping-stones. The scientific impact in public health & health services can be traced to the involvement of African governments in the health sector and the many national and international health-related initiatives on-going on the continent through collaborative programmes aimed mostly at eradicating infectious diseases. This interest of African governments can be determined by considering that the AU Member States invest in average about 6% of the GDP to the health sector and the increases of GERD percentage that is allocated to health sciences (Figure 7).

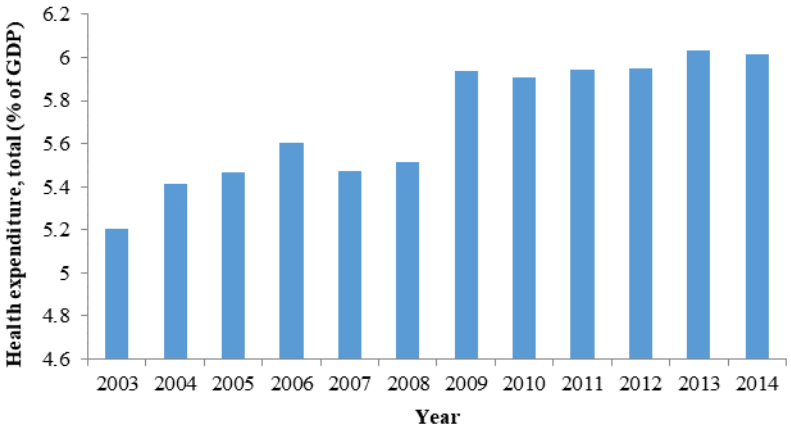

Figure 7: Average Health Expenditure, Total (% of GDP) in AU from 2003 to 2014 [32]

In Member States, countries such as Malawi, Sierra Leone, Lesotho, Djibouti Liberia, and Swaziland, expenditure is more than 10% GDP in the health sector; while Southern Sudan and Madagascar are the least with 2.7% and 3% respectively. In other words, the expenditure of 20 Member States are more than the Africa average; 22 Member States are investing between 4% and 6% GDP while 11 are investing above 2.7% and below 4% (see Figure 8).

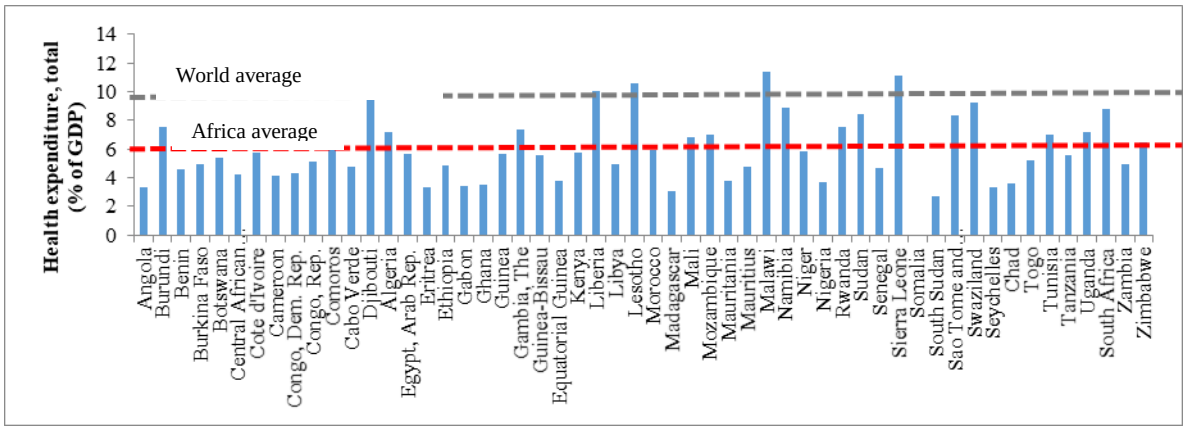

Figure 8: Health Expenditure, Total (% of GDP) in AU Member States Reference Year 2014 [32]

It is worth to mention that the world expenditure is 9.81% of the GDP in the health sector while countries like Austria, Belgium, Brazil, United Kingdom expenditure are 11.2%, 10.59%, 8.3% and 9.1% respectively.

On GERD allocation, there is a remarkable interest in investing in health sciences in most of the AU Member States where Botswana is investing 30% of the GERD in Health research (ref. year 2012) while Kenya is investing 27.7 (ref. year 2010). Countries like Ethiopia; South Africa, and Uganda are investing 15.2%, 17.2% and 18.1% respectively others are allocating less than 10% of the GERD such as Madagascar [30].

This interest can be more evident when examining the attraction of this sector to young researchers where, in Burkina Faso, the number of PhD students in Health increased from 928 to 1554 reference years are 2007 and 2012 respectively; this also can be observed in Niger where in 2011, there were 213 PhD students in health sciences out of the 285 PhD students registered nationwide [30].

Generally, health research is promising and it may change the landscape of research in the continent considering the fact that health research particularly public health and health services not only achieved levels similar to or higher than the world average of 1.00 in terms of research quality impact but also health research accounted for 33% of the papers produced by Africa (Table 7, and Figure 9).

Field of Science	2005 - 2007	2008 - 2010	Growth index 2008 - 2010/2005-2007
Health Sciences	24,959	34,569	1.26
Natural Sciences	22,601	29,829	1.13
Applied Sciences	20,211	29,249	1.2
Economic & Social Sciences	3,552	5,917	1.26
Arts & Humanities	1,406	1,999	1.10
General S&T	1,415	2,460	1.29
General Arts, Humanities & Social Sci.	157	339	1.63
Total	**74,629**	**106,825**	**1.22**

Table 7: Number of Papers, Production in the AU by Scientific Domains 2005- 2007 and 2008–2010 [28]

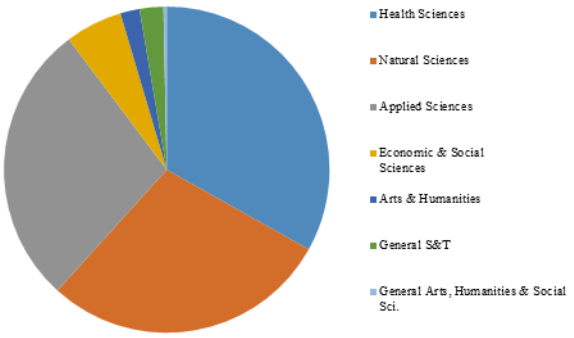

Figure 9: Number of Papers, Production in the AU by Scientific Domains 2008–2010

This large percentage of Africa's papers production (33%) focusing on health research is resulted from the presence of qualified human resources in most of AU Member States. As of the available data, some of the AU Member States have a considerable human capacity in medical and health research/sciences where Burkina Faso has 42% of its research force are in medical and health sciences, this percentage is 40% in the Gambia and 31% in Egypt (Figure 10). That is to say, some of the AU Member States have prioritised medical and health research/sciences in their development plan, while others are following. This could be realized in the case of Kenya 25.5%; Libya 24.4; while Sudan and Botswana are 22%.

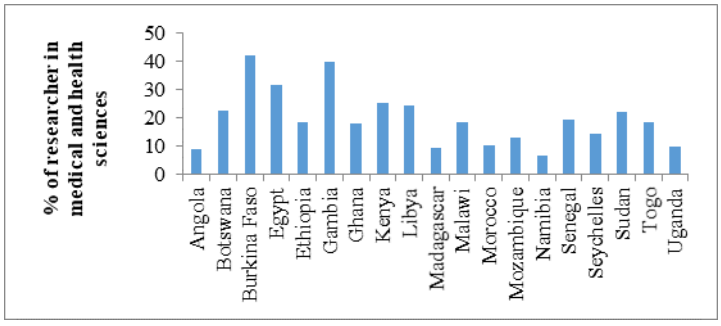

Figure 10: % of Researchers in Medical and Health Sciences in some of the AU Member States Reference Year 2013 [30]

The discussion above on medical and health research/sciences together with the conclusions of the African Science, Technology and innovation outlook Bibliometric [31] under the areas of science in which the AU has a concentration of research effort and demonstrated research excellence "Health sciences: Microbiology, virology, complementary and alternative medicine, general and internal medicine, tropical medicine, health policy and services. The AU is also highly specialized in mycology and parasitology, but the quality of research in these fields remains slightly below the world average" is a testimony that Africa has a comparative advantage in medical and health research/sciences.

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SECTION III: HEALTH CHALLENGES IN AFRICA

3.0 Health Challenges in Africa

Africa is confronted with enormous health challenges because of multifaceted problems that are linked to poverty, food insecurity and malnutrition. The challenges include highly treatable diseases and preventable conditions such as infectious diseases, non –communicable and chronic diseases, shortage of skilled manpower, dearth of infrastructure as well as poor funding and budgetary constraints.

3.1 Pervasive Poverty

Poverty is classified as living on $1.90 or less a day [1]. Poverty is a multidimensional concept while the central aspect of it is income deprivation that restricts an individual's ability to consume certain basic services such as lack of access to health. Pervasive poverty is never considered a disease medically but it is a well-accepted social indicator of health. Africa has the slowest rate of reduction of poverty in the world, particularly in fragile countries and rural areas. Hence, poverty exerts much pressure on the health and well-being of Africans

According to Africa Progress Report 2015, stated that despite some gains over the past decade, Africa has the world's highest incidence of poverty -47% and by some distance, the greatest depth of poverty. The report also cited the International Fund for Agriculture (IFAD) which stated that 60% of rural Africans lives on less than US$ 1.25 a day and 90% on less than US$2 a day [2]. Seventy-five percent of the world's poorest countries are located in Africa, including Zimbabwe, Liberia and Ethiopia. The Central African Republic ranked the poorest in the world with a GDP per capita of $656 in 2016 [3].

Poverty limits access to social services and increase vulnerability to ill-health, which in turn affect productivity, especially in highly labour-intensive economies. The poor are the most exposed to the risks of hazardous environments, and the least informed about threats to their health.

The poverty and poor health nexus worldwide are well known and intrinsically interwoven, and based on this, it was considered as a grave challenge to health care in Africa where vast majority are poor. The causes of poor health for millions of Africans are directly or indirectly rooted in politics, social and economic injustices.

The intrinsic linkage between poverty and poor health outcome is explained [4] as follows

a. Poverty increases your chance of getting ill because of:
    - Poor nutrition
    - Overcrowding
    - Lack of clean water
    - Harsh realities that may make putting your health at risk the only way to survive or keep your family safe.
b. Poor health increases poverty by:
    - Reducing a family's work productivity
    - Leading families to sell assets to cover the costs of treatment. This increases poverty and their vulnerability to shocks/emergencies in the future.

3.2 Infectious Diseases

Africa experiences a disproportionate burden of infectious disease and death with appalling disparities within and between Member States. Infectious diseases are diverse and dynamic; new outbreaks occur frequently and new infectious agents are discovered year on year. The challenge is not only containing the known infectious diseases but also the trend of emerging and re-emerging vector-borne diseases like the Ebola virus pandemic in the West Africa.

3.2.1 AIDS Related Deaths

The World Health Organization's most recent data on global deaths shows an improvement in the death rate for people living with HIV/AIDS in comparison to last decade but the rates in Africa are still the highest of all regions. As such one and half (1.5) million people died of HIV/AIDS in 2005, while in 2015, there was an estimated 760,000 deaths according to the Health Factsheet, this figure in 2015 accounted for 70% of the global deaths from HIV/AIDS and related complications in Africa compared to 1 million in 2010 [5].

This is by far the highest in the world and 90% of the deaths are in Sub-Saharan Africa. 90% of children living with HIV infections and 90% of new infections among children occur in Africa [6]. Africa carries over 60% of the global infected population and women account for 60% of the new infections in Africa. However, the continent represents only 15% of the world's population.

3.2.2 Lower Respiratory Tract Infections

The key infections of the Lower Respiratory Tract include Pneumonia, Influenza, Epiglottitis and Laryngo- Tracheo –Bonchitis (croup). However, tuberculosis is among the respiratory tract infections but it is categorised separately in the WHO classification in the causes of death statistics; hence, we also followed suit in this document. In 2012, lower respiratory tract infections were the second highest cause of death in Sub-Saharan Africa accounting for just over 1 million or 11.5% of deaths in Africa, where tuberculosis alone accounted for a greater percentage than all the rest put together.

Southeast Asia has the highest number of new tuberculosis infections annually but Sub-Saharan Africa has an incidence rate double that of Southeast Asia, and the highest number of tuberculosis related deaths in the world as well as the highest per capita tuberculosis mortality. South Africa and Nigeria have respectively, the fourth and fifth largest number of new tuberculosis cases annually and South Africa by a wide margin has the highest prevalence, incidence, and death rate per capita worldwide [6]. As of 2012, tuberculosis accounted for 230,000 deaths which is 2.4% in the Sub-Saharan Africa [5].

3.2.3 Diarrhoeal Disease

The WHO defines diarrhoeal disease as the passage of three or more loose or liquid stools per day. It is a symptom of infection in the intestinal tract, which can be caused by a variety of bacterial, viral and parasitic organisms [7]. The disease is spread through contaminated food or drinking water, or from person to person as a result of poor hygiene.

Globally, it is the second leading cause of death in children under the age five, from dehydration, shock and electrolyte derangements. the death is Diarrhoea is complicated by the development of Malnutrition which is the result of impaired absorption of nutrients. In Sub-Saharan Africa about 644,000 people died from diarrhoea in 2012 which accounts for 6.7% of deaths in the reference year [5].

According to the US Centre for Disease Control, 88% of diarrhoeal deaths are the result of unsafe water and inadequate sanitation and hygiene.

3.2.4 Malaria

Malaria is a tropical disease caused by Plasmodium parasites. Malaria which can be fatal is transmitted to humans by the female species of the *Anopheles mosquito*. The magnitude of Malaria in Africa is affected by a variety of factors, none of which addressed alone is likely to effect a resolution. It is further compounded by the generally poor social and economic conditions in Sub-Saharan Africa. In most of Sub-Saharan Africa, Malaria is responsible for the largest number of parasitic illnesses. It is also one of the five most important causes of mortality and morbidity, especially among infants, children under five years of age, and pregnant women. Malaria during pregnancy is correlated with low birth weight, miscarriage, stillbirth, and premature birth.

One half of the world's population lives in areas at risk of Malaria, and approximately 214 million people become infected each year. In 2015, Malaria accounted for 80% of cases and 78% of deaths in fifteen (15)-countries; 89% of the cases and 91% of the deaths occurred in Sub-Saharan Africa [8]. Infants and children under the age of five (5) constitute more than 50% of the cases. In 2012, deaths in children under the age of five accounted for 41% of malaria deaths in Sub-Saharan Africa and in the same year Malaria killed 618,000 people around the globe, of which 568,000 (92%) of them were in Sub-Saharan Africa [5].

3.3 Growing Chronic and Non-Communicable Diseases Burden

In addition to the pandemics and other uniquely African infectious diseases, the continent faces a significant and growing non-communicable disease burden and these diseases are a major public health concern. Non-communicable diseases such as Cardiovascular diseases, Cancers, Diabetes, and Chronic Respiratory Disease are considered as leading causes of deaths in the world. Africa has joined the wagon of increased deaths due to non-communicable diseases recently.

Africa, particularly the Northern Region accounts for more than three quarters of deaths from non-communicable diseases [8], (Figure 11). However, it is evident that Sub-Saharan Africa is plagued by infectious disease; it is projected that by the year 2030, non-communicable diseases will be a leading cause of death in the region [9]. It was estimated that about 50% in Africa are already suffering from high blood pressure, a well-known precursor to non-communicable diseases like heart attack and stroke.

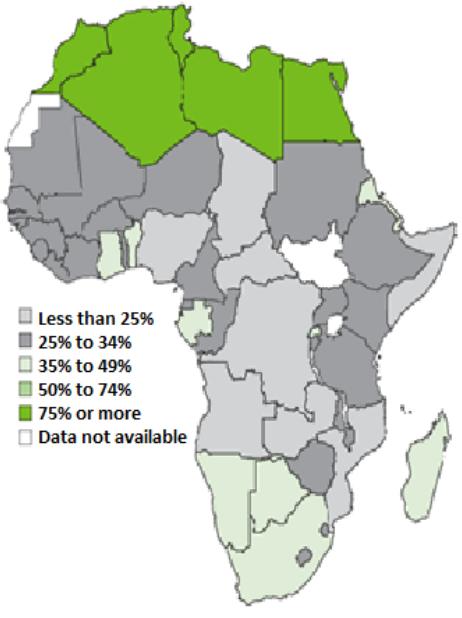

Figure 11: Percentage of Deaths by Non-Communicable Disease per Country 2012 [12].

3.3.1 Stroke

Africa is worst hit by stroke owing to population growth, unchecked industrialization and increased consumption of western diets. These conditions are associated with rise in many modifiable vascular diseases risk factors including smoking, harmful use of alcohol, physical inactivity and unhealthy diets, and invariably resulting in increased prevalence of hypertension, diabetes and obesity [11]. Stroke deaths increased in Africa over the past few years from 406,595 (4.4% of deaths) to 451,000 deaths (4.9%) in 2015 [5]. Data on causes of death from Africa are usually not from standard vital registrations but are gathered from verbal autopsy studies, police reports, sibling histories, and burial and mortuary reports, with the exception of a few high-quality studies.

In a rural hospital in Nigeria, Non-communicable Diseases (NCDs) constituted 63% of deaths, with stroke being the leading cause. Similarly, hypertension related deaths led by stroke was the leading cause of death in a Tanzanian hospital from 2009 to 2011 [12]. In Sub-Saharan Africa, people who die from cardiovascular disease die on average 10 years earlier than in developed countries [8].

Ischaemic heart disease that was previously considered rare in Sub-Saharan Africa is now ranked 8th among the leading causes of death in the region [13]. In 2015, an estimated 441,000 deaths (or 4.8% of the total) were due to ischaemic heart disease. In 2010, this category had a significantly smaller number of deaths at 389,785 (or 4.2% of the total deaths) [5].

3.3.2 Cancer

Cancer is another huge challenge in Africa, the outcome of Cancer in Africa is worse than in developed countries because of late presentation and poor access to early diagnosis and effective treatment. For example, the five-year survival rate of women with breast cancer in Europe is 82% whereas it is 46% in Uganda, a little less than 39% in Algeria, and 12% in Gambia [14]. The recent estimation of cancer incidence, prevalence and mortality in the world shows that in 2012, just less than 1 million new cancers appeared in Africa [14 & 15], while in the same year, almost 600,000 deaths were attributed to malignant disease. The prediction for 2020 is approximately 1,056,000 new cases i.e. an increase of 24% and more than 735,000 deaths are predicted; while in 2030, the region would have more than 85% increase in cancer burden [16].

3.3.3 Diabetes

In 2010 more than 12 million people in Sub-Saharan Africa were estimated to have diabetes and this is projected to increase to 23.9 million in the next 20 years [17 & 18]. Sub-Saharan Africa is expected to have the highest increase in diabetes prevalence than any region of the world; by 2017 more than 15.9 million people had diabetes, and this figure is projected to be increased by 162% by 2045. More challenge can be added to this by considering that Africa is the region with the highest percentage of undiagnosed people - 70% of the people with diabetes do not know they have it [19]. Table 8 below shows the rising profile of diabetes in Member States that are classified as the top 5 in the continent.

	Countries	Number of people with diabetes
1	Ethiopia	2,652,129
2	South Africa	1,865,021
3	Democratic Republic of Congo*	1,738,329
4	Nigeria*	1,731,811
5	United Republic of Tanzania	942,721

*Based on extrapolation from similar countries

Table 8: Shows Top 5 Countries for Number of People with Diabetes (18-99 years) in 2017 [19].

3.4 Other Leading Causes of Death in Sub-Saharan Africa

According to the WHO fact sheet, the five topmost killer diseases in Africa include HIV/AIDS, Lower Respiratory Tract Infections, Diarrhoea, Malaria and Stroke. In addition, the other causes of deaths in Africa, include the following conditions, pre –term birth complications (393, 000), birth asphyxia and trauma (356, 000), Malnutrition (307, 000), Coronary Heart Disease (293, 000) and Meningitis (260, 000) [5].

3.4.1 Shortage of Required Human Resources

The Science, Technology and Innovation Strategy for Africa 2024 (STISA 2024) has underscored the needs and challenges of education in Science, Technology, Engineering and Mathematics (STEM) particularly in medical and health-related fields. The challenge of producing technically and professionally competent labour force in the continent is a enormous task for AU Member States and the entire continent.

Education, in particular, tertiary education, yields significant benefits for young Africans and their societies as it opens up employment opportunities and prospects in the health sector. There is no doubt, enrolment in tertiary education in health science has increased in the last four decades in comparison to the global average of 4.6% which was attributed to new policies and rising population profile of the continent. In contrast, on the education and training of health personnel, for example, in the 47 countries of Sub-Saharan Africa, only 168 medical schools exist and of those countries, 11 have no medical schools, and 24 countries have only 1 medical school [20].

The human resource crisis in the health sector is caused by many factors such as inadequate production of health personnel in the tertiary institutions in some countries, inability to hire in others, brain drain, poor motivation, conflict of interest, corruption and misuse of resources [21]. According to WHO, the world will be in short of 12.9 million health-care workers by 2035; as of 2013 the figures stands at 7.2 million, while the minimal threshold number required globally is 23 skilled health professionals per 10,000 people [20]. In Africa, all categories particularly doctors and nurses are in short supply compared world averages of population ratio.

It is notable that of the 57-countries facing critical shortage of Doctors and Nurses, worldwide, 36 in Sub-Saharan Africa [22]. Figure 12 below shows countries that are in critical need of health workers where health workers are less than 1.15 per 1000 population, which is far below the global threshold and it depicts that the country is in critical shortage of health workers. On the other hand, Table 9 indicates the sub-grouping of health workers into

health service providers and management and support workers per one thousand density population, of all the regions in the world Africa is by far the lowest [23].

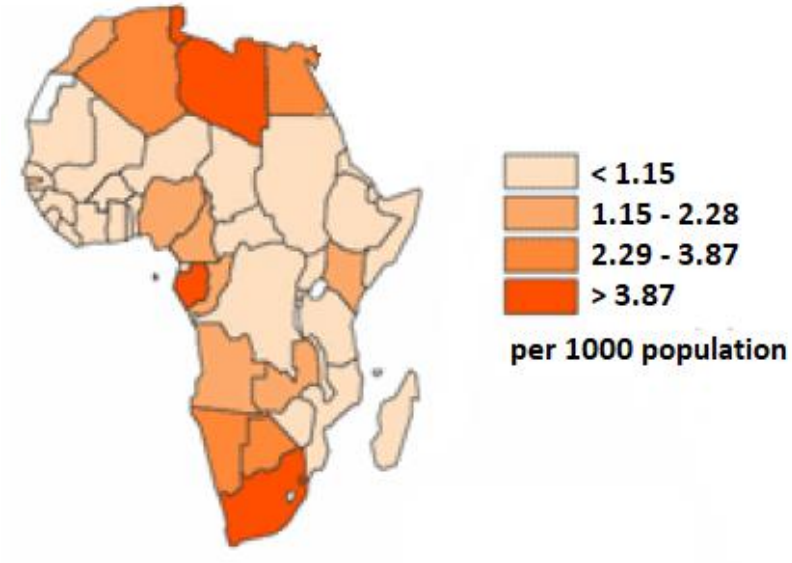

Figure 12: Distribution of Health Workers in the continent and an approximation of actual country figures and border sources [24]

WHO region	Total health workforce		Health service providers		Health management and support workers	
	Number	Density (per 1000 population)	Number	Percentage of total health workforce	Number	Percentage of total health workforce
Africa	1 640 000	2.3	1 360 000	83	280 000	17
Eastern Mediterranean	2 100 000	4.0	1 580 000	75	520 000	25
South-East Asia	7 040 000	4.3	4 730 000	67	2 300 000	33
Western Pacific	10 070 000	5.8	7 810 000	78	2 260 000	23
Europe	16 630 000	18.9	11 540 000	69	5 090 000	31
Americas	21 740 000	24.8	12 460 000	57	9 280 000	43
World	59 220 000	9.3	39 470 000	67	19 750 000	33

Note: All data for latest available year. For countries where data on the number of health management and support workers were not available, estimates have been made based on regional averages for countries with complete data.

Table 9: The Global Health Workforce, by Density [25]

The shortage of health professionals is also due to: migration of health workers to better-paying employment in the developed world; health professionals are being drawn from rural

to urban centres; from the public to the private sector; and from lower-income to higher-income countries even within Africa. For example, Mozambique and Angola have over 60% of their native-born doctors living abroad and experiencing critical shortages of health workers while Sierra Leone, Liberia and Tanzania have over 50% of their native-born doctors living abroad [21].

3.4.2 Rapid Demographic Shift in the Continent

One of the key drivers of environmental change globally is population growth. Africa's demography is unique. In the 1950s, Africa accounted for about 9% of the world population and presently is about 15%, that is over one billion of the world's population and is estimated to account for about 40% of the world's population with a projected total population of 4.4 billion by 2100 [26]. In reality, it is predicted that 83% of the projected increase in global population by 2100 will occur in Africa. It is also going to be that majority of the population will belong to the youth cohort and climate change will increase population risk and geographical range of vector-borne disease has been linked to regional warming and consequently altered the length of seasons.

Climate change could increase the population at risk of malaria in Africa by an additional 170 million by 2030 and the global population at risk of dengue fever by 2 billion by the year 2080 [27]. It is also envisaged that the rapid and unregulated urbanization that is ongoing in the continent poses health hazards, including substandard housing, contaminated drinking water, air pollution, poor sanitation, and sewage systems, stress associated with poverty and unemployment among others.

3.4.3 Sustainable Financing of Health and Funding

Though finance is not the sole requirement for achieving betterment in Africa's health sector but it is considered as an important factor for sustainable health sector as financing is one of the most crucial pillars of building a viable health system and an indispensable prerequisite for improving equitable access to health services. As of that, the average expenditure by AU Member States in the health sector in Africa exceeds 6% of GDP as of 2014. Despite this important fact, most of AU Member States did not meet the Abuja 2001 Declaration target to allocate 15% of their total government expenditure to the health sector (Abuja Declaration) [28].

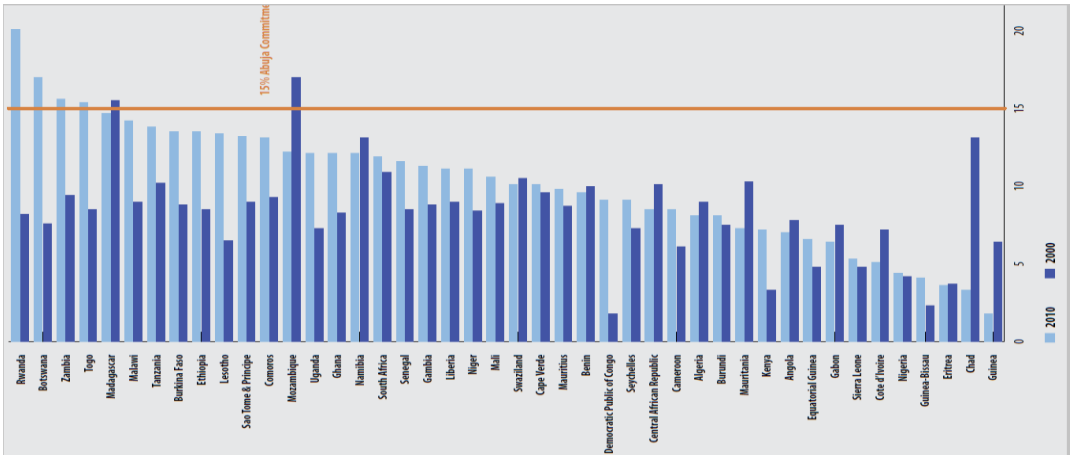

Figure 13. Government Expenditure on Health as a Percentage of Total Government Expenditure in Africa [27]

Figure 13 depicts that Rwanda, Botswana, Zambia, Togo exceeded the Abuja Declaration level as of 2005. It is worthy to mention that these countries received significant external assistance much of which is funnelled through the public sector for use on social programmes such as health and education. Generally external resource for health accounts for 10.2% of total health expenditure in Africa, which is a much higher proportion than anywhere else in the world [27]. On the other hand, figure 13 shows that, Madagascar and Malawi are very close to attaining the Abuja target while Chad, Guinea and Eritrea were below the 2000 level in 2010. These raise concern why the Member States are lagging behind despite the commitment at the Abuja Summit.

Notwithstanding this commitment, the total expenditure on health of the AU 55 Member States is less than 1% of the global health expenditure, considering that the continent carries 25% of the world's disease burden and has 15% of the world's population. In other words, most African countries spending less than US$10 per person per year on healthcare when at least US$27 is needed [29]. Hence, it is not questionable that healthcare financing in Africa remains abysmally low and a patchwork of meagre public spending and reliance on partners' fund. In some instances, health expenditure is based on out of pocket expenses or user fees which constitute great burden on the poorest members of the society.

The World Health Organization's Commission on Macroeconomics and Health (CMH) estimated that in low-income countries, a basic package of health services could be provided for $34 per capita (the so-called "CMH target"). However, the current per capita spending on health is lower in Sub-Saharan Africa than in any other region of the world. In furtherance, the situation of health financing is bleak as even if all AU Member States meet the 15% Abuja target, there are 23 Member States that still will not meet the $34 spending level of CMH [30].

Low domestic financial resource capacity, slow economic growth in the continent, small taxable formal sector, lack of or inefficient social protection systems, health insurance coverage, among others, constrain African governments from significantly increasing the level of resources allocated to health and among the ones that are allocated, significant proportions go to salaries. In addition, value for money and returns on investments are not routinely considered when selecting priority interventions which has further underpinned Africa's health financing. This creates a situation whereby the Ministries of health in Africa spend a lot of time attending workshops and responding to donor inquiries and concerns, and less time providing the needed service to the households [29].

Hence, this shows that Sub-Saharan Africa still faces a grim scenario with respect to the health of its people. The only encouraging and comforting side is that for the first time in the last three decades, the continent started recording sustained economic growth of between 5 to 6 percent per annum [31] that will hopefully spur growth further and health expenditures will eventually be increased.

3.4.4 Health Governance and Management

The concept of governance has been defined in various ways, but the UNESCO's concept is broad and aptly defined it as structures and processes that are designed to ensure accountability, transparency, responsiveness, rule of law, stability, equity and inclusiveness, empowerment, as well as broad-based participation. Its further states that Governance represents the norms, values and rules of the game, and therefore, public affairs are managed in a manner that is transparent, participatory, inclusive and responsive. From this definition, health sector governance in Africa remains a hydra-headed challenge engulfed by weak transparency and accountability mechanisms as well as inadequate engagement of stakeholders in policies, strategies and development plans.

Globally robust health systems cannot be built without strong leadership and governance and greater public accountability. While poor governance impedes the efficiency of African health systems, as discussed above under (**Sustainable Financing of Health and Funding)**, with the meagre allocation of funds by Member States that often fails to reach the front lines, in some cases, this means that 95% of funding fails to reach targeted interventions [27]. Such inefficiencies result from the lack of evidenced-based policies, inadequate provision of resources for high-impact interventions, inappropriate procurement, and poor management of equipment, inappropriate skills mix, and lack of performance incentives. It was also identified that three governance factors particularly relevant to health service delivery are voice and accountability; government effectiveness; and control of corruption [30].

Many can attest that corruption is endemic in Africa and considered a strong retarding force for good governance not only in health but in all spectrums of development. According to the Transparency International's Corruption Perception Index 2016 in Sub-Saharan Africa, only Botswana scored 60, Rwanda 54, Namibia 52, Senegal and South Africa 45 respectively while the rest are below these scores [31].

The Africa Health Strategy 2016 -2030 highlighted that the weak regulation of the private sector and the quality of medical product stocks has resulted in widespread availability of substandard, counterfeit or fake medications as a result of overall ineffective governance framework. There are also major challenges in the health information system of most countries in Africa. Less than two-fifths of Africans have a complete civil registration and vital statistics systems. The poor strategic information found in most Member States has resulted in weak utilization of data and evidence for decision making, including national policy and strategy development and sub-national planning and management of health services [32].

In the Member States where they have shown progress in good governance and management, there is still need for improved harmonization and alignment in a key element of good governance and establishment of national plans, in terms of one governing framework and one monitoring and evaluation system. The centralization of functions and authority based on bureaucracy in the health sector on many occasions results in delayed implementation and execution of programmes and projects. This in itself causes more damage to the health system in Africa in comparison to developed nations systems where functions and authorities are decentralized including resources to improve performance.

Good governance can only be achieved when there is participatory and inclusive approach required to meaningfully and fully engage communities, civil society organizations and private sector.

3.4.5 Health Infrastructure

Health infrastructure is categorised into direct and indirect: The direct health infrastructure refers to medical equipment and production plants while indirect health infrastructure is power, sanitation, roads, rails, information and telecommunication among others. Health infrastructure is further classified into physical and virtual.

The STISA 2024 was developed to respond to the demand for Science, Technology and Innovation to impact across critical sectors such as agriculture, energy, environment, health, infrastructure development, mining, security and water among others. The Programme on Infrastructure Development in Africa (PIDA) has stressed the needs and gaps in the state of infrastructure in Africa across all sectors of development. The former identified building and/or upgrading infrastructure among the prerequisite conditions for its success.

Some have argued that Africa inherited the colonial health infrastructure which may not necessarily fit to our context, hence, making it difficult to build on it. Others have argued that Africa's economy has been low for long and public spending capabilities in infrastructure grows with economic growth, hence, it may not be easy to build health infrastructure. There were many declarations and targets set by highest Decision-Making Bodies in the continent. For example, alongside the Abuja Declaration, Member States have also signed the Maputo Declaration stating that 10% of government expenditure should be for agricultural development while on the other hand, the Education for All Initiative saying that 20% should be for education. There are also agreements on spending targets relative to GDP for social protection (4.5%), water and sanitation (1.5%), 1% of GDP allocation to science and technology and infrastructure (9.6%) [33].

However, only a negligible percentage of Member States met these targets which involve expenditure on infrastructure. In the Member States where such infrastructure exists, they are inadequately distributed in the country. For example, 84% of Africa's urban population have access to improved drinking water sources, compared to just 48% of rural residents. The same applies to sanitation: 47% of urban residents have access to improved sanitation facilities, compared to 26% of rural residents [27].

There a lot of equipment that is obsolete in the developed world but still being used in Africa. In addition, equipment maintenance and spare parts procurement pose a greater challenge in Africa. It takes nothing less than a month or two to procure equipment overseas and import to Africa, from shipment to custom clearance and delivery to the required hospitals or clinics. To date, there are few Member States that have BSL 4 laboratories for testing and analysing samples and the Member States that do not have any rely on foreign laboratories as seen in the case of Ebola epidemic in West Africa. There is also the problem of dearth of skilled manpower to man the laboratories.

The lack of required health infrastructure contributes to poor health outcomes. For example, there is anecdotal evidence that due to the distribution difficulties caused by insufficient

infrastructure in some countries, a percentage of donated drugs expire on shelves in government central medical stores without ever reaching the areas of greatest need in rural clinics and hospitals [15].

Information technology, e-health system infrastructure has revolutionized the health sector but challenges in low bandwidth, less connectivity, and dearth of internet-exchange point in Africa is a serious draw-back. Africa has witnessed benefits of mobile phone technology but communication infrastructure is still limited. As mobile devices become increasingly common, they have become an unexpected resource in delivering better healthcare. This is further strengthened by the fact that Africa has not yet built two-thirds of the infrastructure that will be in operation by 2030 [2]. Despite the importance of e-health in overcoming the triple challenges of inadequate access, finance, and human resources in delivering high-quality healthcare services to Africans including remote areas, it also contributes to greater transparency and accountability in health services, by promoting evidence-based practice and error reduction, diagnostic accuracy and treatment but this indispensable and critical area of health infrastructure is grossly inadequate in the continent.

Nevertheless, Africa is also experiencing the emergence of private hospitals, clinics, laboratories and diagnostic outlets that has contributed to infrastructural development but it is argued that most private sector health services are out of the reach of the common man, that is, too expensive to afford. Another infrastructural challenge in Africa presently, is that health research systems are treated as a separate entity from health systems and its multi-disciplinary and multi-sectorial nature is not emphasized [34].

3.4.6 Limited Access to Essential Medicine and Drug Manufacturing Challenges

Access to health and essential medicine is centred on availability, accessibility and affordability. This topic is multifaceted and depends on a multiple factor and it cuts across many challenges such as lack of local production capacity, weak institutional capacity, poorly regulated supply chain, rampant corruption, ineffective governance, poor funding among others. The fact remains that, in Africa, many people still do not have access to health and essential medicines which they need. The continent on the average has only 9 hospital beds per 10,000 people, in comparison to the world average of 27 per 10,000 [27]. Ensuring affordable access to health services on a continent where one-third of the population lives on less than a $1 per day is a daunting challenge. Public hospitals and health centres often charge user fees (transportation costs are often an additional burden); and private services, which are growing rapidly in urban centres, are prohibitively expensive for a large number of Africans. Disease burden is likely to grow as the global crisis unfolds and remittances, government revenues, and foreign assistance levels across the continent being likely to fall.

If the conventional healthcare is not accessible, the traditional way must takeover. WHO estimated that 80% of the African population makes use of traditional medicine [34 & 35]. In Uganda, the ratio of traditional medicine practitioners to the population is between 1:200 and 1:400 while that of the allopathic (western) practitioners is typically 1:20,000 [35]. For many rural people in Africa, traditional healers are the only source of healthcare within reach. The irony is that traditional African medicine constitutes a very rich cultural heritage that has

sustained Africans for many centuries. Although Africa has over 50,000 plants, less than 10% of the indigenous plants have been subjected to scientific investigations regarding their potential medical use.

There are shortages of crucial medicines throughout the continent, and consequently, only a fraction of those in need receive the treatment. In Sub-Saharan Africa, only 38% of essential drugs are available in public facilities. Access to essential medicines is restricted by high prices, unreliable public health facility supply, and limitations in private sector. The availability of essential medicines averaged 42% in public sector facility, while in the private sector the level was only slightly better at 58% [27]. Most Member States rely on imported medicines to treat their citizens, importing roughly 70% of medicines and 95% of active pharmaceutical ingredients. Meanwhile, the total size of Africa's pharmaceutical industry is less than 1% of the world [15]. Less than 0.01% of new medicines are devoted to treatment of tropical diseases and there is huge gap between appropriate and affordable medical interventions available and their use by those who most need them [34].

It is another matter of concern that, even when medicines are available, their quality is doubted due to the weak nature of regulations and widespread noncompliance with best practices. There is no much research and literature on the impact of substandard drugs on the continent. Development and building of pharmaceutical manufacturing plants is cumbersome as there are issues of regulations, control and compliance. In addition, divergence of regulation across the continent that need to be harmonized and setting up new regulations in Member States where there are none. At present, the continent is situated in an awkward position of being a nearly-net importer of drugs. Drugs vendors are flourishing with less regulation and enforcement in the continent.

Evidently, with all these massive challenges facing the continent's healthcare systems there is need for several major reforms continent-wide to ensure their viability in the long term and to reposition the continent to achieve its vision and missions.

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SECTION IV: INVENTORY ON HEALTH RESEARCH AND RESEARCH TRANSLATION CHALLENGES IN AFRICA

4.0 Inventory on Health Research and Research Translation Challenges in Africa

The STRC designed a programme to develop an inventory on the Health Research and Research Translation in Africa, based on two main approaches which are: Face to face consultation with Scientists that are drawn out from relevant Scientific disciplines related to health and health research; and finally, by conducting a wider consultation with members of the Ethic committees of AU Member States; members of the African network of Drugs and Diagnostics Innovation (ANDI); independent Scientists from the AU Member States by instituting a questionnaire (e-survey) and analysing their output.

4.1 Face-To-Face Consultation

The 3rd UNESCO- MARS Summit was held in Port Louis Mauritius for 2-days, from 27 – 28 November 2017 and featured several interactive sessions Day one of the Summit was largely ministerial interactive sessions, discussions and presentations on strategies for improvement of health and health research in Africa. The participants comprised Ministers and Director Generals from across Africa in the areas of health and science.

The African Union, Scientific, Technical and Research Commission (AU-STRC) conducted the workshops/ breakaway sessions on Day two of the summit. The purpose of the workshop was to collect views and suggestions into the problem "Weak Research Translation and Pathways in Africa". The overall objective was "To Improve the Health of Africans by establishing and implementing Policies that support Research Translation from Bench to Bedside".

The overall problem statement "Weak Research Translation and Pathways in Africa" was categorised into two problem statements, which are accommodated under the policy analysis pillars of the STISA 2024 "Enabling Environment and Technical Support", and "Building/Enhancing Health Research Infrastructure" as follows:

1. Enabling Environment and Technical Support
   Problem Statement: *Inadequate to Absence of supportive mechanisms to Research Translation.*
2. Building/Enhancing Health Research Infrastructure
   Problem Statement: *Poorly Equipped facilities to boost research / drug discoveries and development in Africa*

The output of the focus group discussion further augmented with literature analysis was the basis of the development of the problem tree.

4.1.1 Approach

There were 6 –focus groups made up of 15-participants per group and were randomly selected from the attendees, thus ensuring representation of most AU Member States. The participants were largely mid-career scientists and PhD students. Each group was moderated

by a lead discussant, who had been inducted on the approach of conducting the study in order to achieve the desired output. There were 6 lead discussants and a total of 90 participants took part in the study.

Half of the groups discussed the problem falling under the STISA policy pillar "Enabling Environment and Technical Support", and the remaining three groups discussed the problem falling under the policy pillar "Building/Enhancing Health Research Infrastructure". Each group developed an inventory of the possible factors, which had resulted into the overall problem of "Weak Research Translation and Pathways in Africa".

Each group investigated the problem statements and the following discussant questions:

a) What approach can best control high cost in clinical research and increase governments' investment on vaccine research?
b) What are the hindrances to proper knowledge management and translational systems in Africa?
c) What are the hindrances to a better understanding of the mechanisms in the development of vaccine delivery systems in Africa?
d) What are the factors affecting the development of facilities and incentives to enhance effective care and better disease management systems in Africa?
e) What are the measures that can be employed to enhance vaccines development and potentially useful drugs in Africa?

The final inventory developed was the basis for the Problem Tree Analysis. It was achieved by consolidation amalgamation of the causative factors which in his/her views have given rise to the problem of "Weak Research Translation and Pathways in Africa". The group sessions lasted 20 minutes. At the end of the session, one member of each group compiled, presented and reported on his/her groups output to the plenary session of all participants and groups. Individual participants then further discussed the outputs arising from each group.

Furthermore, the AU-STRC studied the findings using the problem tree analysis from which the problem tree on "Weak Research Translation and Pathways in Africa" was developed (see annex I).

Thereafter, the possible intervention mechanisms for the improvement of research translation in Africa would be considered.

4.1.2 Problem Tree Output

The raw data of the problems presented to AU –STRC, were analysed and resulted in the development of an inventory with 4-pillars as follows-:

In furtherance, AU-STRC took the raw data of problems presented and analysed the output that resulted in clustering the inventory in 4 major pillars identified below:

- Poor/vague protocol on clinical research
- Funds are limited and inadequate for performing research
- Shortfall in Technical/professional competencies

- Public are less interested to participate in clinical research & clinical trials

Realizing from the challenges of science education and research in Africa [1] published in 2017, buttresses the numerous challenges through which the Problem Statement here is considered to be a fundamental factor in the overall development of science. The synthesis of the problems that led to the development of the Problem Tree was done using a step-by-step analysis in hierarchy of the root causes in terms of gravity of the problems facing Clinical Research in Africa. The aim is to map-out a detailed breakdown that enables the development of holistic and effective solutions.

Clinical research is an indispensable tool for the prevention, identification and treatment of diseases and research outcome must be translated to reach the end-users. To overcome the challenges of clinical research translation, a holistic analysis of the 4 pillars was conducted.

4.1.2.1 Poor/Vague Protocol on Clinical Research

Research output and input are not disseminated because decision and policy makers are not well informed or lack awareness about the clinical research potential on addressing health challenges which resulted in incomprehensive guiding principles to clinical research with its existing legislations.

The incomprehensive guiding principles resulted in:

- Poor IP systems that weaken the protection of clinical research output;
- Uncoordinated clinical research standardization in the African Union Member States;
- Insufficient to absence of good clinical practice and guidelines which has caused an adverse effect on the data handling/ sampling protocols in Africa. This created barriers to access and transfer of raw data as well as inappropriate record keeping system in hospitals.
- Inadequate ethical research guidelines which undermine the standard of the ethical approval system and approving committees which made the process of getting ethical clearance very long and complicated.

These factors fall under the category of Poor/Vague Protocol on Clinical Research which is a direct cause of inadequacy/ absence of supportive mechanisms to research translation. In addition, poor protocols and absence of good clinical practice guidelines also compromises research standards.

4.1.2.2 Funds Are Limited and Inadequate for Performing Research

It was identified that fundamental supportive mechanisms are lacking in Africa's clinical research. Poor funding allocation to clinical research hampers the progress of research work, dampens the enthusiasm of researchers, thereby causing them to prefer to work outside the continent. The private sector in Africa does not support research work within the continent and yet import foreign research outputs. Hence, they do not invest in clinical research in Africa.

On the other hand, decision & policy makers are not well informed/aware of clinical research potentials in addressing health challenges. Governments of AU Member States also prefer to

engage the services of foreign research institutions in responding to emerging health challenges. The policy makers in government do not pay the necessary attention to creating institutional framework for the protection of intellectual property and rights of African researchers. The fact that the relevance of research in National development is hardly recognized by the government has limited the encouragement of researchers and made the government to be more interested in hiring foreign experts as a way of responding to emerging health challenges.

Governments are less interested in funding research compared to other development sectors as politicians are not motivated to defend budget reduction on research, and scientists are ignored in research budget development process causing limited transparency and corruption in funding allocation & opportunities.

Moreover, rights of African researchers working with international institutions are not protected due to the lack of institutional framework. Therefore, African researchers are demoralized by the neglecting of their research outputs. The relevance of research in national development is hardly recognized by government and encouragement for researchers is limited. On the part of the researchers, it was also noted that research design does not address the priorities of the government and the general public, which further increases the level of neglect and ignorance associated with clinical research in Africa.

4.1.2.3 Shortfall in Technical/Professional Competencies

In Africa, scientific findings are rarely celebrated or financially rewarded; researchers earn lower income as compared to other jobs. The low income of researchers/mentors have motivated caused the Professors and senior scientists to look for other income opportunities in private Clinics and Hospitals in order to meet their financial obligation, demands/ expectations which they failed to gain out of their research works. This low income has also negatively affected the interest of Professors in research and made them to allocate less time to develop their supervisee/mentee's capacity and drive them to focus more on ways of making money which indirectly makes mentorship for Clinical Research weak and ineffective.

This ineffectiveness of mentorship triggers the lack of communication/understanding between the mentors/Professors and the young scientists to the extent that new ideas coming from the mentees are most times rejected by the Professors. The fear of rejection of ideas gradually killed the creativity and innovation of the young scientists.

Another effect is that the curriculum, training modules and capacity building programmes are not really addressing the knowledge gaps needed and that makes the African researchers to be poorly trained on new research methods and equipment, which results in lack of proper training on grant and proposal writing. As an effect, PhD students face challenges in finding financial sponsorship for their research works and post graduate grants are inaccessible and hard to be gotten. This has led the continent to have poorly trained scientists and professionals in the medical field which in general, causes a shortfall in technical/professional competence.

As a result of poor training, the knowledge and research skills of young researchers are not improved to the required levels. Beyond the difficulties they face during the research designing stage, the financial barriers of publishing their research findings frustrate young scientists and prevent them from continuing their careers in the field of research. This has gradually lowered the number as well as the quality of publications and articles produced by Africa. Another challenge is that the educational curriculums are outdated/poor/ weak. The access to practical classes is very limited and the teaching language is also another barrier for the science students to clearly understand the context and this makes them to lose interest in carrying out research works which leads to poor quality graduates in Africa.

An evaluation of Africa's infrastructural capabilities revealed that, the inadequacy of research facilities to perform Clinical research is a cause effect of the limited encouragement for researchers and is among the major reasons for the discouragement of young scientists. Obsolete machineries and outdated/ inadequate lab facilities for clinical research along with outdated software has made clinical research very difficult and unattractive. The cost ineffectiveness of accessing publications online together with the unavailability of publications in research centres and libraries prevent African researchers from getting access to credible data and publications.

Another perspective to the shortfall in technical and professional competencies is the preference of governments in hiring foreign expertise to respond emerging health challenges. This triggers the deprivation of the rights of research protection for African researchers participating in international institutions' research work. This makes the governments to neglect the research output made by African researchers which in turn demoralizes and diverts the interest of African Scientists to work outside the continent than in their homeland.

Furthermore, compared to other sectors, governments in Africa are less interested in funding research works, this has led African politicians to be reluctant in defending the importance of research funding during the budgetary process. It is a fact that scientists are ignored to participate in the budget development process and this in turn limits the transparency of the process and opens a chance for corruption in funding allocations and opportunities. This improper management of finance has led the continent to have poor funding allocation for clinical research.

The poor allocation of funds has made clinical research to suffer from funding inconsistency, and made research funds to be misplaced and spent on administrative issues such as recruitment of more support staffs than the actual researchers who can do the intended research work. Other than the neglecting of African scientist's research work, the poor fund allocation is also a negative factor pushing African researchers to prefer working outside the continent, thereby causing a shortfall in technical/professional competence in Africa.

4.1.2.4 Public Are Less Interested to Participate in Clinical Research & Clinical Trials

The role of the public in the advancement of clinical research in Africa cannot be disregarded. The fact that the public are not well informed on the potentials of clinical research impact on the development of Africans' lifestyle results in poor support for research

from private sector and industries in the continent as well as minimal investment from public-private partnership, which overall leads to poor funding allocation to clinical research. Also, weak/insufficient communication between stakeholders and the resulting conflicts of interest can also lead to misinformation of the public. In addition to that, insufficient communication has weakened the participation of stakeholders in clinical research and made health problems to look bigger than they appear.

The weak participation of the stakeholders has resulted to incomplete information on the beneficiary's needs. In the African context, cultural values act as barriers to clinical research alongside the absence of guidelines to protect the individual's participation in clinical trials. As a result, research is carried out on patients with no proper guidelines to protect the patient /individual participation in clinical trials. Because of the above-mentioned communication gap, the public is less interested to participate in clinical research and clinical trials.

Lack of expertise-based platform/networks to boost clinical research and weak knowledge sharing among researchers resulted to non-cooperation among African scientists/researchers. These factors added with ineffective data handling/sampling protocols in Africa has made researchers to keep data for themselves rather than sharing it with other colleagues in the same discipline. This as an effect has left African researchers uninformed about the existing clinical challenges which also trigger a shortfall in technical professional competences.

4.2 AU-STRC Questionnaire on Research Translation from Bench to Bedside

Following the evolving challenge which is "Lack of Clinical Research Translation Output in Africa to the inadequate to absence of supportive mechanisms to Research Translation", and the above-mentioned round-table discussion with African scientists and its output that identified the four (4) following gaps that hinder research translation which are: ***Poor/Vague protocol on clinical research***; ***Funds are limited and inadequate for performing research***; ***Shortfall in technical/professional competencies***; ***Public are less interested to participate in clinical research and clinical trials***; A wider consultation was conducted to ensure the consultation and participation of a larger spectrum of stakeholders.

4.2.1 Approach

In this regard, a questionnaire was specifically designed by the African Union Scientific, Technical and Research Commission and sent out electronically, covering the four (4) gaps identified as the major resultant causes of **"*Inadequate to absence of supportive mechanisms to research translation*"** in Africa.

This e-survey system further engaged African scientists in a thorough examination of the problem statement. The data gathering was aimed at achieving a comprehensive data –based analyses of the problems from Clinicians, Clinical Researchers and Bio – Scientists among others. It was expected that the findings would assist in bridging the gap of clinical research translation from Bench to bedside in Africa based on African Inclusive Strategy building as well as dynamic translation models and strategic implementation within major research translation pillars and sub pillars cutting across stakeholders in the dimensions of Mechanisms; Systems and Physical Infrastructure.

The scenario analysis of such data provides a clearer picture or a synopsis of how the problems are generated, interrelated and their impact on clinical research. This analysis engenders a whole new and dynamic approach to tackling the root causes and bridging the existent gap in research translation from Bench to Bedside in Africa.

4.2.2 The AU-STRC E-Survey on Research Translation

As mentioned earlier, an e-survey (questionnaire) was developed by the AU-STRC to ensure a wider consultation with stakeholders. The questionnaire was generally designed in four clusters which are:

- Poor/Vague protocol on clinical research;
- Funds are limited and inadequate for performing research;
- Shortfall in technical/professional competencies;
- Public are less interested to participate in clinical research and clinical trials.

A copy of the questionnaire is annexed (see Annex II).

The participatory group (sample) in the questionnaire drawn from the AU Member States and categories were 64% male and 36% female with a total number of 209 participants. In terms of age groups, the sample: age 25 -29years (21%); 30 -35years (28%); 36 to 40years (11%); 41 to 45 Years (7%); 46 to 50 years (5%); 51 to 60 years (17%) > 60 years (11%).

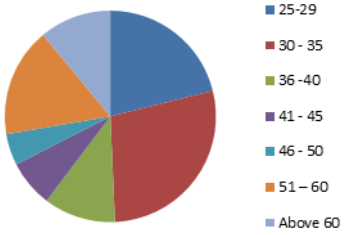

Figure 14: Distribution of the Sample by Age Group

The sample was designed to ensure a wider participation of scientists and stakeholders who are involved in research translation; with the distribution per major as shown in figure 15.

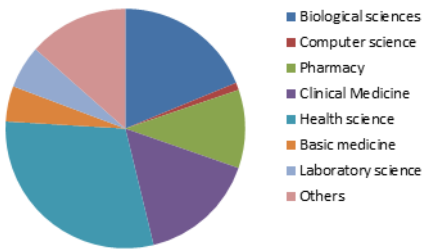

Figure 15: Distribution of the Sample by Major Field of Study

The distribution by affiliated institutions and occupancy is presented in Figures 16, and 17 respectively.

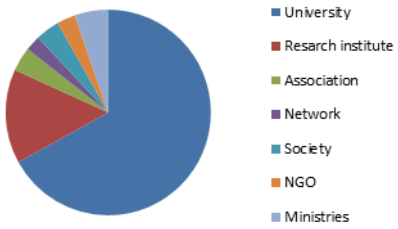

Figure 16: Distribution of the Sample by their Affiliated Institutions

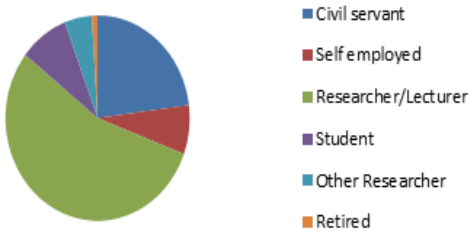

Figure 17: Distribution of the Sample by Occupancy

Finally, it is important to highlight the fact that response was received from 28 out of the 55 AU Member States that were requested to participate in this survey. The participating countries include Algeria, Benin, Burkina Faso, Burundi, Cameroon, DR Congo, Egypt, Ethiopia, Gabon, Ghana, Kenya, Lesotho, Liberia, Mali, Morocco, Namibia, Niger, Nigeria, Rwanda, Senegal, Somalia, South Africa, Sudan, Tanzania, Tunisia, Uganda, Zambia and Zimbabwe.

The highest number of respondents were drawn from the age group 30 to 35 years (28%) and followed by age group 25 to 29 years (21%); these represent the active work force age group.

4.2.3 Analysis of the Survey and Its Output

The analysis of the survey focused on examining the four clusters namely "***Poor/Vague protocol on clinical research***; ***Funds are limited and inadequate for performing research***; ***Shortfall in technical/professional competencies***; Public ***are less interested to participate in clinical research and clinical trials"*** and the output is shown thereafter.

4.2.3.1 Poor/Vague Protocol on Clinical Research

Under this pillar, questions in the questionnaire were clustered to address Research Ethic issues; Data handling and Recorder Keeping; Existence of Intellectual property systems; and Good clinical practice.

a. Ethic Committee and Approval Guidelines

The result shows that 25 Member States out of the sample size (28 Member States) do have an Ethics Committee, while ethic approval systems in Member States was not satisfactory to 17% of the participants and considered to be weak; 64% of the sample shows indecisive response on the strength of the ethic approval system.

On the existence of ethical research guiding principles, 90% of the sample reported that their Member States have guiding principles for Ethical Research i.e., 23 Member States out of 28 have an ethical research system.

Sample participants from the same Member States came with different/ contradicting opinions on the existence of such guidelines; for example, in Nigeria 74% agreed and 26% opposed, in Ethiopia 74% and 26% opposed. While in Cameroon and Kenya 89% agreed, 11% opposed; 80% agreed and 20% opposed.

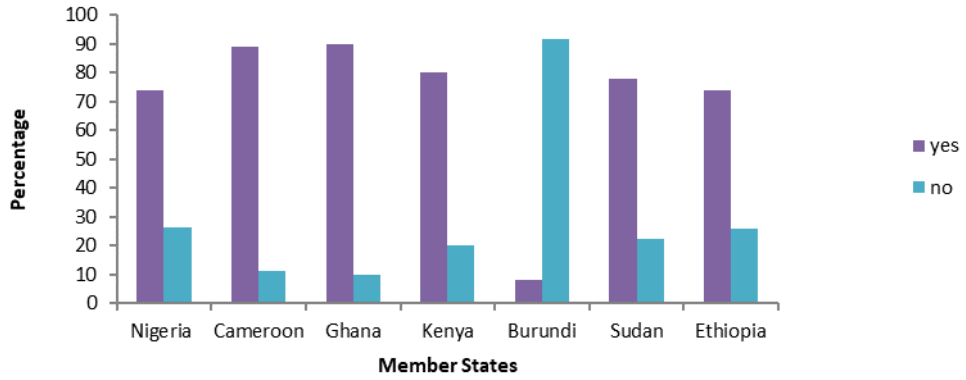

Figure 18: Distribution of Ethic Research Guide Line in Some Selected Member States.

On the quality of those research guidelines, it was observed that 64% of Member States that participated in the survey are confident that this ethical research guideline is adequate to perform clinical research while 34% either denying or indecisive.

b. Data Handling and Record Keeping

Data handling and record keeping, and the accessibility of such data is vital to conduct clinical research; 47% of the sample (13 Member States) have data handling and sampling protocols while 47% of those who have protocols rate their protocols are efficient. In other words, 53% of the sample dose not has protocols, while 50% of those that have protocols are not satisfied with them. That is to say, the opinion of 77% of the sample was either there are no protocols or weak protocols exist in the Member States.

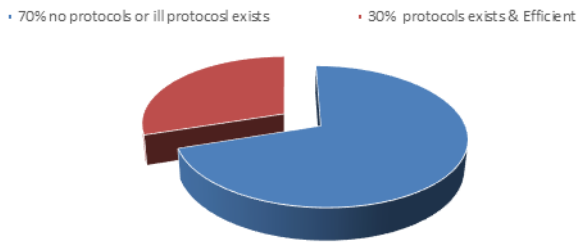

Figure 19: Data Handling Protocols in Member States

This was confirmed by the participants when they expressed low trust in the data recording systems in the National and Private Hospitals in their respective Member States where 65% of the sample showed no trust in the data recording system.

On the accessibility of such data and record, it was recorded that in 78% of the participating Member States, it is difficult to access such data and records.

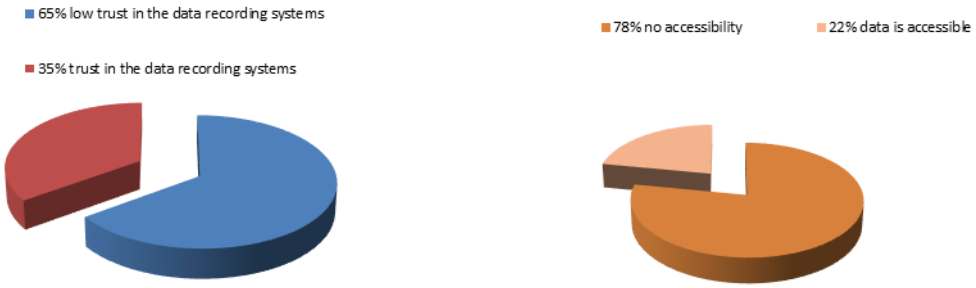

Figure 20: Data Recording System in National and Private Hospitals

(a. Quality of the Data & b. Acceptability to the Data)

c. Existence of Intellectual Property systems and its Effectiveness

Most of the responses received from Member States that participated in the survey shows that they do have intellectual property systems. However, there is irregularity in the responses that are given in some of the Member States. In Nigeria 29% of the sample stated that they do not have an intellectual property system; the case is similar in Cameroon (27.7%), Rwanda (28.5%), Sudan (50%), Ethiopia (34.7%), and Tanzania (50%).

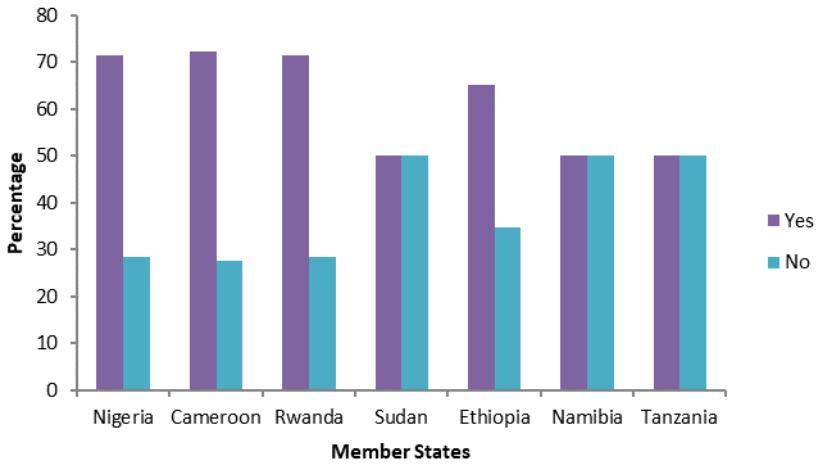

Figure 21: Informed Scientist on the Existence of IP systems in Some Selected Member States

On system efficiency, most of the sample expressed that their country's system needs improvement and needs to be more efficient. 10% of the sample was satisfied with the level of protection of research output in their respective Member States; 39% saw the system as adequate; 14% clearly stated that there is no protection of intellectual property; while the rest 37% were uncertain and could not answer.

d. Good Clinical Practice

The opinions on the existence of good Clinical practice in Member States re mostly fair; on the other hand, there was a disagreement between the sample within the same Member State where in Senegal, 14% saw it as good, 72% considered it to be fair and the rest consider it to be poor. In Nigeria, 75% of the samples considered good clinical practice as fair while 18% considered it as poor. Figure (22) explains better the irregularities within these same Member State.

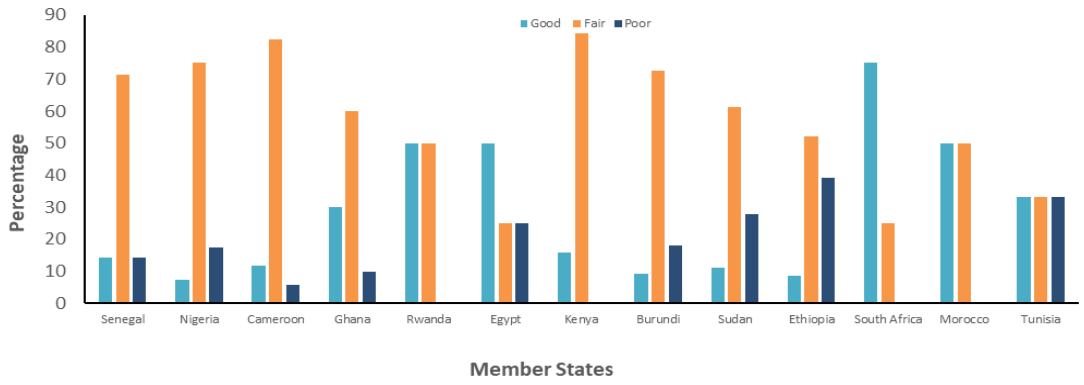

Figure 22: Distribution of Good Clinical Practice in Some Selected Member States

4.2.3.2 Fund Allocation to Clinical Research

Out of the 28 Member States in the sample, 57% said that fund allocation to clinical research is insufficient, while (25%) said that there is no fund allocation in their respective countries. On the level of individual scientists who participated in this survey, 77.5% indicated either the funds were insufficient or no fund had been allocated to clinical research.

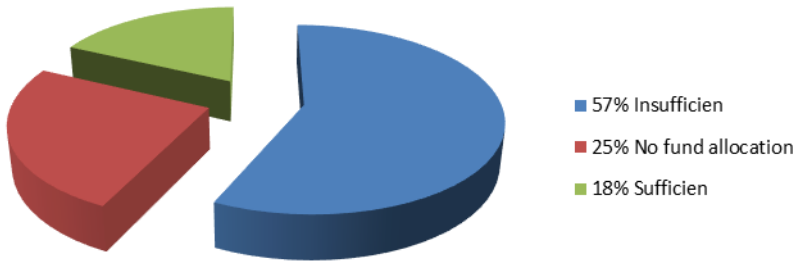

Figure 23: Fund Allocation to Clinical Research

This is confirmed by analysing the interest of Governments on clinical research 66.5% (majority of the scientist) recognize that their governments do not prioritize clinical research. On the level of Member States, 25% of the participated Member States prioritized clinical research e.g. Senegal, Rwanda, Zambia, Libya, Tunisia, Algeria, Uganda and Democratic Republic of Congo. On another hand, it is worth mentioning that 25% of the sample size in Egypt and 50% of those from Republic of South Africa considered their countries as prioritizing clinical research.

In summary, 25% of responses said that clinical research is prioritized in their Member States (including the countries listed above). The output of the survey shows that this interest (in 25% of the Member States) has never been recognised as a financial investment. Whereas all the results show that Member States invest inadequately in clinical research except for Senegal. On this issue of investment in clinical research, about 69.9% of the participants show that their respective Member States invest less in clinical Research i.e. government investment in the sector was hardly recognised nor appreciated by the participants in the questionnaire. Private sector investment in clinical research was analysed where 60.3% of the participants (individual level) denied that any investment was being made by the private sector in clinical research. While at the national level, 29% affirmed the presence of investment from the private sector in clinical research.

This low level of fund allocation to clinical research may result from the fact that most of the Member States do not invite scientists to participate in their budget development processes, though this is not the case in the Republic of South Africa.

On retaining African researchers in their respective Member States, the sample shows that only 34.5% of African scientists prefer to work in their respective Member States while 10.5% showed interest to work in Africa, that is, in another country other than their respective Member State, while 55% of the sample showed interest to work outside the Continent.

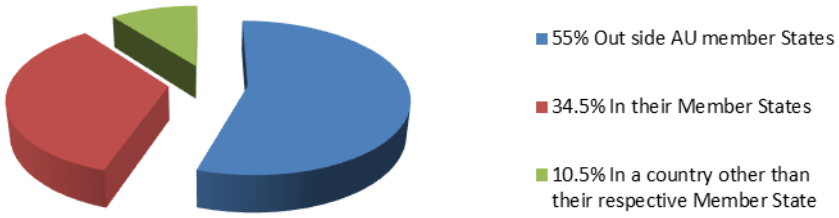

Figure 24: Retaining of African Scientists in their Respective Member States

This could be further established when reflecting on the recognition that is given to scientists for their scientific findings, where 80% of the sample participants said that scientific findings are not celebrated in their respective Member States and 65% said that there is no financial reward system in the African Union Member States.

In addition, the low wages and income could be the causative factor for 55.5% of health researchers choosing not to work in their countries. The survey shows that 91.4% of the participant scientists receive low income and that they are poorly paid, with the exception of South Africa and Tunisia that have disparity levels of 25%, 33% respectively.

4.2.3.3 Shortfall in Technical & Professional Competence

This section of the questionnaire was to examine the level of technical and professional competencies in each Member States and the continent at large on one hand; while on the other hand to identify the root cause of the challenges Africa is facing in its scientific and knowledge production from the angle of technical and professional competence. This was achieved by examining the quality of the African graduate researcher's capabilities and output; infrastructure within Africa's learning and research institutions along with the knowledge and databank in individual Member States and the continent at large.

On the knowledge and data banks in individual Member States and the continent at large, 58.4% of the sample agreed that there is a considerable effort by individuals to share their data and knowledge within their scientific communities. This was however disadvantaged by lack of networking and platforms as only 28.5% (i.e. 8 Member States) that responded to the questionnaire had active networks and platforms to boost interaction among scientists. On the other hand, interdisciplinary cooperation within the same Member States was at an advantage where 71% of the individuals who participated in the questionnaire highlighted the existence of such cooperation.

The accessibility for publication and journals in Africa is limited, where 35.4% of the scientists have access to journals and publications; and the libraries are mostly furnished with old or outdated journal based on the opinion of 81.8% of the sample. This can also be seen when considering the lack of reference books and other materials where the percentage is 87.2%.

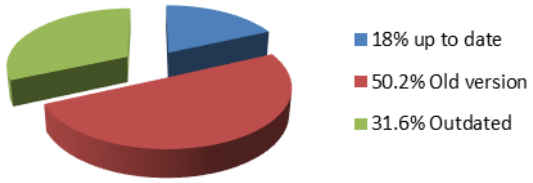

Figure 25: Libraries are Mostly Furnished with Old or Outdated Journal

E-libraries exist in 15 Member States (out of 28 Member States that responded to the questionnaire) but the e-libraries accessibility to world class and up to date scientific product was denied by 32.6% of the individuals that participated in the survey, while 35.4% are indecisive.

Research output was also investigated since this is the fruit that comes out of research and it presents the final product of education/knowledge sharing, data sharing and all the processes that are discussed in this context.

The level of trust the scientists have in research output produced in their Member States was inconclusive as there was a large contradiction between the participants (see Figure 26).

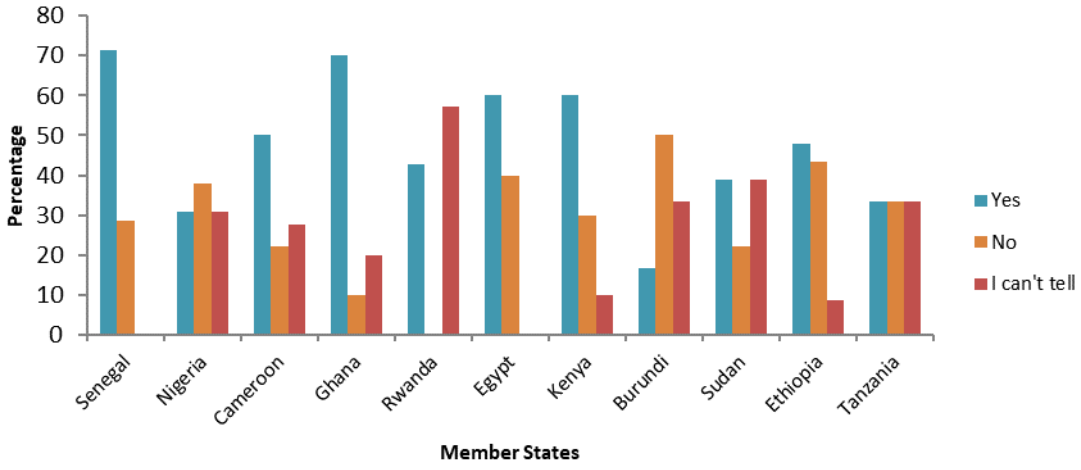

Figure 26: Trust in the Output of Research

Half (50.2%) of the participants see quality as the most important aspect in publishing their article, and it was found that 54.5% are interested in publishing articles in a quantitative manner.

N.B. the sum of the percentages is not up to 100% since the statements was presented in two different questions in the survey.

This was shown again when examining the responses received on valorisation of research standard in African Union Member States; where 33% of the respondents refused to give an answer; 30% had no answers (could not tell); 12% said that research standards are compromised; and 24% said that there was no compromise of research standards (Figure 27).

This could be attributed to poor payment of the researchers which makes them more interested in promotion and career advancement to acquire better pay, recalling that 70% of the sample agreed that their salary/payment was very low and only 22.5% said that their salary is ideal.

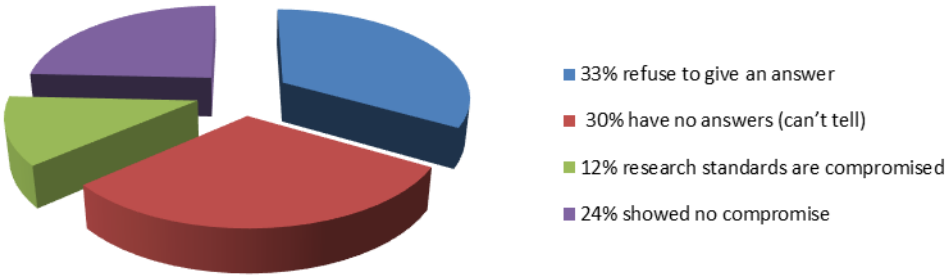

Figure 27: Valorisation of Research Standard in African Union Member States

Considering training and capacity building for African scientists in Member States, the results show that 40% of participants are not trained on new research methods while 27.8% declined to respond.

Since education is a process and its product are graduates, and from these graduates Africa builds its researchers' community, in other words, the more Africa has high quality graduates, the greater the possibilities of having pioneer researchers that contribute to scientific knowledge and to their nation's development. The questionnaire investigated the quality of the existing curricula in the learning institutions, where 23.9% of the participants agreed that the existing curricula is updated while 76.1% declined and saw the curricula as outdated. Furthermore, the low availability and/or absence of mentorship is a major reason that may contribute significantly to the low quality of African graduates; 78% of the sample agreed that mentors and research teams' leaders rarely allocate time to build their supervisees' capacities. This weakness in mentorship is worsened if we considered the authoritative relationship between lecturers/heads/supervisors over students. This authoritative relationship was confirmed by 73.7% of the sample.

It is undeniable that having adequate laboratory equipment and experiment materials is the backbone for conducting an experiment; building the capacity of a learner, and ultimately to conduct any meaningful research. In this aspect, the responses received from the majority of Member States that participated in the survey showed gross inadequacy in the laboratory infrastructure and materials necessary for conducting clinical research. This was the exact conclusion received from the scientists who participated in the survey, where 88.5% said that the laboratory equipment and materials available in their laboratories are inadequate for performing research.

On the contrary, the survey shows that African Students are considered to be creative and do have innovative ideas which was agreed by 63% of the sample while their talents were

confirmed by the agreement of 62.7%. However, most of the responses on the quality of the African graduates said that they are ***fair to poor*** (60.8% and 16.7% respectively), i.e. 77.5% of the responses see the quality of Africa's graduates as fair to poor, which could be considered as a reason for all the above-mentioned challenges and facts.

4.2.3.4 Public are Less Interested to Participate in Clinical Research and Clinical Trial

The participation of study participants and the public is mandatory for good clinical research,. Additionally, larger communities must be consulted and involved in the design, conduct and evaluation processes. Moreover, the clinical research should consider the cultural aspects of the targeted communities. In this regard, the survey evaluated the interest of the public to participate in clinical research and the findings are presented in this subsection.

There is a weak communication with the public on the potential impact of clinical research in improvement of health and lifestyle of Africans, where 32.1% of the sample said that the public is not informed while 67.5% said that they are inadequately or poorly informed.

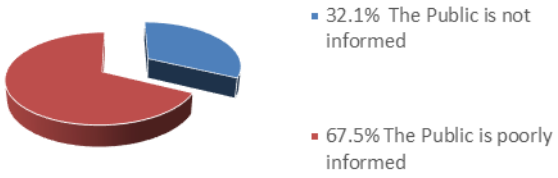

Figure 28: Public Awareness on the Impact of Clinical Research

The beneficiary needs (study participants and communities) are not well known to the scientists during the development of their experiments and research work. In this regard, 53% of the participants supported the argument as against 31.6% that were undecided.

On the issue of involving the study participants and carrying them along during the clinical research exercise, 62.2% said that study participants are sometimes carried along, while 22.5% said that study participants are always involved in the clinical research exercises. Finally, 15.3% of the sample said that study participants are not carried along during the process.

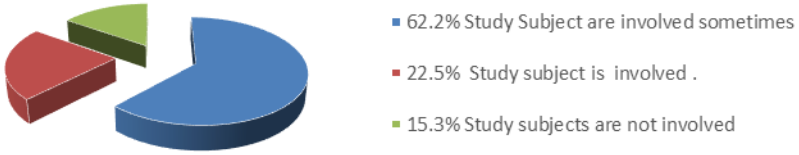

Figure 29: Study Participant's Involvement and Carrying Out during the Clinical Research Exercise

The above-mentioned has resulted in the fact that cultural values have stood as a hindrance to effective clinical research, as this was the opinion of 73.2% of the sample.

4.3 Conclusion – Inventory on Health Research and Research Translation Challenges in Africa and Way Forward

The AU-STRC conducted a two-phased thorough inventory on Health Research and Research Translation Challenges which was comprised of the Face-to-Face consultation with scientists; and e-survey on research translation in Africa. Comparatively, both inventories depict closely related or similar challenges that hinder the effective translation of research from bench to the bedside in Africa. These overarching challenges of research translation in Africa predominantly cut across four identified pillars which are the main obstacles to research translation. For Africa to achieve an efficient/comprehensive system of research translation, the need to overcome such obstacles is imperative by taking all the necessary measures and actions to ensure that research translation in Africa meets the world's best practices.

The first pillar which is the ***Poor / Vague Protocol on Clinical Research*** is primarily caused by reactive factors that weaken the collective system as well as strategies that should standardize operational ethics. During the in-depth interview it was indicated that the lack of awareness about the potentials of clinical research in addressing health challenges in Africa affects the dissemination of research out-put and in-put, therefore, guiding principles for clinical research with its existing legislation are incomprehensive. On the other hand, factually, the e-Survey points out the existence of ethical research guiding principles /systems across 90% of the 28 Member States covered by the survey.

However, there is an imbalance in the agreement of the functionality of the system within the same Member States where in Ethiopia 74% agreed and 26% opposed the existence of such guidelines. This encapsulates the incomprehensiveness of the existent ethical research guiding principles, the frail IP systems and the overall low trust on the capabilities of research output in addressing health challenges owing to the vague protocols on clinical research.

Furthermore, during the In-depth interviews of key participants, it was identified that funding which is one of the fundamental supportive mechanisms that boost research work is lacking in Africa. This has unleashed untold impacts on the motivational drive and enthusiasm of researchers, considering the fact that the relevance of research in national development is hardly recognized by the Governments and there is little or no interest at all to fund research in Member States. Categorically, the e-Survey shows that 57% of Member States have insufficient funds to carryout research. In this regard only 18% have sufficient funds while 25% have no fund allocation for research. This further depicts the lack of prioritization of clinical research across Member States where 66.5% of the participants of the e-survey indicated that their Governments do not prioritize clinical research; hence it has never been viewed as investment in the development of the country.

Among the factors affecting clinical research translation, the scientists who participated in the consultation noted that low income of researchers, lack of recognition and reward of scientific findings has forced Experts, Professors and Senior Scientists to resort to other income opportunities whereby knowledge transfer to build the capacities of supervisees is

adversely affected. This has contributed to the Shortfall in Technical/Professional Competencies. On the other hand, this challenge "Shortfall in Technical/Professional Competencies" is more tangibly expressed by the low quality of Africa's graduate; researcher's capabilities; research output; infrastructure within Africa's learning/research institutions; and the size of the knowledge and databanks in AU Member States.

Results from the e-Survey also reveal that journals and publications in the libraries that should benefit researchers are either old or outdated (this is the opinion of 81.8% of the sample from the survey). While, 32.6% indicate the e-libraries inaccessibility to world class and up to date scientific products. Following a combination of causative factors to the problem identified above, it is important to note that African students though considered being creative and having innovative ideas are graded as fair to poor by 77.5% of the responses.

In addition, it is undoubtedly true that the role of the public in the advancement and authentication of clinical research in Africa cannot be underemphasized. The fact remains as observed in the face-to-face consultation that the public are not well informed on the potentials of clinical research impact in the development of health and lifestyle of Africans. Therefore, the public are less interested in participating in clinical research and clinical trials. This inadequate communication of the potential impact of clinical research in development is revealed statistically where 32.1% of the sample said that the public is not informed, while 67.5% indicated that they are poorly informed. A major cause of the poor information of the public is tied to the existing cultural values as indicated by 73.2% of the samples.

In general, the root causes for the weak research translation in Africa could be linked to the need to have strong ethical practices, financial systems and more involvement of senior scientists in building the capacity and mentoring young / early career ones, while public participation and awareness is an important factor that is not less important than the above-mentioned.

Reference

1. Ahmed Hamdy et al (2017) Towards Women Participation in Scientific Research in Africa. AUSTRC Publication Series. www.austrc.org

Part 2: STRATEGIC ANALYSIS TO ACHIEVE RESEARCH TRANSLATION FROM THE BENCH TO THE BED SIDE IN AFRICA

SECTION I: STRATEGIES TO ACHIEVE EFFECTIVE RESEARCH TRANSLATION FROM BENCH TO BEDSIDE

The challenges hindering health research and effective research translation from the bench to the bed side were interrogated through an analysis of the output identified from the face to face consultations and the e-survey with scientists resulted in identified interventions for the four individual pillars that hinder the translation. Additionally, three cross cutting pillars were identified to enhance stakeholder interventions "Member States and Regional Economic Communities among others" in addressing the gaps so as to create an environment which will encourage ethical practices, mechanisms, policies and guidelines to disrupt the low support towards research translation in Africa. Thus, this will improve measures and actions aimed at enhancing the culture of best practices for effective implementation of research translation in health research.

Each intervention identified is interlinked with the other and has some commonalities that aim at achieving a comprehensive system for research translation in Africa, through proposed solutions to obtain desirable and achievable outcomes for each pillar to attain to the ultimate goal. Further a deeper analysis was conducted in respect of the individual and the cross-cutting interventions by highlighting the necessary sub-pillars; physical infrastructure; systems; mechanisms and the accompanying stakeholder analysis; along with the prospective partners.

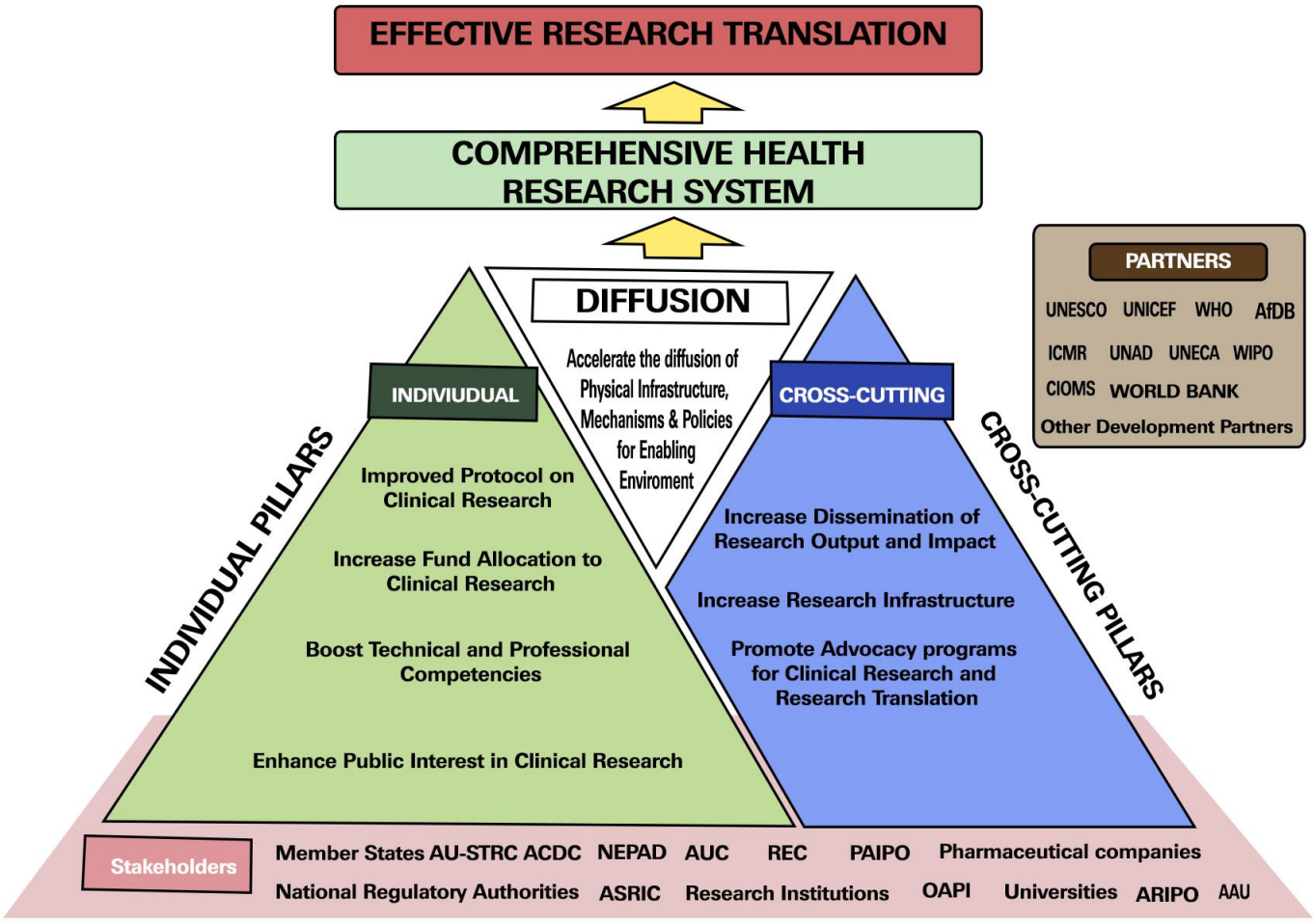

Figure 30: Achieving Effective Research Translation from the Bench to the Bed Side

1.0 INDIVIDUAL PILLARS

1.0.1 Intervention to poor/ vague protocol on Clinical Research- Pillar 1: Improved Protocol on Clinical Research

Improved Protocol on Clinical Research					
Sub-Pillar	**Physical Infrastructure**	**Systems**	**Mechanisms**	**Stakeholders**	**Partners**
Develop harmonized good clinical practice guidelines for AU Member States	• Establish AU Regulatory Council on Clinical Research • Upgrade existing laboratories and research facilities	• Formulate Continental framework/policy on clinical research • Review and harmonize existing national policies on clinical research	• Adopt continental frameworks and guidelines at national levels • Align guidelines with world best practices • Conduct periodic system reviews	• AUC-DHRST • AU-STRC • AUC-DSA • AU-CDC • Member States • National CDCs • National Regulatory Authorities • Research Institutions • Universities • Pharmaceutical companies	• WHO • ICMR • CIOMS • UNFPA • UNAIDS
Build Strong Ethical Approval Systems	• Establish National Independent Ethics Committees (IECs) • Establish Institutional Review Boards (IRBs) in National Universities and Research Institutions	• Establish Comprehensive Ethics Approval Processes • Review & Upgrade structures for ethical reviews	• Develop a standardized ethics guideline for clinical research • Develop Standard Operating Procedures for IECs and IRBs • Develop data management, handling and record keeping protocols	• Member States • Pharmaceutical companies • Universities • Research Institution • AU-STRC • AUC-DSA • AU-CDC	• WHO • ICMR

1.0.2 Intervention to limited/inadequate funds – Pillar 2: Increased Fund Allocation to Clinical Research

Increase Fund Allocation to Clinical Research					
Sub-Pillar	**Physical Infrastructure**	**Systems**	**Mechanisms**	**Stakeholders**	**Partners**
Increase Government budget for clinical research	• Establish Government committees on Clinical Research budgeting and monitoring • Set up parliamentary Committee on clinical research in Member State	• Formulate a continental framework/policy on clinical research funding within the context of Abuja declaration on health sector fund allocations (April, 2001 Abuja, Nigeria) • Review and harmonize existing national policies on clinical research funding • Budget quota allocation to clinical research within national Health care and R&D allocations	• Involve scientists in research budget development process • Improve transparency in research fund allocation • Ensure proper management of research funds • Setup advocacy and pressure groups • Increase the commitment of development partners to clinical research	• AUC-DHRST • AU-STRC • ASRIC • Member States • Universities/Research Institutions • National parliaments/ Parliamentarians • National ministries of Finance; Science and Technology and Health	• World Bank/IMF • AfDB • Pan Africa Parliament • Development partners
Promote Private Sector investment in clinical research in Africa	• Establish networks of industry and research institution • Establish public-private working groups	• Develop/Review national public- private partnership policies in clinical research • Formulate frameworks/guide-lines to strengthen mutual benefit of research output • Review & strengthen existing policies on cooperate social	• Build broad awareness on the benefit of public private partnerships • Promotion of research investment and sponsor ship culture • Establish/ promote linkages and cooperation between industry (private sector) and research (academia)	• Member States • Private Sector • NGOs and CSOs • AUC-DEA • AUC-DTI • ASRIC	• World Bank • AfDB • UNDP • UNECA • Development partners

		responsibilities to support clinical research			

1.0.3 Intervention to shortfall of Technical and Professional Competencies- Pillar 3: Boost Technical and Professional Competencies

Boost Technical and Professional Competencies					
Sub Pillar	**Physical Infrastructure**	**Systems**	**Mechanisms**	**Stakeholders**	**Partners**
Build critical mass of practitioners, (MDs, MSc, PhDs)	• Improve research facilities in universities/ institutions • Enhance the enrolment of students in Medical education	• Frameworks on the establishment, development and/or improvement of research facilities in universities/institutions • Strengthen continental and national frameworks on science education • Review existing enrolment policies for Medical education in higher institutions • Upgrade existing research & under/post graduate curricular • Upgrade remuneration schemes for Medical Scientists and practitioners	• Quality assurance guide line to audit existing facilities • Expand the capacity and enhance the quality of existing facilities • Institute higher education trust fund, scholarships, loans, awards, grants • Promote professional capacity building programs • Industrial attachment programs • Improve teaching methods in universities • Promote science education at lower levels of education • Develop annual assessment numeration guidelines for MDs and Medical Scientists/ Researchers in the AU Member States • Establishment of national fund on retaining MDs and	• Member States • Universities/ Research Institutions • AUC-DHRST • PAU • AfDB • National labour organizations	• AAU • UNESCO • UNICEF • Development partners

			Medical Scientists / Researchers		
Promote effective mentorship, knowledge exchange and brain circulation	• Establish platforms to promote mentorship and networks of African medical researchers • Strengthen existing networks of scientists such as AUNS • Build national data repositories and libraries	• Formulate national and continental policies to promote knowledge exchange and brain circulation • Formulate conducive policies for bilateral and multilateral collaborations & partnerships • Establish/review open data policies to promote access to data among universities in Africa and abroad	• Establish structured mentor mentee relationships for all MSc & PhD students • Form Technical/ Scientific networks • Provide incentives for intergenerational collaborations • Form networks of health researchers • Establish exchange programs for African students • Establish national travel grants for clinical research exchange • Promote Sister University programs • Establish and strengthen capacity of international offices in universities and research institutions • Development of comprehensive programme on university chairs and visiting professors	• AUC-HRST • AU-STRC • Universities/ Research Institutions • National professional bodies • Member States Ministries of Higher Education, Foreign Affairs and Health	• ICMR • AUNS • UNESCO • UNAIDS • Development partners
Promote professional associations & memberships	• Establish professional organizations&	• Strengthen professional regulatory bodies in all AU levels	• Develop statutes, codes of conduct &Ethics for professional bodies	• AU-STRC • AUC-DSA	• CIOMS • Development

	Associations at the national RECs, and AU levels		• Advocate for establishment of professional bodies • Build capacity of regulatory bodies • Encourage professional mobility	• AU-CDC • RECs • Member States • Registrar general departments in Member States • Universities/ Research Institutions	partners

1.0.4 Intervention to low Public Interest - Pillar 4 Enhance Public Interest in Clinical Research

Enhance Public Interest involvement in clinical research					
Sub Pillar	**Physical Infrastructure**	**Systems**	**Mechanisms**	**Stakeholders**	**Partners**
Encourage strong public participation in clinical research	• Establish advocacy groups and committees to advocate for public interest in clinical research • Establish community information centers within Universities/ Research Institutions and rural health care centers	• Formulate policies/ strategies on public engagement in clinical research	• Awareness campaigns on the potentials of clinical research impact for improved health & wellbeing • Build capacity of community leaders and communities to appreciate clinical research • Develop advocacy programs to address challenges in participating in clinical research • Develop the capacity of researchers to prioritize research areas to address public needs, interests considering community cultural values.	• Member States • Research Institutions and Universities • National councils on clinical research • National Ethics committees • Regulatory bodies • Community leaders • Medical practitioner Societies and associations • AUC-DSA • NGOs • National/ international pharmaceutical companies • AU-STRC • AU-CDC	• WHO • UNESCO • CIOMS • Development partners

Promote the protection of human participants in clinical research	• Establishment or strengthen IECs and IRBs in the AU Member States	• Develop guidelines to protect the rights and the wellbeing of research participants	• Increase adherence to protocols & guidelines • Increase public awareness on their rights in clinical research • Continual monitoring and auditing of clinical research and experiments • Develop a comprehensive guideline to strengthen communication between researchers, human participants, research sponsors and IECs/IRBs	• National Ethics committees • National food and drugs authorities • Medical practitioner Societies and associations • Community leaders • NGOs • National/ international pharmaceutical companies • AU-STRC • AUC-DSA • AU-CDC	• WHO • UNESCO • CIOMS • Development partners

2.0 CROSS-CUTTING PILLARS

2.0.1 Intervention to week Dissemination of Research Output - Pillar 5: Increase Dissemination of Research Output and Impact

Increase Dissemination of Research Output and Impact					
Sub Pillar	**Physical Infrastructure**	**Systems**	**Mechanisms**	**Stakeholders**	**Partners**
Strengthen/ improve Clinical Research output dissemination	• Establish an AU Journal on Health Research • Upgrade and align existing journals (in Member States & Regional level) with world best practices • Strengthen African Union network of sciences (AUNS)	• Establish strong channels of communication between governments and researchers • Build periodic reporting systems • Develop policy briefs on Clinical Research • Develop a robust partnership with Journalist and Media	• Capacity building modules and programs to enhance researchers experience in conducting research; writing skills (research proposal/ publication); resource mobilization; and mass communication • Promote innovation in health research • Promote publications in high quality journals	• Ministries of Science in the AU Member States • AU-STRC • AUC-DSA • AU-CDC • AUNS • ASRIC • National Journals and media agencies • National parliaments • Publishing Companies	• WHO • African Journals Online (AJOL)

			• Capacity building schemes for Journalist and Media on Clinical research • Information days on clinical research targeting government officials, parliamentarians, and the public at large		
Build strong IP systems that protect clinical research output	• Establishment/ Functionalization of the Pan African Intellectual Property Organization • Establish/ Strengthen national IP registration offices • Establishment of IP units in Research Intuitions and Universities	• Develop Clear IP protection policies for AU Member States. • Strengthening & harmonizing existing national policies on IP issues. • Build proper legal enforcement systems in all AU levels	• Build strong IP standards and registration processes • Develop guidelines for agreements & contracts • Develop guideline protocols to protect Africa's indigenous Knowledge and traditional medicine • Develop robust strategy to educate the public, Scientists and Researchers on IP related issues	• AUC-HRST • AU-STRC • AU- Legal Council • PAIPO • ARIPO • ASRIC • OAPI • Member States' IP offices and organizations • National Parliaments • Research Intuitions and Universities • Pharmaceutical companies	• WIPO • WHO

2.0.2 Intervention to weak/absence of Research Infrastructure -Pillar 6: Increase Research Infrastructure

Increase Research Infrastructure					
Sub-Pillar	**Physical Infrastructure**	**Systems**	**Mechanisms**	**Stakeholders**	**Partners**
Strengthen national health research institutions	• Existing Universities Polytechnics, Research Institutions and Centers	• Investment policy on clinical research infrastructure development • National strategy on the establishment of research infrastructure	• Increase fund allocation for research infrastructural development and improvement • Maximize the use of existing infrastructures	• National Universities and Research Institutions • Ministries of Finance; Science and technology; Higher	• World Bank • AfDB • Development partners

	• New research Universities Polytechnics, Research Institutions and Centers		• Virtual lab and laboratories networking • Joint Research project with pharmaceutical companies • Tax waivers on imported medical devices and manufacturing parts and equipment • Boost governments' commitment to research infrastructure funding development • Structure smart partnerships for health infrastructure development with relevant private institutions	Education and Health • PAU • AAU • pharmaceutical companies • NGOs	
Encourage private universities /higher education institutions	• Establish private universities /higher education institutions in predefined priority sectors	• Regulation on the establishment of private universities/higher education institutions • Standardization system for private universities/higher education institutions	• Provide incentives to attract more private sector investment in higher education • Curriculum guidelines and audit system • Strong Monitoring and evaluation system	• Ministries of Finance; Science and technology; Higher Education and Health • AAU • AUC-HRST • NEPAD Education hub	• World Bank • AfDB • UNESCO • Development partners

2.0.3 Intervention to inadequate Advocacy programs - Pillar 7: Promote Advocacy programs for Clinical Research and Research Translation

Develop Advocacy Program					
Sub-Pillar	**Physical Infrastructure**	**Systems**	**Mechanism**	**Stakeholders**	**Partners**
Develop advocacy programs to create more awareness on the importance of clinical research and research	• Establishment of the national advocacy board on clinical research and research translation	• Continental policy to publicize the benefit of clinical research and research translation • National policy on	• Utilizing network of media organizations at all levels of the AU, RECs & MS • Capacity building schemes for Journalist and Media	• AU-STRC • AU-CDC • AUC-DSA • National councils on clinical research	• WHO • UNESCO

translation		clinical research and research translation advocacy	on Clinical research • Establish advocacy groups and committees to advocate for clinical research • Awareness campaigns on the potentials of clinical research impact for improved health & wellbeing • Outreach programs to communities, Government officials and Parliamentarians	• Research Institutions and Universities • National Ethics committees • Regulatory bodies • Community leaders • Medical practitioner Societies and associations • NGOs • National/ international pharmaceutical companies	

Key for the Table

AAU	Association of African Universities	IRB	Institutional Review Board
AfDB	African Development Bank	MSc	Master of Science
AJOL	Africa Journal Online	NEPAD	New Partnership for Africa's Development
ARIPO	Africa Regional Intellectual Property Organization	NGO	Non-Governmental Organization
AU	African Union	OAPI	Organization Africaine de la Propriété Intellectuelle
AUC	African Union Commission	PAIPO	Pan African Intellectual Property Organization
AUNS	African Union Network of Sciences	PAU	Pan African University
AU-STRC	African Union- Scientific, Technical and Research Commission	PhD	Doctor of Philosophy
ASRIC	Africa Scientific, Research and innovation Council	R&D	Research and Development
CDC	Center for Disease Control	REC	Regional Economic Community
CIOMS	Council for International Organization of Medical Sciences	SMEs	Small and Medium Enterprise
DEA	Department of Economic Affairs	UNAIDS	United Nations Program on HIV/AIDS
DHRST	Department of Human Resource, Science and Technology	UNDP	United Nations Development Programme
DSA	Department of Social Affairs	UNESCO	United Nations Educational, Scientific and Cultural Organization
DTI	Department of Trade and Industry	UNFPA	United Nations Population Fund
ICMR	Indian Council of Medical Research	UNICEF	United Nations Children's Emergency Fund
IEC	Independent Ethics Committee	WHO	World Health Organization
IMF	International Monitory Fund	WIPO	World Intellectual Property organization
IP	Intellectual Property		

SECTION II: ROADMAP TO THE CREATION OF MECHANISMS TO SUPPORT RESEARCH TRANSLATION FROM BENCH TO THE BEDSIDE IN AFRICA

The creation of mechanisms to support research translation can be made realistic, building upon four (4) major key players that are triggered by some determinant forces that characterizes a reinforced operationalization of the **"Pillars"** to unleash effective ***Research Translation from Bench to Bedside.*** While ensuring that professional ethics are adhered to, both technical and professional competencies remain enhanced, along with a stable financial resource inflow and the interest of the public to participate in research is upheld, this will lead to the synchronization in clusters, the major forces to drive Research Translation from Bench to Bedside in Africa.

Nevertheless, building upon a strong foundational roadmap with a comprehensive guideline on research principles for each AU Member State, will improve protocols on clinical research holistically by addressing core areas such as harmonization of clinical research standardization for unique model adoptable and applicable across AU Member States; good clinical practice guideline that is tailored towards the enhancement of effective data handling & sampling protocols in Africa; and uninterrupted access to raw data and its transmission; as well as top notch / best practice model of ethical research guidelines that foster strong ethic approval systems and committees for a more comprehensive and precise process to get ethical clearance in any part of Africa, in addition to strong IP Systems.

It is undoubted that awareness of the public on the potentials of clinical research in the development of Africans' health and lifestyle will bring about increased participation of stakeholders in clinical research, especially harnessing the special interest of the private sector and industries to support clinical research work within the continent. Public-Private Partnership will leverage on this competitive advantage to increase their investment in clinical research leading to more funding allocation to clinical research in the continent. Consequently, clinical research in Africa will thrive with consistent and adequate funding.

Furthermore, there is an array of salient instrumental factors that serve as a springboard to boost technical and professional competencies in clinical research. These multidimensional forces are rooted in the awareness of the decision and policy makers on the potentials of clinical research in addressing pertinent health challenges, whereby the relevance of clinical research is recognized by some governments in the continent and they prioritize research funding as other development sectors bringing about a sharp decline of interest in hiring foreign expertise/firms to address their current health challenges. The encouragement for researchers is increased through the celebration of scientific findings along with financial rewards and provision of adequate research facilities.

Apparently, as a result of the recognition of the importance of clinical research and the increased encouragement and financial rewards for researchers, there is an increased passion for research which brings about a greater adherence to research standards and protocols by researchers, building up and mentoring young scientists effectively through the utilization of well-designed curriculum /training modules and capacity building programs that address the knowledge gaps and needs.

This effective mentorship in clinical research creates the existence of a robust relationship between supervisors and students where lecturers and heads of departments allow students to give their opinions and ideas, which enables them to develop more innovative and creative ideas from young scientists. This will in turn enhance the quality of applications for postgraduate grants and increase their chances of accessing more opportunities.

Building upon a well-structured and well-designed training module, targeted at addressing the knowledge gaps and needs, African researchers will be properly trained on new research methods and equipment which also covers a proper training on grants and proposal writing that enables postgraduate students to attract sponsorship and financial support. On the other hand, researchers' skills and knowledge are improved upon, making more researchers in the continent able to design their research and receive financial support in publishing its output, which results in increase in publication (qualitative & quantitative) of articles, thereby increasing the trust in research output from stakeholders.

The existence of updated proper curricula makes students to be properly educated, having enough access to practical problems, experiments, world class laboratories, well-furnished up-to-date libraries. In such teaching environment, the participation of students in research is enhanced and students easily understand research context which also increases the interest of young practitioners in research work, resulting in the production of high-quality graduates.

In the pursuance for enhanced cooperation and collaboration among researchers in Africa, platforms/networks to boost clinical research for better output based on expertise will not only enhance collaboration among researchers, but they will also be well informed about existing clinical challenges in different ramifications taking advantage of the increased inter-disciplinary collaboration, sufficient data and its dissemination /circulation. Therefore, strong cooperation and knowledge sharing among researchers in Africa is a realistic goal.

On another note, the dissemination of research output and impact, informs the public on the potentials of clinical research impact in the development of health and lifestyle of Africans, thereby encouraging stakeholders to prioritize their common interest building upon efficient/sufficient communication to surmount pertinent health issues while enhancing participation by stakeholders in clinical research. This increases public support for research and enables researchers to acquire complete database /information on the beneficiary needs more easily. Guidelines are hereby available to protect individuals' participation in clinical research with patients' consent. In so doing, the public will be more interested to participate in clinical research and clinical trials.

Summarily, the roadmap to the existence of effective mechanisms to support Research Translation from Bench to the Bedside in Africa is a broad spectrum of cognitive forces inter-dependently clustered to drive the needed actions and policies achievable through a carefully fragmented approach and application in the different spheres of development sectors across Africa. In addressing the pertinent need towards achieving a harmonized/standardized operating system in clinical research across AU Member States, the next chapter outlines a guideline for improved harmonized good clinical research practice adoptable across AU Member States that is in line with the world best practices.

Part 3: GUIDELINE FOR IMPROVED HARMONIZED GOOD CLINICAL RESEARCH PRACTICE FOR AU MEMBER STATES

GUIDELINE FOR IMPROVED HARMONIZED GOOD CLINICAL RESEARCH PRACTICE FOR AU MEMBER STATES

Motivation: The fundamental principle of Good Research Clinical Practice is that in research involving human participants, the interest of science and society should never take precedence over considerations related to the wellbeing of the study participants [1].

The current system of Good Research Clinical Practice has evolved partly in response to revelations of past experience in which research participants were grossly abused. Exposure of these incidents provided much of the momentum for the development of regulations and ethical guidelines on the protection of human research participants [2]. The unethical experiments that were conducted by Nazi scientists during the Second World War led to the formulation of the Nuremberg Code of research ethics in 1946 which since then, has influenced the international research ethics environment in several ways [3].

The Nuremberg trials led to the inclusion of a statement on voluntary participation in research in the Human Rights Charter of 1948 [4]. The trials also led to the Declaration of Helsinki by the World Medical Assembly in 1964, as well as the development of the International Ethics Guidelines for Biomedical Research Involving Human Participants (CIOMS Guidelines) of 1982 [1,5].

Africa has not been immune to human research abuses, with numerous reports having documented unethical experimentation and unethical clinical trials in Africa [2]. For instance, in Zimbabwe, during the early 1990s, Dr. Richard Gladwell McGown, a British anaesthetist working in Zimbabwe, was charged with conducting dangerous human experiments without the approval of the National Drugs Authority, and without the knowledge of his patients [6]. In Nigeria in 2001, 30 families sued the Pfizer pharmaceutical company over trials of trovafloxacin (Trovan), an antibiotic that was intended to treat Meningitis. The new drug was tested on nearly 200 children during a Meningitis outbreak comparing Trovan with the recommended drug Ceftriaxone. Unfortunately, children in the control arm allegedly received Ceftriaxone at an inadequate dose. Eleven children died, while some survivors suffered permanent brain damage and paralysis. Investigations later revealed that, the clinical trial had not been approved by a local research ethics committee, and the families concerned were not adequately informed that their children were research participants in a study employing the use of Trovan [7]. In South Africa, in 1999, Dr. Werner Bezwoda, tested the efficacy of breast cancer chemotherapy in women without; neither research ethics approval, nor individual informed consent [8]. Research misconduct in developing countries such as African countries is largely due to the existence of weak regulatory systems and lack of a harmonized good research clinical practice guidelines.

The above mentioned was more evident by considering the output of the inventory on health research and research translation challenges in Africa “Section IV Part 1 of this document” where the findings revealed that poor or vague protocol on clinical research, is a direct cause of inadequate or absent supportive mechanisms for research translation in AU Member States. In addition, poor protocols and absence of good research clinical practice guidelines lead to compromise of research standards. It therefore became evident that Africa needs a harmonized clinical research practice guideline that not only protect the rights of human

participants in clinical studies, but also ensures quality research output to influence practice, policy and further research.

This Guideline on Good Clinical Research Practice was developed considering best practices and guidelines from India, Brazil, European Union, World Medical Association in the Declaration of Helsinki, the Council for International Organization of Medical Sciences (CIOMS) and the existing guidelines in AU Member States. It is developed to guide all biomedical studies including research on pharmaceuticals, medical devices, medical radiation and imaging, surgical procedures, biological samples, as well as epidemiological, social, and psychological investigations. This Guideline was developed with the aim to improve/ harmonize Clinical Research Practice in African Union Member States. It is to serve as a model guideline to assist African Union Member States to develop their own guidelines for good clinical research practice.

The objective of this Guideline is to provide a harmonized standard across the African Union to facilitate the mutual acceptance of data from clinical studies by National Regulatory Authorities. It describes extensively ethical justification and scientific validation of biomedical research involving humans. It discusses the establishment and composition of independent ethics committees (IECs), informed consent process, confidentiality, and research involving vulnerable population. It also describes the responsibilities of the sponsor, investigator and monitor as well as the necessary research protocol and record keeping systems.

Finally, this guideline is a complement of existing laws, regulations, and practices in Member States and is developed to serve as a basis upon which countries can develop, evaluate or refine their own specific written guideline for good clinical practice.

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SECTION I: ETHICAL CONSIDERATIONS IN CLINICAL RESEARCH

1.0 Overview of Ethical Considerations in Clinical Research

Ethics are the norms or standards of conduct that distinguish between acceptable and unacceptable behaviour [1]. Ethics is an integral part of research involving humans because it greatly impacts the integrity of research study results as well as encourages an environment of trust, accountability, and mutual respect among researchers and the public. Because ethical considerations are so important in research, many professional associations and agencies such as the World Health Organization have adopted codes and policies that outline ethical behaviour to guide good clinical practice [2].

All research involving human participants must respect the three ethical principles of ***justice*** (fair distribution of risks, burden and benefits), ***respect for persons*** (obligation to treat participants as autonomous agents and protect those with diminished autonomy) and ***beneficence*** (to maximize benefits and to minimize harms and wrongs) to ensure greater protection for participants [3]. That leads to the result that all research involving human participants must be reviewed by a special committee (a research ethics committee) set up to safeguard the rights of the study participants as well as to ensure the authenticity of data generated from such studies.

A research ethics committee is a group of people appointed to review research protocols to formally assess if the research is ethical. This means the research must conform to recognized ethical standards. In other words, any clinical investigation involving a product regulated by the Food and Drug Administration/Authority (FDA) of any Member State must be reviewed and approved by an Independent Ethics Committee (IEC). An IEC has specific authority over the conduct of research under its jurisdiction. No clinical study may begin enrolling participants until it has received approval from the IEC.

The Independent Ethics Committee (IEC) is the conscience of the scientific research community, and the protector of human research participants. Its primary role is to safeguard the dignity, rights, safety and wellbeing of all actual and potential human participants within the research enterprise [4]. In this regard, it is of paramount importance for the IEC to be properly constituted and have all the resources that it requires to execute such an important duty.

Member States should endeavour to develop Independent Ethics committee (IEC) at national level that is independent, multi-disciplinary, multi-sectoral, and pluralistic in nature. The IEC will serve as the overall umbrella body for all other institutions involved in ethical review of research involving humans. This is to ensure the broadest possible coverage of protection for potential research participants and contribute to the highest attainable quality in the science and ethics of biomedical research. States should also promote, as appropriate, the establishment of Institutional Review Boards (IRBs) at institutional levels which will conduct scientific reviews to ensure research protocols make scientific sense and make sure all relevant documents are available for submission to the Independent Ethics Committee.

2.0 Ethical Research

Ethical Research is to be governed by the standards of conduct for scientific research. It is important to adhere to ethical principles in order to protect the dignity, rights and welfare of research participants [5].

Ethical principles underpin decision making in the research process and serve as a criterion upon which the Independent Ethics Committee arrive at a conclusion of whether research is ethical or not. These principles stem from the fundamental ethical principles of ***justice*** (fair distribution of risks, burden and benefits), ***respect for persons*** (obligation to treat participants as autonomous agents and protect those with diminished autonomy) and ***beneficence*** (to maximize benefits and to minimize harms and wrongs) to ensure greater protection for participants [3]. For research to be ethical, it must satisfy all the principles mentioned below;

a. Essentiality:

Refers to whether the research is considered to be absolutely essential after a due consideration of the existing scientific knowledge in the proposed area of research. Research must have social and/or scientific value to either participants, the population they represent, the local community, the nation and/or the world in order to justify the use of resources and the risk level that participants may be exposed to. Research should evaluate issues that lead to improvements in health and contribute meaningfully to knowledge. In addition to that, the research project has to demonstrate lasting impact, technology transfers where appropriate, and contribute to capacity building [6].

b. Scientific Validity:

The Scientific Validity of a research work is to be judged upon the fact that the research work has clear scientific objective(s); appropriate methodology; clear data analysis and dissemination plans; and endeavours to benefit humanity and/or the environment.

c. Fair selection of participants:

Research site, Communities and Participants in research should be selected through fair processes that are guided by the scientific objectives of the research. A clear guideline on recruitment of research participants should be declared before the recruitment process is started. This guideline should always exclude participation of people that are at excessively increased risk of harm. These include “Children; pregnant women; socially, culturally, economically, politically, educationally, physically and psychologically disadvantaged groups; and groups with constrained autonomy and other vulnerable populations”. However, in very rare/limited cases, these groups may be included in the research work as a recruit in case the research is intended to improve their health and wellbeing.

d. Respect for Potential and Enrolled Participants:

Respect entails that participants must be treated as partners in the research enterprise with every opportunity taken to inform them of the progress of the research and any new findings that may have potential impact on their health and wellbeing, and on their continued participation in the research. It also entails protection of the welfare of research participants.

This means that the process of research must be carefully monitored to ensure that participants are not exposed to excessive risks and all adverse events are examined in detail and promptly. Such adverse events must also be reported to the National Independent Ethic Committee and efforts should be made to prevent future occurrences. Full medical care must be provided to participants who have suffered such adverse events and where warranted compensations paid.

The requirement to respect both enrolled and potential participants means that researchers should engage with communities where research is being conducted whenever this is appropriate. In certain instances, community consultation or assent may have to precede research activities in order to engender community buy-in and to respect the socio-cultural values of the community and its institutions. It may also be necessary to inform the community from time to time about the progress of the research, pertinent findings that may influence their health and wellbeing, and the outcome of the research [7].

e. Non-Exploitation:

The research design and implementation plans must satisfy the principle of non-exploitation by ensuring that participants irrespective of their social status or educational level, should be made aware of all the possible dangers that may arise during the research so that they are well informed on all the physical and psychological risks as well as moral implications of the research whether to themselves or others, including those yet unborn. Consequently, the research should include a mechanism for compensation for the human participants either through insurance cover or by any other appropriate means.

f. Accountability and Transparency:

The research or experiment should be conducted in a fair, honest, impartial, and transparent manner after full disclosure is made by those associated with the research or experiment of each aspect of their interest in the research, and any conflict of interest that may exist. Full and complete records of the research should be retained for such reasonable period as may be prescribed or considered necessary for the purposes of post-research monitoring, evaluation of the research, conducting further research, and scrutiny by appropriate legal and administrative authority, if necessary.

Ethical research should maintain trust in the researcher(s)-participant(s) relationship(s). This requires that there is transparency including clear description of goals and risks, considerations for sharing financial benefits of research, determination of social value, creative approaches for effective representations and involvement of researchers and communities. This trust principle encourages the engagement of communities, respect for socio-cultural values, relevant and timely feedback to communities [7].

g. Minimizing Risk and Maximizing benefits:

The research team is to conduct risk assessment studies where risk benefit analysis is to be part of their research proposal. Not only that but also the researchers need to ensure that research procedures are consistent with internationally recognized research design; using procedures that are already in existence whenever possible; and/or do not expose the participants to undue risk.

Furthermore, due care and caution should be taken at all stages of the research and experiment to ensure that the research participants and those affected by it including the community are put to the minimum risk, suffer from no known irreversible adverse effects, and generally, benefit from the research or experiment. There should be a plan for interim reviews to detect whether any intervention arm (active or control) is associated with increased risks, so that undue harms are avoided by stopping the research. In addition, for research to be ethical, the design, conduct, and reporting procedures should be in accordance with the principles of good clinical and laboratory practices.

h. Professional Competence:

Research should be conducted by competent and qualified persons who act with total integrity and impartiality and who have been made aware of the ethical considerations to be borne in mind in respect of such research or experiment.

i. Protection of Research Stakeholders' Intellectual Rights:

The interest of participants, researchers, sponsors and communities must be protected and must be taken into consideration and adequately protected and compensated, particularly where research leads to tangible or intangible benefits. Satisfactory parameter(s) that shall determine sharing of commercial and other benefits should be clearly articulated and where indicated, benefit sharing agreements, materials transfer agreements, patent rights, intellectual property and royalties' distribution agreements should be signed before initiation of research.

j. Informative Public:

The research findings should be brought into the public domain so that its results are generally made known through scientific and other publications. This would help in consolidating the scientific knowledge base of the field being studied and would prevent undue replication of studies which poses risks to some participants.

k. Observing Good Clinical and Laboratory Practices:

International standards for designing, conducting, and reporting clinical trials that involve human participants should be observed. The compliance with these standards is an additional assurance that the rights, safety and well-being of trial participants are protected in a manner that is consistent with the highest ethical and scientific standards.

l. Observing National Laws:

All research projects to be conducted should observe the national laws, legislations, and regulations guide lines that are produced or published in each individual AU Member States.

m. Independent Review:

The Research programme should be scrutinized by an independent review, through a system of ethical review and oversight of such systems assures society that reasonable attempts have been made to minimize the potential impacts of these conflicting interests and ensure balanced judgements. On the other hand, an independent review should be conducted to examine the qualifications of the investigator, monitor and sponsor to make sure that they

have the requisite qualifications and experience to conduct the research according to ethical standards.

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SECTION II: INDEPENDENT ETHICS COMMITTEE

2.0 Introduction

Independent Ethics Committee (IEC) must be well structured with clear terms of reference for appointment, termination and replacement of its Members. Members must be capable of providing competent and thorough review of research protocols and other mandates assigned to them. This section describes the constitution and composition of the Independent Ethics Committee. It also describes the terms of reference and educational requirements of the IEC's members. Independent ethics committee should also have written standard operating procedures (SOPs) to ensure standardised best practices for health research, compliance with national and international ethical and regulatory requirements, consistent processes about ethical issues in health research, declarations regarding confidentiality and conflict of interest for each meeting.

2.1 Mandate of the Independent Ethics Committee

The mandate of the Independent Ethics Committee is to oversee the conduct of research involving human participants and to ensure that research is conducted in such a manner as to safeguard the rights, safety, and wellbeing of all human research participants. The committee fulfils its mandate by:

a. Reviewing the full study plan for a research study to ensure that the research meets the criteria specified in all regulatory guidelines concerned;
b. Confirming that the research plans do not expose participants to unreasonable risks;
c. Reviewing and approving proposed payments or other compensation to study participants;
d. Ensuring that human participant protections remain in force throughout the research by conducting continuing review of approved research. This continuing review is conducted at intervals appropriate to the degree of risk posed by each study, but not less frequently than once a year;
e. Considering adverse events, interim findings, and any recent literature that may be relevant to the research;
f. Assessing suspected or alleged protocol violations, complaints expressed by research participants, or violations of institutional policies;
g. Reviewing proposed changes to previously approved studies;
h. Suspending or terminating ongoing research that:
    - Is not being conducted in accordance with IRB[3] requirements;
    - Is associated with unexpected or serious harm to participants;

[3] Institutional Review Boards (IRBs)

Institutions engaged in research involving human subjects are encouraged to have their own IRBs to oversee research conducted within the institution or by the staff of the institution. On the other hand, IRBs is the advisor for researchers, sponsors, and human participants ;to conduct initial scientific reviews; and to help in filing the applications to the IEC for approval. The IRBs should be registered by the IEC and should follow the rules and protocols of the IEC.

- The IEC may also suspend or terminate research when additional information results in a change to the study's likely risks or benefits.

i. Granting approval where research proposals meet ethics standards and regulatory requirements.

2.2 Organogram of the Independent Ethics Committee

2.2.1 Structure of the Independent Ethics Committee

The committees shall be consisting of at least 5 members and/or as many members as possible to function effectively. The members of the committee to be appointed by the Director of Health Services (or by any relevant authority as may be identified at the Member State level); considering the following:

2.2.1.1 Constitution of the Independent Ethics Committee:

The membership of the Independent Ethics Committee must be multidisciplinary and multi-sectoral including scientists and non-scientists members. Scientific members may include researchers, physicians, psychologists, nurses, and other mental health professionals. Non-scientific members may have special knowledge of a certain population (pregnant women, children, or prisoners), as well as community members or representatives of patients' groups who can represent the cultural and moral values of study participants. Ideally, one or more members should have experience as study participants since there is growing recognition that knowledge gained through personal experience as a participant can supplement the professional understanding of illness and medical care.

There should be adequate representation of age, gender, community; etc. in the Committee to safeguard the interests and welfare of all sections of the community/society. Members should be aware of local, social and cultural norms, as this is the most important social control mechanism. If required, subject experts could be invited to offer their views.

Collectively, IEC members must have the qualifications and experience to review and evaluate the scientific, medical, behavioural, social, legal, and ethical aspects of a proposed study.

2.2.1.2 Composition of the Independent Ethics Committee:

The committee is to be composed of voting members and non-voting members as follows:

I. The Composition of the Voting Committee shall be as follows:

a. A Chairperson to be appointed by the Director of National Health Services (or by any relevant authorities as may be identified at the Member State level) in mature stage, consequent Chairperson to be elected from the IEC members by the Members of the committee;
b. One or two Basic medical scientists (preferably one pharmacologist) to be identified from various Research Institutes;
c. One or two Clinicians to be identified from various Research Institutes;
d. One Legal expert or retired judge;
e. One Social scientist / representative of non-governmental voluntary agency;

f. One Philosopher / Ethicist / Theologian;
g. One representative from the community;
h. Secretary of the IEC; and
i. Special appointment when the need arises

II. Non-Voting Members

The committee may invite individuals with competence in special areas (Independent Consultants) to assist in the review of issues that require expertise beyond or in addition to that of its members. These consultants are not voting members of the committee. However, when research involves vulnerable populations, individuals specializing in these areas must be voting members of and maintained on the committee roster.

III. Special Membership Appointment

Special considerations are to be given to certain studies especially those involving vulnerable people and when conflict of interest is declared. The composition of the committee can vary in the following cases:

a. Vulnerable Population:

When a proposed study involves vulnerable individuals or groups, as may be the case in research involving prisoners, Children, Adults with incapacity or illiterate persons, representatives of relevant advocacy groups shall be invited to meetings where such protocols will be reviewed. Members should receive training on health research review before they commence work. Those members should be considered as voting members.

b. Conflict of Interest:

No member may participate in the review of any project in which he or she has a conflict of interest, except to provide information requested by the committee.

An investigator may be a member of a committee. However, the investigator (or any other member) cannot participate in the review or approval of any research in which he or she has a current or potential conflict of interest. The investigator should be absent from the meeting room while the IEC discusses and votes on the research in which he or she has an interest.

2.2.1.3 Criteria for Appointment

The following criteria shall be used to appoint the Independent Ethics Committee members where applicable.

I. Chairperson of the IEC:

a. Chairperson to be appointed by the Director of National Health Services (or by any relevant authorities as may be identified at the Member State level) in muter stage the Chairperson to be elected from the IEC members by the Members of the committee;
b. A person with high standing in society;
c. Have at least 1-3 years' experience of serving on an ethics committee.

II. Secretary of the IEC:

a. Shall be a member of the committee and thus referred to as the Secretary;
b. Shall head the IEC secretariat;
c. Preferably be a medical professional;
d. Should have a recognized postgraduate degree in a health-related field; and
e. Should have domain specialty experience, clinical research and ethics knowledge, personal interest and capacity, and good communication skills.

III. Members of the IEC

a. Members will be appointed based on their qualification, experience in domain field, interest, ethical and/or scientific knowledge and expertise, as well as on their commitment and willingness to volunteer the necessary time and effort for the IEC;
b. Members must be persons of professional integrity with no known record of professional misconduct;
c. Medical scientists and clinicians should have post graduate qualifications; and
d. Conflicts of interest should be avoided while making appointments, but where unavoidable, there should be transparency with regard to such interests.

IV. Special appointment

This is when a proposed study involves vulnerable individuals or groups, as may be the case in research involving prisoners or illiterate persons, representatives of relevant advocacy groups should be invited to meetings where such protocols will be reviewed (2.2.1.2.III.a of part 3 of this document). Members should receive training on health research review before they commence work. The special appointee is considered to be a voting member and he/she should exercise the rules and privilege as any other Member of the IEC.

V. Conditions to be fulfilled by a member after appointment

Members to be appointed on the IEC will need to fulfil the following conditions:

a. Members must submit a recent signed CV;
b. Training certificates in Ethics and/ or Good Clinical Practice (GCP) if available (members must submit these within 6 months if not available at time of appointment).
c. Signing no objection form to publicize his/her full name, profession and affiliation
d. Signing the Confidentiality Agreement form
e. Maintain confidentiality regarding meetings, deliberations, research proposals, information on research participants and related matters.
f. Read, understand, accept and follow the Conflict of interest policy and sign the Conflict of interest agreement/form.

2.2.1.4 Tenure of Membership

The tenure of IEC will be for a continuous period of 3 years from the date of appointment, however in certain cases and if the need be the IEC members could be re-nominated for two consecutive tenures.

2.2.1.5 Resignation and Disqualification of Members

The following are the rules to be used in cases of Resignation and Disqualification:

I. Resignation:

A member may resign from membership by submitting a letter of resignation to the Chairperson with or without reasons for resignation. The resignation will become effective from the day it is accepted by the Chairperson and presented to the IEC regular meeting.

II. Disqualification for misconduct of an IEC member:

A member may be disqualified from his/her membership by voting two third majority of the IEC members in a specific meeting called for the purpose of disqualification of a membership.

II.1 Grounds for disqualification:

The Grounds for disqualification include but are not limited to:

a. Failure to attend three consecutive scheduled meetings without prior permission;
b. Failure to attend at least 20% of the Committee meetings in any given year;
c. Serious assault, verbal or physical, harassment, or threats to other IEC members;
d. Immoral, indecent or disgraceful conduct including disruptive behaviour at meetings;
e. Undeclared conflicts of interest including taking or giving bribes or any illegal gratification;
f. Theft, fraud, dishonesty, forgery, misappropriation or misuse of IEC funds, stores or property including electronic data, files, records and documents;
g. Disclosure of official information without permission;

II.2 Disqualification Procedure

The Disqualification procedure should be as follow:

a. The process will be initiated if the Chairperson or the Secretary receives a communication in writing (provided by an IEC member, the secretariat, the public, or any of the stakeholders) alleging misconduct by a member;
b. If the Chairperson is satisfied that a prima facie case exists, and that the matter is of grave significance where the integrity of the IEC could be questioned, the chairperson should suspend the membership of the concerned IEC member till final decision is to be taken. During the period of suspension, the concerned individual will not have any rights, privileges or responsibilities of an IEC member and will not perform any duties as IEC member;
c. The Chairperson shall call for a special meeting to discuss this issue. The meeting convened will follow the usual rules of quorum;
d. The allegation will be discussed at the IEC meeting and the member alleged of misconduct will be provided adequate opportunity to defend himself / herself;
e. The Chairperson with the approval of IEC members may appoint an investigation committee from the IEC and any relevant authority that to investigate the allegation;

f. The member would stand disqualified, if members present approve of disqualification by 2/3rd majority by voting members present at the meeting; and
g. The Chairperson will convey the disqualification to the concerned member through a written communication.

In all the above cases the Chairperson shall announce the vacant position for the recruitment of a new member within two days of the disqualification meeting.

In case the allegation of misconduct is to face the Chairperson, a temporary chair to be elected in accordance with article (2.2.2.2/ I), and He/she shall take all the above actions defined in the Disqualification procedure. The Disqualification of the Chair should be discussed on emergency meeting.

2.2.1.6 Appointment of New Members

In the case of new appointments during an existing session of the replacement of vacant seat that may result from:

a. A regular member completes his/ her tenure;
b. A regular member resigns before the tenure is completed;
c. A regular member ceases to be a member for any reason including death or disqualification; and
d. To fulfil the membership requirements.

The new members will be identified and appointed by the Director National Health Services in consultation with the Chairperson of the IEC and to be selected in accordance with the membership requirements.

2.2.1.7 Appointment of Independent Consultant

The Chairperson, the IEC Secretary or any Member may have to suggest to the IEC meeting the appointment of independent consultant to perform one task or another that to complement facilitate the work of IEC and to ensure its quality/timely attendance to its objectives and mandates, that may include validation and assessments of study protocols. An independent consultant is an expert in a specified field who gives advice, comments and suggestions upon review of study protocols. The secretariat is to ensure that the independent consultant has no affiliation to the sponsor, investigators proposing the research protocols; and to ensure that he/she signs the confidentiality and conflict of interest agreements.

The Independent consultant shall be invited to the IEC meeting when the need arises to provide additional information or clarifications that may be sought by the IEC members or chairperson. The Independent consultant is not to be in the meeting room during the voting and decision-making time.

2.2.1.8 Training of the Independent Ethics Committee (IEC) Members in Research Ethics

The IEC needs to ensure that its members are up-to-date in their knowledge of all the aspects that relate to its mandate and objectives. The following highlights the needed training for the

IEC members:

a. A new member of the IEC will be required to attend one meeting as an 'Observer' before being inducted as a member of the IEC.
b. The Secretary or an IEC member will provide introductory training in Research Ethics, Good Clinical Practice (GCP) and Standard Operating Procedures (SOPs) to the new member.
c. A newly inducted member should submit certificate of training within 6 months.
d. All members including Chairperson and Secretary will be encouraged to receive continuous training by participating in workshops, conferences and/ or re-training program related to research ethics, as a delegate or facilitator.
e. The IEC will conduct workshops on ethics in clinical research, GCP and SOPs from time to time to impart training and update the IEC Members and Institutional faculty members.
f. The IEC may nominate and / or sponsor the expenses of (as applicable) an IEC member or prospective members for attending conference, continuing education session workshop and/ or training program etc.

2.2.2 Functionality of the IEC

The IEC shall function in accordance with a term of reference (TOR) that govern its internal procedures that includes its regular sessions, extra-ordinary session, establishment of ad-hoc sub-committees, financial/procurement controls and also addressing any other aspects that to facilitate the work of the IEC. On the other hand, the Terms of Reference (TOR) of the IEC need to clearly highlight the responsibilities of its Chairperson, Secretary, and Members.

2.2.2.1 IEC Meetings

The IEC has to conduct a meeting on a regular basis once every month to attend to its objectives and mandates. In cases of emergency, the Chairperson or the IEC Secretary shall call for extraordinary session when the need arises.

I. Modes of Conduct of Meetings

The IEC meetings shall generally be held by face-to-face. At the discretion of the Chairperson, they may be held via audio conference, or video conferencing or any other electronic communication medium that allows the committee members to follow and contribute to the meeting discussions as they occur in real time. The IEC Chair shall decide on the medium used for each meeting, after consultation with the IEC members.

II. Quorum

A quorum of the IEC is the minimum number of voting members that must be in attendance at a meeting for the meeting to be regularly constituted. A quorum must be met for the committee to conduct its business legally.

a. There must be the presence of 3/4 of the ICE voting members in the meeting to have a quorum, i.e. a meeting can only commence once a quorum is obtained.
b. If at any time during the meeting the quorum is lost, the meeting must be concluded.

c. Members of the Secretariat and other experts or observers do not count towards the quorum.

III. Attendance

a. Committee meetings may only be attended by members, the Secretary and the Secretariat staff and such additional people as Independent Consultants (ICs) and/ or guests or observers permitted to be present for a particular meeting or a portion of it;
b. Committee members are responsible for attending the meetings they agree in advance to attend or, if they are unable to do so, for notifying the Secretariat as far in advance as possible to enable the Secretariat to arrange for alternate dates of the meeting if the required quorum is not obtained;
c. The responsibility of attending and participating in Committee meetings shall be borne equitably by all members and the Secretariat shall keep records of attendance;
d. At the invitation of the Chairperson, the Principal Investigator, Monitor or Sponsor may attend meetings at which the protocol will be reviewed for the purposes of offering additional information and clarifications requested by the Committee;
e. The Chairperson may invite additional members (Independent Consultants) to provide expert advice on special issues when the Chairperson considers that their expertise is needed for the review of a research protocol or for other matters before the Committee. When consulted on a research proposal, such experts may attend those portions of the meeting at which the proposal is being reviewed and participate in the discussion; and
f. In the interest of transparency and improving the wider understanding of the work of the Committee, the Chairperson may at his or her discretion, invite a limited number of individuals as observers to the Committee meetings. Observers may attend the entire meeting to which they have been invited but may not take part in discussions unless explicitly invited by the Chairperson to do so. Observers shall be requested to leave the meeting room during specific portions of the discussions and in the voting time.

IV. Meeting Confidentiality

a. The project documentation and the deliberations of the Committee are confidential and all Committee members are bound to respect such confidentiality;
b. All Independent Consultants (ICs) and observers invited to any Committee meeting must commit to maintain confidentiality regarding the Committee's work for each meeting that they are invited to attend; and
c. The experts and observers will sign and date the Confidentiality Agreement form.

V. Decision Making

a. The final decision on each protocol or issue discussed in the meeting shall be by voting. A majority vote is defined as 2/3rd of the members, present at the meeting and voting.

b. Decisions will include approval, disapproval, conditional approval, suspension or termination of an ongoing study.
c. The following will not vote at the meeting:
    - Member(s) of the committee who is/are listed as investigator(s) on a research proposal
    - An investigator or study team member invited for the meeting
    - An independent consultant invited for the meeting to provide specific opinion.
    - A guest or observer

VI. Extra-Ordinary Session

Any member of the IEC in consultation with Chairperson or the Secretary may call for an extra-ordinary session for any one or more of the following reasons:

a. Urgent issues (which, if not decided upon early could adversely affect or have adverse impact on patient safety, public safety or national economy etc.)
b. Occurrence of unexpected serious adverse event(s).
c. Other reasons, as deemed appropriate by the Secretary and/or the Chairperson.
d. The Secretariat will endeavour to contact each and every IEC member and inform about the date, time and venue of the meeting as well as the justification for calling for such meeting.
e. In case there is a allegation of misconduct against the chairperson or any other member of the IEC;
f. The quorum for such extra-ordinary session is 2/3 of the voting members.

2.2.2.2 Responsibility of the IEC Members

The following are the responsibilities of the Chairperson, Secretary, and other Members of the IEC.

I. IEC Chairperson Responsibility

The IEC Chairperson's responsibilities may include the following:

a. Preside over the proceedings of the IEC;
b. Oversee and follow-up the implementation of the decisions of the IEC;
c. Ensure scientific excellence, promote creativity and innovative research for all programs/projects supported by the IEC;
d. Ensure the smooth running of the ethic approval processes through the establishment of Institutional Review Boards (IRBs) and IRBs networks; and
e. Coordinate activities/ processes with other National IECs in African Union Member States.

In the absence of the Chairperson to chair any regular or extraordinary meeting, the meeting is to vote for the temporary chair on the meeting day; the Secretary shall not be voted as temporary chair.

In case of disqualification (for Health reasons or any other reasons presented in 2.2.1.5) of the Chairperson, the IEC is to conduct a special meeting to elect a new chairperson (definite Chairperson) to stand in the Chair position.

II. IEC Secretariat Responsibilities

The Secretariat shall be headed by the IEC Secretary and shall comprise of scientific officers and administrative staff responsible for maintaining records and other secretarial duties. The staff shall support the IEC Secretary in his/her duties to fulfil the function of the secretariat which may include the following:

a. Provide administrative and secretarial services to the IEC;
b. Manage the overall activities related to the implementation of the IEC programs in coordination with the IEC Chairperson;
c. Prepare and implement the budget of the IEC and carry out financial programming and resource mobilization in accordance with the IEC financial rules, policies and practice;
d. Establish Pan African platforms connecting institutions, networks, and other actors to strengthen synergies and scientific knowledge exchange;
e. Establish Institutional Review Boards (IRBs) and networks in national research institutions and universities;
f. Promote the establishment of strategic partnerships, and advance Africa's cooperation in clinical research;
g. All the staff of the Secretariat will sign confidentiality agreement which should be filed with the IEC; and
h. Perform any other functions to ensure the smooth running of the IEC.

III. IEC Members Responsibilities

The IEC members shall assist the IEC Chairperson and the Secretariat in performing their duties and need to attend to the following:

a. Adhere to all issues related to the confidentiality and maintain confidentiality regarding meetings, deliberations, research proposals, information on research participants and related matters;
b. Give proper advice that relate to the performance of IEC objectives and responsibilities;
c. Review, discuss and consider research Proposals submitted for evaluation;
d. Monitor Serious Adverse Event reports and recommend appropriate action(s);
e. Review the progress reports and monitor ongoing studies as appropriate;
f. Do onsite visit whenever needed;
g. Evaluate final reports and outcomes;
h. Maintain confidentiality of the documents and deliberations of IEC meetings;
i. Declare any conflict of interest in writing to the Chairperson, if any, at each meeting; and
j. Work collectively on the implementation of the decisions of the IEC.

SECTION III: STANDARD OPERATING PROCEDURES

3.0 Introduction

For smooth running of any national Independent Ethic Committee and to ensure that it attends to its mandate and objectives, Member States' relevant authorities and the national Independent Ethic Committee need to work together towards the development of a guideline on Standard Operating Procedures (SOP) which is a compilation of step-by-step instructions to help carry out routine operations of the IEC. On the other, the SOP is to achieve efficiency, quality output, and uniformity of performance while reducing miscommunication and failure to comply with good clinical practices and other national regulations [1, 2].

A general guide line was developed to assist Independent Ethics Committees in African Union Member States to develop their own Standard Operating Procedures that fit their specific contexts. Additionally, it is to serve as a basis upon which countries can evaluate or refine existing Standard Operating Procedures (SOPs) for Ethical Review. The Guideline covers operations of the Ethics Committee such as, management of submission of research protocols and related documents, review of study protocols and management of conflict of interest. It also describes the processes involved in site monitoring and post monitoring activities, participants' requests and complaints, ethics committee audit and record keeping.

3.1 Management of Submission of Research Study Protocols and Related Documents

Management of submission of research study protocols and related documents focuses on the processes involved in receiving study protocols for initial or continuing review. It also describes the communication procedures between the IECs and Principal Investigators (PIs) regarding approval of protocols.

Submission of research protocols is done by the Principal Investigator to the IEC Secretariat after initial authorization or approval from the Institutional Review Board (IRB) if any[4]. The protocol should include approval letters from the IRB, names of investigators and their CVs, names of participating institutions and/or sponsors, a complete study protocol that contains brief background and objectives of the study, methodology, questionnaire and individual informed consent document.

The secretariat is to ensure that the protocol includes all essential documents and check for required new information or amendment to existing ones.

3.2 Review of Research Protocols

Every research conducted using human participants or data, from human participants require review and approval from an Independent Ethics Committee (IEC) [3]. Some of such research includes studies of physiological and experimental interventions with drugs or

[4] In cases where there is no IRB in a particular institution, the IEC is advised to conduct the initial scientific reviews or to refer the case to another national institutional IRB.

devices among human populations. The review of research protocols by the Independent Ethics Committee are guided by ethical principles described in the guidelines for good clinical practice. The following protocols and reports are to be reviewed by the IEC: Research Study Protocols; Proposals involving Vulnerable Population; Resubmitted and Amended protocols; Continuing Review of Study Protocols; Review of Protocol Deviations/Violations; and Review of the Reports on Serious Adverse Events.

3.2.1 Research Study Protocols Review

Research study protocols submitted to the IEC are to be categorised into three groups namely, full board, expedited or exemption from review depending on the risks involved for prospective research participants. Where **Full Board review:** shall be categorized when new research protocols involving more than minimal risk, and /or vulnerable populations. **Expedited Review** if the study involves not more than minimum risk such as non-invasive procedures (application of Electrocardiogram, Blood pressure measurement) or involve data that have already been collected. Research on interventions in emergency situations or disaster management may also be reviewed with expedited process if they meet other criteria mentioned above. It is also to be considered when resubmitted documents with minor modifications previously approved through full board review by the IEC. While, **Exemption from Review** include research that does not involve live human participants or involve data already in the public domain. Examples of such research include but are not limited to audits of educational practices, research on microbes cultured in the laboratory or research on cadavers or death certificates with identifying personal data. The type of review will be determined by the decision at initial review.

3.2.1.1 Full Board Review

A full board review involves all members of the committee with or without independent consultants and representatives of special groups to be conducted when new research protocols involve more than minimal risk, and/or vulnerable populations.

- The Secretary/Chairperson appoints two or more primary reviewers comprising of a clinician and a non-technical person with expertise and experience in the related field of each study.
- The Secretariat will then send a cover letter and a package including the study assessment form, study submission application form and protocol with all related documents to the designated IEC Members requesting initial review.
- The protocol is to be reviewed by each member as per guidelines and the assessment form to standardize the review process. The duly signed and dated assessment form will be returned to the secretariat within a specified time period; agreed upon between the Secretariat and the reviewers.
- Final decision on the protocol shall be made by 2/3rd majority vote at a fully convened meeting and recorded as full approval, conditional approval or disapproval. All decisions in this regard (review decisions) should be made on the basis of specific reasons, which are communicated to the principal investigator in the letter of notification.

- In case of a conditional approval, the committee will decide whether final decision should be taken by the secretary or full board.

3.2.1.2 Expedited Review of Research Study Protocols

Studies that carry not more than minimal risk fulfil criteria for expedited review except in the case of research involving vulnerable populations. This sub-section describes the procedures involved in the review of protocols that meet the criteria for expedited review.

- The Secretary, in consultation with the Chairperson will nominate two or more IEC members to review the protocol after establishing with appropriate checklists that the protocol satisfies all conditions for expedited review.
- The Secretary will discuss the comments of the reviewers with the Chairperson and a decision about the protocol will be taken if there are no queries.
- In case of queries, these will be communicated to the Principal Investigator and his replies shall be obtained before a final decision is reached.
- The final decision will be communicated to the Principal Investigator and then to the rest of IEC members at a full board meeting.
- In case a protocol is disapproved, the decision will be communicated to the Principal Investigator with reasons and justifications.
- Whenever deemed fit by the reviewers, the Secretary or Chairperson, protocols submitted for expedited review may be referred for full board review.
- The duration of expedited review shall be determined by the IEC.

3.2.1.3 Exemption from Ethics Review of Research Study Protocols

Any research not involving live human participants, but the data is already in the public domain or anonymized data was derived from participants qualify for exemption from IEC review [3].

- The secretariat to forward all protocols submitted for exemption from review by the Principal Investigator to the Secretary of the IEC.
- After determining that the protocol meets the criteria, the IEC Secretary to consult with the Chairperson for brief review of the project summary and make recommendations.
- The final decision will be communicated to the Principal Investigator and kept on record to be announced at the next full board meeting.
- In some circumstances however, research that meet exemption criteria may need to be reviewed by the IEC due to demands from the publisher or the funding organization.

3.2.2 Review of Proposals Involving Vulnerable Populations

All protocols involving vulnerable populations should be reviewed in full Board meeting by the IEC. The review should ascertain the justification of the research and establish the fact that the research could not be performed among non-vulnerable population [4].

- The Secretary or the Chairperson to appoint two or more members of the IEC who have thorough understanding of the ethical review process and experience in the field of research to review such type of protocols. They (reviewers) should also be well versed with the potential harm or risk of such population participating in the study. The review must address all points to be considered in the checklists for different vulnerable populations.
- The secretariat to provide a suitable checklist to the investigator depending on the type of participants and provide appropriate reference materials relevant to vulnerable populations upon request.
- Reviewers shall review the protocol with the informed consent document or assent form as per the IEC standard operating procedures and provide their comments on the assessment form.
- IEC members to discuss these comments at a full board meeting and arrive at a decision which is to be communicated to the Principal Investigator.
- The IEC's approval should clearly state that if the vulnerability of the study participants changes for example in the case of an unconscious person regaining consciousness or a person with mental disorder regaining insight, the participant should be re-consented.

3.2.3 Review of Resubmitted and Amended Protocols

Resubmitted protocols are protocols and related documents that have been resubmitted with clarifications or replies to queries sought by the IEC at initial review, while amended protocols are previously approved protocols that have undergone some modifications or changes.

Resubmitted protocols are reviewed according to the IEC decision at the time of the initial review. On the other hand, the Chairperson or Secretary would recommend a full board review if an amended protocol is related to safety or data capture, and expedited review if the amendment is of administrative nature.

The secretariat upon receiving the revised protocol or documents will verify if all queries have been answered and all clarifications provided as requested before forwarding to the Chairperson, Secretary or IEC members according the decision at initial review.

The IEC members, Secretary or Chairperson will refer to the query letter to serve as a guide and to determine if all queries have been responded to. Whichever decision is taken regarding the review, due procedures will be followed as per the SOP and the Principal Investigator informed through writing.

In case of protocol amendment, the secretariat shall receive and check for completeness of all required documents and notify the Secretary. After review of the materials, the Chairperson or Secretary will determine whether the protocol requires a full board review or expedited review. A full board decision will be required if the amendment changes the risk-benefit assessment such as a change in the study design or dose of treatment. Appropriate documents will be distributed to the designated IEC members as per the decision regarding review. The reviewers will review the amended documents and note their comments in writing.

In case of full board review, final decision regarding the research project shall be reached by voting (2/3rd majority of the members present and voting). The secretariat shall communicate the IEC decision to the Principal Investigator in writing within a period determined by the IEC.

3.2.4 Continuing Review of Study Protocols

The IEC continues to review protocols after initial review to monitor the progress of the study and continuous protection and welfare of participants. The interval of this review is to be determined by the IEC at the time of the final approval considering a number of factors including: the duration of the study; the study design; degree of risk involved; and the vulnerability of study participants. The frequency of continuous review may increase based on serious adverse events and monitoring reports or safety concerns. The IEC is to review items that may include the number of recruitments, dropped outs and reasons for drop out in the occurrence of unexpected events or problems.

Prior to continuous review due date, the IEC Secretariat will send a reminder to the Principal Investigator who will in return submit his/her study documents for review. The form may undergo **the same procedure for the type of review deemed appropriate by the IEC Chairperson or the Secretary**. Decisions reached will be either "noted", "modification recommended" or "discontinuation of the project" which will be communicated to the Principal Investigator.

Failure on the part of the Principal Investigator to submit continuing review report after subsequent reminders will result in the matter being taken up to full board meeting for appropriate actions to be taken which could be sending further reminder letter; request for explanation for non-submission; or order to put new recruitments on hold.

3.2.5 Review of Protocol Deviations / Violations

Review of protocol deviations/violations describe action(s) to be taken by the IEC when investigators or trial sites fail to follow due procedures in the approved protocol, comply with mandated guidelines, or fail to respond to the IEC requests regarding statutory, ethical/scientific, or administrative matters.

A protocol deviation is any change, divergence, or departure from the study design or procedures of a research protocol that is under the investigator's control and that has not been approved by the IEC. Upon discovery, the Principal Investigator is responsible for reporting protocol deviations to the IEC using the standard reporting forms [5].

A protocol violation is a deviation from the IEC approved protocol that may affect the rights, safety or wellbeing of participants as well as the completeness, accuracy or reliability of the study data [6]. Protocol violations include but are not limited to the following;

- The deviation of the protocol has harmed or posed a substantive risk to the research participant as in the cases of administering a wrong treatment or incorrect dose, failure to withdraw participants who meet criteria for withdrawal, or giving an excluded concomitant medication to participants;

- The scientific integrity of the data collected is compromised as in enrolling participants who do not meet the eligibility criteria, failure to treat study participants as per the protocol or changing the protocol without prior IEC approval and inadvertent loss of samples or data;
- Wilful breach of human participant protection regulations, policies, or procedures by the investigator(s) including failure to obtain informed consent prior to initiation of study-related procedures, falsifying research or medical records, and performing tests or procedures beyond the individual's professional competence;
- Serious or continuing noncompliance with national, local or institutional human participant protection regulations, policies, or procedures in the form of working under an expired professional license or certification or refusal to follow good clinical practice guidelines and IEC regulations; and
- Inconsistency with medical, and ethical principles, for example; a breach of confidentiality or inadequate informed consent procedure.

Protocol deviation or violation may be detected either by the Principal Investigator, sponsor, contract-organization or by the IEC members during monitoring at trial sites, or when scrutinizing periodic reports or any other communication received from investigators or sponsor. Similarly, the secretariat detects deviations from failure of investigators to comply with statutory requirements or failure to respond to requests from the IECs. The IEC could also receive notification from study participants, individuals approached for enrolment or independent persons.

The Principal Investigator would usually submit protocol deviation report if he/she detects a deviation or as requested by the IEC in situations where the deviation is detected by any other person(s).

The actions of the IEC regarding protocol deviation shall include request for written clarification from Principal Investigator or call for emergency full board meeting depending on the seriousness of the deviation where $2/3^{rd}$ majority vote will determine whether to reprimand the Principal Investigator, conduct audit of the trial, suspend the study till further information is available. Further actions could be to revoke approval, inform relevant authorities or terminate the study. These decisions will be taken based on the nature, seriousness and/or frequency of the deviation or violation in order to ensure that the safety and rights of the research participants are safeguarded. A signed notification letter will be sent to the Principal Investigator, Departmental/institutional Head(s) and relevant national authorities as required on a case by case basis.

3.2.6 Review of Serious Adverse Event (SAE) Reports

In general terms, Serious Adverse Event is any untoward medical occurrence associated with the use of a drug in humans, whether or not considered drug related Serious Adverse Event is any untoward medical occurrence. Therefore, an Adverse Event can be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a medicinal (investigational) product whether or not considered related to the medicinal (investigational) product (attribution of unrelated, unlikely, possible, probable, or definite). In other words, it can be defined as any untoward medical occurrence

that at any dose results in: death, life-threatening; study participant hospitalization or causes prolongation of existing hospitalization; significant disability, congenital anomaly/birth defect, or permanent impairment damage [7].

This sub-section describes procedures for the review of initial and follow-up reports of serious adverse events (SAE) for any study under the oversight of the Independent Ethic Committee (IEC). The IEC is to set up a serious adverse events sub-committee to review reports of this nature. Details of the sub-committee are expounded below.

3.2.6.1 Formation of Serious Adverse Event Subcommittee

A Serious Adverse Event (SAE) Subcommittee should be constituted within the IEC to review and evaluate the scientific, medical and ethical aspects of adverse event reports particularly institutions having a large number of SAE reports for review.

The Subcommittee will consist of members who collectively have the qualifications and experience in clinical studies involving human participants.

3.2.6.2 Composition of the SAE Subcommittee

Members of the SAE Subcommittee are to be appointed by the IEC Chairperson and it should be multidisciplinary and multi-sectoral and composed of at least 5 and at most 10 IEC members. The composition shall be as follows:

a. Head of the SAE Subcommittee
b. Executive Secretary (rapporteur) of the SAE Subcommittee
c. At least one member with post graduate qualification in the discipline of Medicine, Medical Pharmacology or any other relevant clinical specialties.
d. IEC Secretary (Ex-Officio member)
e. Legal expert of the IEC to provide opinion on the legal implication of adverse events.

For the SAE Subcommittee meeting, a quorum will consist of at least 4 members including pharmacologist/clinician, legal expert, secretary and Head/Acting head of the SAE subcommittee; the acting head is to be nominated by the Head of the SAE and to be approved by the members of the subcommittee.

3.2.6.3 Functions of the Head of the SAE Subcommittee

The Head of the SAE Subcommittee will be responsible for the following:

a. Conducting SAE subcommittee meetings and leading all discussions and deliberations pertinent to the review of adverse event reports; and
b. Signing the minutes of the SAE Subcommittee meetings.

3.2.6.4 Functions of the Executive Secretary of the SAE Subcommittee

The Executive Secretary of the SAE Subcommittee will be responsible for the following;

a. Schedule and organize the SAE Subcommittee meetings;
b. Prepare and maintain meeting agenda and minutes;
c. Prepare the communication letters related to the adverse event reports;

d. Communicate with IEC members, regulatory authorities and investigators in a timely manner;
e. Provide necessary administrative support for SAE Subcommittee related activities;
f. Ensure adherence of the SAE Subcommittee functioning as per SOPs.

3.2.6.5 Membership Requirements

a. The IEC Members will be appointed to the SAE Subcommittee if they show willingness and commitment in terms of time to perform the role and responsibility as SAE Subcommittee members. The members shall be appointed by the IEC Chairperson while the IEC members may suggest names of new members to be appointed;
b. The tenure of the SAE Subcommittee will be for a continuous period of two (2) years from the date of appointment;
c. An SAE Subcommittee member may resign from membership by submitting a letter of resignation to the IEC chairperson and copied to the Executive Secretary of the SAE Subcommittee with or without reasons; and
d. An SAE Subcommittee member may be disqualified from the SAE Subcommittee membership if the member fails to attend more than three regular consecutive SAE Subcommittee meetings without prior permission. The Head of the SAE Subcommittee will inform the IEC Chairperson, in writing, if a member has not attended more than three consecutive regular meetings of the SAE Subcommittee. The Chairperson will take up the issue of disqualification for discussion at the full board meeting and allow the concerned SAE Subcommittee member to state his reasons for unauthorized absence.

3.2.6.6 Receipt of On-site SAE Report

Initial onsite SAE report shall be submitted by the Principal Investigator within a day of its occurrence. This will be followed by a due analysis report submitted by the Principal Investigator and the sponsor within days specified by the IEC. Follow-up reports of all onsite to the SAE will also be submitted till the event is resolved.

The IEC secretariat is to receive and verify any SAE reports timely. Reports submitted after specified timelines will be considered as protocol violations and treated accordingly.

3.2.6.7 Review and Decision on SAE Reports

Serious adverse reports are first reviewed by the Executive Secretary of the SAE subcommittee who will in turn present it to the full board/SAE subcommittee. The SAE review focuses specially on relatedness to the clinical trial, medical management and financial compensation to be given to the research participants using applicable regulations and guidelines. If necessary, an emergency IEC meeting will be held to discuss financial compensation.

Decisions taken by the IEC will be communicated to the Principal Investigator requesting replies to all queries raised within stipulated days specified. Likewise, the IEC opinion

regarding relatedness, medical management and compensation to research related injury will be communicated to the licensing authority in case of regulatory clinical trials.

The investigator is further mandated to submit SAE reports occurring at other sites along with covering letters specifying the total number of reports, whether causality is related or not related. This report will be reviewed by the SAE's Executive Secretary to be discussed in the forthcoming scheduled meeting.

Following detailed review of all SAE reports and related documents, the IEC/SAE subcommittee may request additional information, suggest follow-up till events resolve, seek outside expertise opinion or provide recommendations regarding compensation for study related injury or death.

Final decisions of the IEC following full board meeting will include; suggest changes/ amendments in the protocol and related documents, suspend the study till additional information is available, suspend the study till amendments requested by the IEC are carried out, suspend enrolment of new participants, direct the Principal Investigator to inform participants already enrolled in the study about the serious adverse and re-consent regarding continuation in the research trial is to be submitted or the study to be terminated.

Communication from the IEC regarding suspension of any kind and re-consenting of research participants will be conveyed to the Principal Investigator through telephone, fax or email within 24 hours. This will be followed up with complete recommendations within specified days of the IEC meeting.

3.3 Management of Conflict of Interest

Conflict of interest is a set of conditions in which professional judgment concerning a primary interest like patient's welfare or the validity of research appears to be unduly influenced by a secondary interest like financial or non-financial (personal, academic or political) gain [8].

The avoidance of conflicts of interest is important to safeguard the quality and credibility of research ethics review.

The IEC Chairperson ensures that there is no conflict of interest in the ethics review process. Members who have conflict of interest are to disclose their interest and be absent from the meeting where the particular protocol is being revised.

In the event that the Chairperson declares conflict of interest for a particular project, this should be so declared and handled as such and an acting Chair appointed for discussion on such a project as per article (2.2.2.2/ I).

3.4 Management of Premature Termination / Suspension / Discontinuation of a Study

Protocols may be terminated/suspended/discontinued at the recommendation of the IEC, Principal Investigator, Sponsor, Regulator or other authorized bodies wherein participant enrolment and follow-up are discontinued before the scheduled end of the study. The IEC may revoke approval and recommend to permanently stop all activities in a previously approved research protocol. The decision to prematurely terminate/suspend/ discontinue a

study may result from protocol non-compliance/violation, occurrence of unexpected SAEs, Zero accrual for 1-2 years or long-term low accrual. While suspended protocols remain open and require continuing review, terminated protocols are considered closed and no longer require continuing review. On the other hand, a Principal Investigator/ Sponsor may put a previously approved research on hold when considered appropriate to protect the rights or welfare of participants or when new safety information becomes available or evolved from the ongoing or similar research.

The process will be as follows: The IEC Secretariat shall receive a study protocol termination/suspension/discontinuation report that includes detailed reasons and covering letters to the IEC secretariat. The Secretariat will then inform the Chairperson regarding the receipt of the report. The Chairperson/ Secretary shall review the report and either call for an emergency meeting or discuss the report at the forthcoming regular full board IEC meeting. The person or the authority that filed the recommendation may be requested to provide additional information in case the report is unclear, otherwise, the Chairperson will sign the report in acknowledgement of the report. In case the suspension or termination is authorised by the IEC, regulatory authorities; the Principle Investigator; and the Head of the institution will be informed.

3.5 Review of Study Completion Reports

It is important to review study completion reports for studies approved by the Independent Ethics Committee (IEC) to ensure the study was conducted according to the protocol and guidelines and to ascertain that the rights of human participants were protected throughout the study.

The study completion report is expected from the Principle Investigator within one month of completion of the study. The Secretariat will receive the report which will be forwarded to the IEC Secretary. The Secretary will review the Study Completion Report, confirm that it is complete and present it at the next full board meeting. The chairperson will approve the report or ask for additional information following the discussion at the full board meeting.

The study shall be considered as closed if the decision by IEC Chair is “Noted” or “Approved” and the Principle Investigator notified accordingly by the Secretariat.

3.6 Waiver of Written / Verbal Informed Consent

The Independent Ethics Committee (IEC) may grant waiver for obtaining written or verbal informed consent to protocols that meet the following requirements;

a. The proposed research presents not more than minimal risk to participants. Example, a retrospective review of patient case records to determine the incidence of disease / recurrence of disease;

b. When it is impractical especially in the case of written consent. Example, conducting phone interviews (In case of telephone interview, verbal consent is mandatory);

c. When the only record linking the participant and the research would be the consent document and when there is a possible legal, social or economic risk to the participant entailed in signing the consent form;

d. Research on publicly available information, documents, or records;

e. Research on anonymous biological samples example; from deceased individuals; and

f. In emergency situations when no surrogate consent can be taken (Information about the intervention should be given to the patients whenever he / she gains consciousness or to relative / legal guardian when available.

The Principle Investigator will fill the waiver of consent application form and submit to the IEC secretariat together with the following documents:

a. A script for verbal consent - a verbal consent script provides all of the elements of consent in a more informal style. In addition, each participant should be provided with an information sheet that describes the study and gives contact names and numbers.

b. The interview schedule with details such as duration of the interview and statement to affirm that no questions will be asked that compromise a person's confidentiality or position.

c. A log book with a chart indicating the participants as participant 1, participant 2, etc. and a column indicating that verbal consent was given along with the date.

The IEC Secretariat will check the documents for completeness and forward to the Secretary.

The Secretary shall distribute the documents to the designated IEC members for review. The IEC reviewers will ensure that there are adequate mechanisms described in the protocol for protection of the identity of the research participants and maintaining of confidentiality of study data. The final decision concerning consent waiver is taken at a full board meeting and the decision communicated to the Principal Investigator in writing. The IEC will provide reasons for disapproval (as applicable).

3.7 Site Monitoring and Post-Monitoring Activities

Routine and for-cause on-site monitoring are conducted for studies approved by and under the oversight of the IEC. Decision to visit particular study sites is made during full board meetings at the time of approving the study.

Routine monitoring is done periodically within specified intervals while for-cause is done in response to events such as protocol violations/ deviations, SAE reports, high recruitment rate, complaints received from participants or other persons, failure to submit required documents and any other cause as decided by the IEC.

3.7.1 Before the Visit

Before the IEC embarks on a monitoring visit, the Chairperson will designate one or more IEC members (henceforth referred to as monitors) to conduct the monitoring specifying the

agenda. The final date will be decided on and communicated to the Principle Investigator (with a request to be available). The Secretariat will provide Monitors with relevant reference materials and documents like the Site Monitoring Visit Report Forms to document findings.

3.7.2 During the Visit

At the study site, the Monitor will check if the site is using the latest versions of the IEC approved protocol, informed consent documents and case record forms and also the log of delegation of study team.

The Monitor(s) will also observe the informed consent process, if possible, and check if investigational product accountability is adequately controlled and documented throughout the product flow including storage times, conditions and expiry dates.

It is also critical for the monitor to verify that the investigator follows the approved protocol and all approved amendment(s) in enrolling eligible participants, reporting SAEs appropriately and any other requirements on the checklist.

3.7.3 After the Visit

The Monitor will submit the completed Site Monitoring Visit Report Form to the IEC describing the findings of the monitoring visit. The IEC will discuss the findings of the monitoring process and take appropriate action by voting.

The final decision taken at the full board IEC meeting by the Chairperson will be conveyed to the Principal Investigator in writing.

3.8 Dealing with Participants' Requests and/or Complaints to the Institutional Ethics Committee

The IEC may receive requests and complains from human participants of studies, it is important that the IEC handles such requests confidentially, promptly and efficiently to sustain the trust of participants and the public at large.

Complaints received by the IEC Secretariat will be forwarded by the Secretary who will ascertain the details of the request/ complaint by examining any relevant documents and by interviewing the participant if necessary. The Secretary, in consultation with the Chairperson will initiate a process to address any injustice that may have occurred. The Chairperson will determine the best means to resolve the matter depending on the seriousness of the complaints. The final decision will be communicated to the research participant and the Principle Investigator through the Secretariat.

3.9 Ethics Committee Audit

Activities of the Independent Ethics Committee will be audited from time to time. The audit process applies to all the IEC members and the Secretariat.

On receipt of written or mailed communication regarding audit visit, the Secretary will inform the Chairperson and IEC members about the date and purpose of the audit. The IEC shall develop a checklist to include a step by step procedure before, during and after audit visits.

The IEC Secretariat shall ensure that all documents are kept in the right order for easy and quick access, while the Chairperson makes sure that IEC Members are available to answer questions during audit or inspection by national administrative and regulatory authorities.

The Secretary/ designated IEC member/ Secretariat shall make notes and review comments and recommendations of the auditor.

Upon receipt of Audit Report the Chairperson shall implement corrective and preventive measures and set the timelines for implementation of corrections as stated by the auditor.

3.10 Record Keeping and Archiving

One of the essential functions of the IEC is maintenance, archival and retrieval of all study files and study related documents. This sub-section entails processes in the preparation and maintenance of active study files, IEC administrative documents as well as archival and retrieval of documents.

3.10.1 Maintenance of the Active Study Files

A study master file is a file comprising all essential documents and correspondence related to the study. This should be created for all proposals at the time of initial submission to the IEC office. All related documents of the approved study will be gathered, classified appropriately and placed in the study master file: These could include;

a. All original research proposals reviewed and approved;
b. Reviewer's assessment forms;
c. Study approval letter;
d. Reviewed and approved consent documents;
e. Amendments and any other correspondence;
f. Study progress reports and interim reports;
g. Serious adverse event report forms submitted by investigators;
h. Any other relevant reports; and
i. IEC correspondence

Confidentiality of the contents of the files shall be strictly maintained with active files kept secured in a controlled accessed file cabinet.

3.10.2 Maintenance of the IEC Administrative Records

The IEC administrative records include;

a. IEC members' records
    i. Appointment and acceptance letters of each members;
    ii. Signed and dated confidentiality agreements;
    iii. Updated Curriculum vitae for the IEC Members and associated personals (hard copy or soft copy);
    iv. Training records for each IEC member; and
    v. Documentation of Members' resignations / terminations.
b. IEC membership roster - An IEC roster will be maintained which will contain:
    i. Names of IEC members
    ii. Age

iii. Gender
iv. Evidence of qualifications
v. Role on the IEC
vi. Status of affiliation to institution (e.g., unaffiliated or affiliated)
vii. Regular/ Alternate member to the IEC (if applicable)

c. IEC mandate
d. Correspondence related to changes in IEC membership with concerned authority
e. IEC attendance roster
f. Agenda and Minutes of IEC meetings
g. Standard operating procedures (SOPs)
h. Annual reports
i. Documents related to Workshops & conferences organized by IEC (Continuing education for members & staff)
j. SOP training and distribution logs

3.10.3 Maintenance of Closed Study Files

Once the study file is closed (following completion/ premature termination), the related study files will be shifted to the IEC Archival room for period determined by the IEC before being disposed of (such studies' files should be kept for a period not less than 5 years). Study files and administrative records will be made available to regulatory authorities and for audit, or any other purpose (e.g., research on SAEs) on request if authorized by the Secretary or Chairperson. It is also important to consider that the SAEs reports are to be kept for longer period as a reference document.

3.10.4 Accessibility / Retrieval

Study files and administrative records will be made available for audit on request if authorized by the Secretary/ Chairperson.

Representatives of regulatory authorities may have access at all times and a log book of retrieval of documents maintained.

3.10.5 Disposal of Closed Files and Copies of Protocols and Documents Submitted for IEC Review

At the end of the archival period, the closed files will be shredded and disposed of by authorized IEC personnel. Extra copies of protocols and documents submitted for the IEC review and any other extra copies will be shredded by authorized IEC personnel after the IEC approval in general meeting. A formal disposal log will be maintained, providing details of documents that to be disposed.

3.10.6 Record Keeping on Data Handling and Sampling

Records on data handling and sampling must be well documented to ensure accurate collection and efficient use of information collected on study participants. The IEC sees to it that researchers have access to relevant protocols to guide them on procedures for data collection, sampling and dissemination. All procedures for data handling and management should be thoroughly explained in research protocols submitted for IEC review, a guideline

protocol on data handling and record keeping is fully described in section IV of this document.

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SECTION IV: DATA HANDLING PROTOCOLS

4.0 Introduction

Data are the most important elements in clinical research. The ability to collect, store, analyze and retrieve information for use is crucial for conducting a successful clinical research. In order to produce accurate and valid data to support reliable conclusions, the procedure for sampling, handling and record keeping must be taken seriously.

Clinical data management (CDM) is the process of collecting, cleaning, and handling of participants' data in compliance with regulatory standards. The prime objective of CDM processes is to generate high-quality data for analysis and minimize the number of errors and missing data as much as possible [1]. For this objective to be realized, the research team must adopt best practices and adhere to protocols to ensure that data are complete, reliable, and processed correctly.

High-quality data should be absolutely accurate and suitable for statistical analysis as well as satisfy the protocol-specified parameters and requirements.

Whether the research involves the use of personal records and/or biological material, all processes including study design, data collection, analysis and data storage must be statistically sound and comply with appropriate guidelines and regulations.

4.1 Statistical Significance of Data

Statistics is the science of collecting, analyzing and making inference from data, while ***biostatistics*** is the application of statistics in the design, analysis, and interpretation of data in public health and medical research [2].

For a study to influence policies and practices, its results must be trustworthy and to be statistically significant. To achieve this, it is necessary to involve a qualified and experienced biostatistician from the planning stage and throughout the study to assist in designing a statistical model to help the sponsor and the Investigator in writing the protocol. The number of participants to be included, justification for the kind of data to be collected, data analysis and dissemination plan is determined in relation to the statistical model on which the protocol is based.

The biostatistician will assist the research team in designing the protocol to include appropriate study design, statistical analysis, and method of randomization. Randomization is one of the fundamental principles of experimental design which ensures that all participants have equal chance of being administered the intervention product.

4.2 Data Collection

Data collection refers to the process of recording information in a given research project. The aim of successful data collection should always be to uphold the integrity of the project, the institution and the researchers involved [3]. For data to be reliable, the process should occur consistently and systematically throughout the course of the project.

The design and objectives of a study determine the kind of data to be collected. Information and rationale regarding the type of sample should be included in the protocol stating the

amount and method of collection; type of analyses; mode and duration of storage and intended use(s). This should also be included in the informed consent form and thoroughly explained to potential study participants.

Clinical research data collection involves the collection of patients reported data/health information record such as questionnaire surveys and patient reported data, proxy/informant data, review of ambulatory or hospital medical records and collection of biomedical materials called bio-specimen [4].

4.2.1 Patient Reported Data/ Health Information Records

Personal data collected for research purposes usually include socio demographic characteristics (age, gender, place of residence, employment status etc.) present and past medical history (hypertension, diabetes, asthma, allergies etc.), lifestyle practices (diet, smoking, alcohol intake etc.) and/or hospital health records (date, history, diagnosis, lab results). These could be collected through questionnaire surveys/patient reported data, proxy informants or through the review of medical records.

In clinical research, data collection is done using the Case Record Form (CRF), which is a document designed in consonance with the protocol, to record data and other information on each trial participant. The Case record form should be designed in such a foreplace with e - Diariesrmat that allows accurate input, presentation, verification, audit and inspection of the recorded data. Data could be collected in printed or electronic form (eCRF) [1].

In the traditional printed format, data is collected by the investigator and recorded on paper CRFs. These responses will later be translated to a database by means of data entry. In Electronic CRF method, data is directly collected by the investigator into the clinical data management system. Electronic data collection reduces errors as discrepancies are resolved faster usually at the data collection site.

In some cases, the study participants are required to record data (e.g. daily symptoms) into a diary provided by the investigator. Patient diaries may be developed in either paper or electronic (e-Diaries) formats. Such e-Diaries generally take the form of a handheld device which enables the subject to enter the required data and transmits this data to a centralized server.

4.2.2 Biological Specimens

The collection, processing and storage of biological samples often involve complex processes and usually occur in repositories known as biological resource centers or bio-specimen resources.

Essential decisions made about biological sample collection such as type of sample, amount, type of laboratory analysis, affect the quality of the samples and the outcome of the study must involve qualified personnel with research and professional competency. Consideration must be given to the proper storage conditions to maintain sample quality until analyses are completed. All of these activities must be monitored and controlled by appropriate sample tracking and laboratory informatics systems. A comprehensive quality management system, standard guidelines and protocols are necessary to ensure that biological samples are of consistent quality and right for the intended analyses and the study goals [5].

4.2.2.1 Biological Specimens Context and Public Health Significance

Biological specimens such as blood, urine, saliva, and others are collected for a variety of reasons, either for routine patient monitoring and care or for clinical and epidemiological research studies. Many medical advances, including studies of heart disease, HIV/AIDS and cancer, have resulted from preliminary developmental studies that have relied on access to and proper use of appropriate bio-specimen [6, 7].

For molecular epidemiology studies, the ultimate success depends on reliable laboratory analyses of these specimens. In order for laboratory analyses to be reliable, the collection, processing and storage of specimens must be performed under strictly controlled procedures and under a well-planned quality assurance program in accordance with ethical guidelines described in this book.

4.2.2.2 Essential Considerations in Biological Specimen Collection

Several factors need to be considered prior to initiating a study that involves specimen collection. First and foremost, the goals of the study must be carefully outlined and this will determine the type of laboratory analysis needed to accomplish the study goals and consequently the type and amount/volume of specimen suitable for such analysis. A biostatistician is needed to determine the amount of specimen required to reach statistical significance. Additionally, it is necessary to consider frequency of collection, quality standards the specimens need to meet, the most effective and efficient way to store them bearing in mind the study goals and the strength of analytical techniques available. If specimens need to be shipped to distant locations for analysis, packaging and shipping protocols need to be validated to guarantee the stability and safety of the specimens and personnel who will handle them.

Other logistical issues such as additional data collection, proper coding, labelling and identification of types of storage vessels need to be resolved in addition to ensuring that all appropriate informed consent, privacy and other ethical, legal rules and regulations been reviewed and adhered to in the study planning.

Finally, it is important to consider costs of analyses and storage, especially if long-term storage will be necessary. Sources of funding and budget must be adequate for the processes involved if not, cheaper alternatives should be considered as much as possible without compromising the targeted standards.

4.2.2.3 Specimen Ethical, Legal and Policy Issues

In addition to technical considerations related to the physical quality of bio-specimen, multiple ethical, legal and policy issues also affect the ability of researchers to use these resources [8]. The ethical, legal and policy aspects of bio-specimen collection vary from place to place. IEC in consultation with National regulatory authorities need to develop regulations to govern their specific locations or study sites. Ethical considerations ensure proper and thorough informed-consent procedure and privacy protection of research participants while legal and policy issues regarding the use of bio-specimen describe data access, ownership and intellectual property protection [9]. Researchers must be abreast with these regulations governing research involving biomedical specimens and adhere to them.

I Ethical Issues in Bio-specimen Research

Ethical issues involving bio-specimen include informed consent process, privacy protection and confidentiality and participants' safety considerations. These issues must be addressed in order that the rights and safety of human participants are protected.

a. Informed Consent Process

The informed consent process is an integral part of clinical research and more so research involving biomedical specimen. Clinical research must not be conducted to exploit a particular group of people based on their vulnerability and reduced autonomy or low social status. The purpose and objectives of the study as well as risks, benefits and costs (if any), should be explained to participants including contacts of the study team for further interactions. Additionally, the kind of procedure, type of samples, amount and number of times the specimen will be taken should be carefully explained to the participants and their informed consent obtained and documented with a signed consent form. The language of the consent document must be simple to understand giving special considerations to cultural issues relevant to the informed consent process [6].

b. Privacy Protection and Confidentiality

Due to advances in genomic technologies, the public is becoming increasingly concerned about the protection of privacy. Potential study participants need to be assured that their identity will be protected, with respect to use of specimens they have donated and any resulting data. Stored data must be void of identifying information through appropriate de-identifying processes. Strict security systems should be put in place to restrict data access to only authorized persons. Specimen and data sharing must be regulated and careful done in a way that does not expose privacy information about donors. Applicable guidelines concerning privacy protection must be adhered to by all researchers.

c. Participants' Safety Consideration

Participants' safety concerns are of utmost priority in clinical research. As much as possible, risk involved in clinical studies should be kept at minimal level. Sponsors must recruit qualified professionals to collect biomedical specimen to ensure maximum safety. Compensation packages must be arranged for participants should unforeseen events occur such as serious adverse events and death.

II Legal and Policy Issues in Bio-specimen Research

As the use of biomedical specimen have become important in the conduct of clinical studies to advance medical research, so has legal and policy issues become necessary to protect all stakeholders and ensure integrity in the research process. Legal and policy issues in research involving biomedical specimen include ownership of bio-specimen and intellectual property issues [10].

a. Ownership of Bio-specimen

Ownership of bio-specimens is a global concern in recent times as study participants continue to demand and claim rights over their bio-specimen. National Laws and policies need to be formulated to address ownership of bio-specimen in consultation with IEC and National

regulatory authorities. Contract agreements should be signed between participants, investigators and sponsor institutions regarding data ownership. Also, researchers and regulatory bodies must ensure contract agreements are signed after data transfer or data sharing agreements are reached.

b. Intellectual Property of Bio-specimen Data

Inventions and data arising from research using annotated bio-specimens may have commercial value. Institutions should have clear intellectual property guidelines and use material transfer agreements to ensure that the sharing of specimens and data are well controlled. The final disposition of specimens and data should be understood before initiating a transfer.

4.2.2.4 Specimen Collection

In many molecular epidemiology studies, more than one specimen may be collected depending on the study goals. These may include, blood and blood fractions (plasma, serum, buffy coat, red blood cells), tissue (from surgery, autopsy, transplant), urine, saliva/buccal cells, placental tissue, meconium, cord blood, bone marrow and many others.

Each of these specimen types need to be collected, processed, and stored under conditions that preserve their stability with respect to the intended future analyses.

For molecular epidemiology studies, special consideration is given to those specimen types that can be collected most conveniently and efficiently, and at the lowest cost for large population-based studies. The most common specimen types collected are blood, tissue, urine and saliva.

Collection procedures vary from specimen to specimen and the intended analyses, but all procedures should be carefully designed and documented in a step by step manner. Pilot studies are necessary to validate new specimen collection methods and protocols. Procedures for the most common types of specimen are discussed in the next sub-sections.

a. Blood Collection

Blood specimen collection should be done by trained phlebotomists to avoid causing discomfort to study participants or compromising the quality or quantity of the sample. Relevant standard protocols should be followed.

An evacuated tube system with interchangeable glass or plastic tubes is commonly used to collect blood. The tubes, some with additives appropriate to a specific application, are differentiated by their colour-coded stoppers. Blood collection tubes should be drawn in a specific order to avoid cross- contamination of additives [5].

Blood should be collected uncoagulated (consisting of plasma, buffy coat and red blood cells) or coagulated depending on the intended analysis. The temperature, time period between collection, or removal from storage and subsequent processing may be important, depending on the intended analyses.

b. Tissue Collection

Tissue is part of the body of a living thing that is made of similar cells, like the cardiac tissue of the heart. Human body tissue makes up organs and other body parts. There are four main types of tissue: muscle, epithelial, connective and nervous tissues. Each is made of specialized cells that are grouped together according to structure and function.

Tissues must be collected under strict ethical and legal guidelines, and the collection of samples for research must never compromise the diagnostic integrity of a specimen. It is recommended for a trained pathologist to be involved in the procedure for obtaining tissue specimen during a surgical or autopsy procedure.

The time between tissue collection and stabilization depends on the intended use but the best approach is to collect, stabilize (freezing or fixing) and process tissue specimens as rapidly as possible. It is recommended that surgical or biopsy specimens be preserved within 1 hour (or less if possible) of excision [8]. Detailed records of the timing of events from excision to fixation or freezing should be kept. The appropriate method of preservation should be planned and specified in the study protocol and necessary preparations put in place before the start of the study.

Tissue samples usually collected for research include surgical samples, autopsy specimen and transplant tissue or organs.

Surgical samples may be collected as remnants from diagnostic procedures or resected specifically for research through biopsy with proper IEC approval. Depending on the intended use, specimens may be transported or frozen immediately. Samples requiring snap freezing can be frozen appropriately at the time of collection, otherwise, it is recommended that samples be transported in saline on wet ice to the repository or laboratory for additional processing.

Autopsy specimen should be collected and processed as soon as required as specimens may degrade quickly after death. Autopsy procedures may yield “normal” tissues (i.e. normal lung), or large quantities of a specimen that would not otherwise be available from surgical procedures. Tissue specimens collected at autopsy should be appropriately labelled as to the organ site, tissue type, and time of resection, and then immediately placed in a container of saline on wet ice for transport to the tissue repository for processing.

Transplant tissue and organs that are inappropriate for transplant may sometimes be made available for research. Often transplant tissue is of a higher quality than either surgical or autopsy specimens, due to the special efforts made to preserve the integrity of the transplant organs.

c. Urine Collection

Urine sample is a convenient specimen for a variety of studies because, many analytes, such as steroid hormones, pesticides and a wide variety of drugs and their metabolites, can be measured in urine. The collection can be performed under several conditions, depending on the study design and analytical goals [5].

Urine collections should be maintained on ice or refrigerated for the duration of the

collection. Collection vessels may range from 50 to 3000 ml. Preservatives may be added depending on the analyte to be measured and differ according to test methodologies, time delay, and transport conditions. Plans for preservation and appropriate preservatives should be determined and included in the study protocol before submission.

d. Saliva/Buccal Cell Collection

Saliva, with exfoliated buccal cells, is an excellent source of DNA for genetic studies. Self-collection of buccal cells is a safe, convenient method that can be used to reduce the cost of specimen collection. Several methods have been developed for collecting buccal cells, including swabs, cytobrushes and a mouthwash protocol. The mouthwash protocol has shown to yield DNA of good quality and quantity for genetic analyses when used in large population-based studies [11].

4.2.2.5 Preserving Specimen Stability during Collection

The elapsed time for collection, and between collection and stabilization, should be minimized, and the tissue temperature reduced as soon as possible after collection. This is especially important if freezing is the stabilization endpoint. Rapid processing may not be as critical for other types of bio-specimens, such as blood. Optimal processing times vary depending on the analysis method for which a bio-specimen is used.

4.2.2.6 Specimen Processing

Specimens are processed according to the study design and the methods most appropriate for preserving the analytes of interest. For a particular specimen type and analysis, several processing methods may be appropriate. The research team ensures that standard guidelines are adhered to when choosing processing methods for specimens most commonly used in molecular epidemiology studies.

a. Blood – separation into fractions (e.g. plasma, serum, buffy coat, red blood cells)

The processing method used for blood specimens depends on the laboratory analyses to be performed. Cryopreservation which typically involves the use of a cryoprotectant, such as dimethyl sulfoxide (DMSO) is a cost-effective way of preserving. Whole blood may also be cryopreserved as an efficient and cost-effective approach to centralized processing and storage of viable cells in large- scale epidemiological studies [12].

b. Tissue – processing after surgery, autopsy

Specimens resected specifically for research may be processed either in the operating room or pathology suite, shortly after the time of collection, or may be transported to the repository for processing, depending upon the requirements of the specific protocol.

c. Urine sample Processing

Processing of urine before storage is done by the size of the portion to be stored and based on the expected analyses. If the analytes are stable to thaw/refreeze cycles then larger portions can be stored.

d. Saliva/buccal cell processing from mouthwash protocol specimens

Buccal cells collected using the mouthwash protocol [11] are processed by centrifugation of

the cell suspension, re-suspension in a buffer, and either processed immediately or frozen for future use.

4.3 Data Handling

Data handling is the process of ensuring that research data is stored, archived or disposed-off in a safe and secure manner during and after the conclusion of a research project. This includes the development of procedures to manage data handled electronically as well as through non-electronic means. Data handling is important in ensuring the integrity of research data since it addresses concerns related to confidentially, security, and preservation/retention. Proper planning for data handling can also result in efficient and economical storage, retrieval, and disposal.

4.3.1 Data Tracking

Clinical data tracking involves monitoring and checking clinical data for correctness and completeness.

4.3.1.1 Case Record Form (CRF) Tracking

A case record form is a printed or electronic document designed to record all of the protocol-required information to be reported to the sponsor for each participant in a clinical trial. Entries made in the CRF will be monitored by the Clinical Research Associate (CRA) for completeness. This is done by tracking all CRFs for missing pages and illegible data manually to assure that the data are not lost. Clarifications are to be obtained from the investigator when necessary, such as in case of missing and/or illegible data.

In electronic (e-CRF) based studies, data validation process will be run frequently for identifying discrepancies. Ongoing quality control of data processing is undertaken at regular intervals.

4.3.1.2 Specimen Tracking

Bio-specimen collections are documented and tracked by many forms of data management tools, spanning from laboratory notebooks to multiuser software implementations. Automated information systems are ideal where available and affordable. Information technology software for specimen tracking features secure validated environments that adhere to ethical practices.

Biorepository information systems should support inventory functions by tracking all phases of sample acquisition, processing, handling, quality control and distribution from collection site (patient/subject) to utilization (researcher). The inventory tracking should include intentional or accidental events such as thaws, loss, depletion and destruction of specimens. Restocking of returned, unused samples from the researcher, if allowed per protocol, must also be documented. Current guidelines for biorepository information systems recommend the use of electronic labels or barcodes to document and associate a unique identification number to the samples making sure not to include identifying information about the specimen.

4.3.2 Data Entry

Data entry is done after retrieving information from the sites. Usually, double data entry is performed wherein the data is entered by two operators separately [1]. This helps in

verification and reconciliation by identifying the transcription errors and discrepancies caused by illegible data. It also helps in getting a cleaner database compared to a single data entry.

4.3.3 Data Validation/ Discrepancy Management

Data validation is the process of testing the validity of data in accordance with the protocol specifications. Edit check programs are written to identify discrepancies in the entered data, which are embedded in the database, to ensure data validity. A discrepancy is a data point that fails to pass a validation check mainly due to inconsistent or missing data, range checks or deviations from the protocol.

Discrepancy management is then carried out to review inconsistencies, investigate the reasons, and resolve them with documented proof or declaring them as irresolvable. This helps in cleaning the data and gathering enough evidence for the deviations observed. A discrepancy database is created where all discrepancies will be recorded and stored for audit purposes. Managing discrepancies is the most critical activity in the clinical data management (CDM) process and must be handled carefully.

Electronic data must always be adequately safeguarded to ensure validation including a signed and dated printout and backup records. Computerized systems (hardware and software) should be validated and a detailed description of their use be produced and kept up-to-date.

4.3.4 Medical Coding (Data Consistency)

Medical coding is the method used to properly classify reported medical terms on the CRF to standard medical dictionary terms in order to achieve data consistency and avoid unnecessary duplication. It helps in identifying medical terminologies associated with the clinical trial. Commonly, Medical Dictionary for Regulatory Activities (MedDRA) is used for the coding of adverse events as well as other illnesses and World Health Organization–Drug Dictionary Enhanced (WHO-DDE) is used for coding the medications. These dictionaries contain the respective classifications of adverse events and drugs in proper classes. Medical coders need the knowledge of medical terminology, understanding of disease entities, drugs used, and a basic knowledge about the structure of electronic medical dictionaries.

4.3.5 Database Locking

Database lock for a study is done to ensure no manipulation of study data during the final analysis. The database is locked after a proper quality check and assurance is completed and the final data validation is run. If no discrepancies are detected, the datasets are finalized in consultation with the biostatistician. All data management activities should have been completed prior to database lock. To ensure this, a pre-lock checklist is used to confirm the completion of activities. Once the approval for locking is obtained from all stakeholders, the database is locked and clean data is extracted for statistical analysis.

Generally, no modification in the database is possible except for a critical issue or for other important operational reasons. This should be properly documented and an audit trail maintained with sufficient justification for updating the locked database.

4.3.6 Data Storage

Data storage is the means of preserving biomedical samples (bio-specimen) and data derived from clinical studies for continual or future use. The emergence of genomics, molecular therapies and biomarker discoveries in medical research has created the substantial need for high-quality tissue, blood and other samples for use to advance a wide range of medical endeavours. As such, preserving/storage of samples to the highest standards has become a critical component of clinical research management.

4.3.6.1 Bio-specimen Storage

Clinical research depends partly on the availability of and access to high-quality specimens stored at large-scale biorepositories. Specimens may be stored under different conditions depending on the intended laboratory analyses, and other considerations. Usually, mechanical and liquid nitrogen freezers are used to store samples at low temperatures. In situations where freezer systems may not be available, a lower-cost option may be collection of saliva or blood spots on filter cards stored at room temperature.

a. Freezer temperature monitoring

Most common specimens such as plasma, serum or DNA may be securely stored in mechanical freezers at -80 °C, where temperatures are displayed on each freezer and must be monitored periodically. However, lymphocytes, or other cellular specimens, should be stored in the vapour phase of liquid nitrogen at -150 °C or lower, when long-term cellular viability is necessary [13].

Liquid nitrogen freezers are less susceptible to mechanical failure and can withstand power outages for long periods with no temperature deviations but require monitoring of both temperature and liquid nitrogen levels. Automated systems that can detect and sound alarms for undesired levels of liquid nitrogen should be kept especially in large repositories [14]. In small biorepositories, temperatures must be maintained by keeping manual log at specified intervals.

b. Storage system maintenance

Freezers and other storage equipment should be validated and maintained according to the manufacturer's recommendations. Biorepositories should develop protocols to ensure that the equipment functions properly. A preventive maintenance program should be in place to maintain equipment at regular intervals. The power supply must be connected to a back-up generator system that immediately provides power during an electrical outage.

c. Proper packaging and shipping

Specimen shipment may be regulated as infectious substances or as diagnostic specimens depending on the intended analyses or whether it contains infectious agents. To properly classify the specimens to be included in a shipment, it is important to consult the appropriate regulatory authorities such as IEC for guidelines and advise on handling the shipment that may include safety precautions for packaging; dispatching conditions such as uploading and offloading; unpackaging and etc.

d. Safety in biorepository

A small percentage of bio-specimens could pose a risk to the biorepository workers who

process them. Biorepositories should adhere to key principles of general laboratory safety and treat all bio-specimens as biohazards. Appropriate vaccination protocols should be offered to all personnel who may be potentially exposed to bio-specimens or other potentially infectious materials. In addition to biosafety, biorepositories should follow strict general safety regulations and procedures regarding chemical, electrical, fire, physical and radiological safety. The relevant authority in the national level such as IEC should develop a comprehensive guideline that address the Biorepository over all safety and the personnel self-protection guidelines.

4.3.6.2 Data Storage and Record Keeping

All steps involved in data handling should be guided by standard operating procedures and protocols that govern data recording and documentation in order to allow step-by-step retrospective assessment of data quality and study performance for the purpose of audit and reuse. Such protocols for data management should include details of checklists and forms that record actions taken; dates and names of individuals responsible for the action; confidentiality and privacy/sensitivity of the data; permission of data accessibility and etc.

Data can be documented and kept in either traditional written/ printed forms or electronic record forms. Written documents, information and other materials used in the study should be in a language that is clearly understood by all stakeholders (i.e. the participants, paramedical staff, Monitors etc.). Corrections in the Case Report Forms (CRFs) or any other study related documents should be made in a way that does not obscure the original entry. The correct data should be inserted with the reason for the correction if such a reason is not obvious, the corrections should carry the date and initials of the Investigator or the authorized person.

Electronic records allow researchers to efficiently access and compare information from different sources across similar projects [2]. There are numerous programs that allow researchers to enter, store and audit research data. To ensure security of electronic data processing, only authorized persons should be allowed to enter or modify the data in the computer and there should be a recorded trail of the changes and deletions made. A security system should be set-up to prevent unauthorized access to the data. If data is altered during processing the alteration must be documented and the system validated. The systems should be designed to permit data changes in such a way that the data changes are documented and there is no deletion of data once it has been entered. A list of authorized persons who can make changes in the computer system should be maintained. Adequate backup and protection policy/measures should be in place with adequate infrastructure to ensure record keeping and protection.

The data “Written and/or electronic forms” should be archived at a national or international data repository for a period recommended by relevant authorities. If that is not possible, the data should be archived by the institutional repository.

4.3.7 Data Sharing and Reporting

Data sharing is the practice of making data used for scholarly research available to other investigators as of to share any supplemental information (raw data, statistical methods or

source code among others) it is the way research is accurately represented to the scientific community and the general public.

Existing research data can be used to answer questions beyond those planned in the original study, to analyze outcomes that were not included in the primary analysis, and to investigate new methodologies for analyzing data. By sharing research results, a project may advance new techniques and theories to benefit other ongoing research. In general term, sharing is cheaper, allows for transparency as published results can be independently validated and reduces risk of participating in clinical research whereas reporting of clinical research data can have a direct impact on the quality of care provided to patients.

Independent Ethics Committees should provide a comprehensive guideline for data sharing with detailed procedures for data ownership and participant protection. Member States should have data protection regulations to govern data protection and facilitate data sharing. All stakeholders in the clinical research process are responsible for ensuring the integrity and accuracy of shared research data to meet desired quality standards

Researchers should prepare an anonymized dataset with appropriate level of anonymization if they before share the trial data. Anonymization or de-identification is the process by which personal information that can be used to identify an individual is removed from a set of data. The dataset preparation should be done by individuals with an understanding of data management and basic statistics. The dataset should be in a form that is recognized by a range of software while the pack for sharing should contain supporting documentation including the protocol and annotated data collection forms (including any amendments throughout the study).

4.3.8 Direct Access to Source Data/Documentations

The sponsor should ensure that it is specified in the protocol or other written agreement that the investigator(s)/institution(s) will permit study-related monitoring, audits, IEC review, and regulatory inspection(s) are provided a direct access to source data and documentations.

4.3.9 Data Retention and Continued Storage

The continuous keeping of research data after a clinical study conclusion is at the discretion of the IEC and other regulatory bodies concerned. In some cases, the time and/or the period is determined by the sponsor institutions and the research protocol. Such data could be needed at any time, however continued storage especially of confidential data increases risk of possible violation. Once the minimum storage period is over, the PI in consultation with the sponsor institution and the IEC to decide whether to continue storage of the data or not, by evaluating the risk and benefits associated with this decision.

4.3.10 Data Destruction

Data should be completely destroyed when a decision is reached to destroy data after minimum storage time. Effective data destruction makes sure that the data cannot be extracted or reconstructed in future. Onsite shredding and secure destruction of written and electronic records are often recommended. The study protocol should suggest secure data destruction methods.

4.3.11 Data Informatics System Security

Clinical research data management utilizes simple to complex Information Technology (IT) tools usually connected into robust software systems to ensure accuracy of data and improve the overall efficiency of the whole clinical research. Maximum cybersecurity and physical security of such systems is needed to protect clinical research data. Strong biorepository management systems provide controlled user access for system security which should include role-based security for all repository staff, study coordinators and scientists with the need to access the bio-specimens inventory. If the study annotation is held within the same data system, there should be security measures to protect study participants' personal health information (PHI) from disclosure to unauthorized users of the data. It is important to design system security guidelines to guide all research team members.

4.4 Data Management Team

For a proper data management to produce and maintain quality data, a strong and qualified clinical data management team must be established. In a clinical data management team, different duties are performed by the team members. A clinical data management team member must be a graduate in life sciences with knowledge of computer applications. Ideally, medical coders should be medical or paramedical graduates [14].

The minimum composition of the team is as follows;

- Data Manager;
- Database Programmer/Designer;
- Medical Coder;
- Clinical Data Coordinator;
- Quality Control Associate; and
- Data Entry Associate.

The data management is not only the responsibility of the data management team but the responsibility is extended towards the investigators and the research sponsor. A description of the roles and functions of each team member; and the responsibility of the investigator and sponsor are given in this sub-section.

4.4.1 Functions of the Data Manager

The Data Manager is a professional with at least four-year baccalaureate degree in computer science, Information Technology with additional qualification in health informatics.

He/she performs the following functions;

- Supervises the entire clinical data management (CDM) process;
- Prepares the Data Management Plan;
- Approves the CDM procedures and all internal documents related to CDM activities; and
- Controls and allocates the database access to team members.

4.4.2 Functions of the Database Programmer/Designer

The data base programmer usually has a BSc in Mathematics, Statistics, Computer Science or related field with experience in data programming. The following are his/her core functions;

- Performs the CRF annotation;
- Creates the study database;
- Programs the edit checks for data validation;
- Designs data entry screens in the database; and
- Validates the edit checks.

4.4.3 Functions of the Medical Coder

The Medical Coder must be a medical or paramedical graduate who has certification for medical coding. He/she needs the knowledge of medical terminology, understanding of disease entities, drugs used, and a basic knowledge about the structure of electronic medical dictionaries.

- He/she is responsible for preparing the coding for adverse events, medical history, co-illnesses, and administered concomitant medications

4.4.4 Functions of the Clinical Data Coordinator

The clinical data coordinator is in charge of organizing data and coordinating activities relating to clinical administrative tasks. He/she must have basic MSc in Statistics, Mathematics with additional Master's degree or PhD in the aforementioned courses or related fields. He/she performs the following duties;

- Designs the CRF;
- Prepares the CRF filling instructions;
- Develops the data validation plan and discrepancy management plan; and
- Develops all other CDM-related documents, checklists, and guidelines.

4.4.5 Functions of the Quality Control Associate

The quality control associate is a qualified quality control personnel with additional qualifications in medical sciences or clinical study. He/she performs the functions below:

- Checks the accuracy of data entry and conducts data audits; and
- Verifies the documentation pertaining to the procedures being followed.

4.4.6 Functions of the Data Entry Associate

The data entry associate is the member of the team that enters data from paper to the computer. He must have a baccalaureate degree with additional knowledge in typing, computer and software packages.

- Tracks receipt of CRF; and
- Performs the data entry into the database.

4.4.7 Responsibilities of the Investigator and Sponsor in Data Management

The oversight of data management represents a significant investment of time and effort by the Principal Investigator (PI) and the Sponsor of the research project. PIs and Sponsor must understand the basic concept of data management and ensure every member of the research team is involved in the planning, implementation and maintenance of data management policies and procedures.

4.4.7.1 Principal Investigator

The Principal Investigator should;

- Ensure that findings are correctly recorded in the CRFs and signed by designated person(s);
- Ensure laboratory values are recorded on or enclosed with the CRF;
- Evaluate and comment on laboratory values outside the reference range or differ from previous values; and
- Ensure units of measurement are documented.

4.4.7.2 The Sponsor

The sponsor should;

- Ensure that electronic data processing systems conform to the documented requirements;
- Maintain SOPs for the use of data procession systems;
- Take adequate measures to prevent data overlook and manage discrepancies;
- Safeguard the blinding, if any, particularly during data entry and processing; and
- Ensure documentation and disclosure of data ownership and to the concerned party(ies).

4.5 Data Quality Assurance and Control

The clinical research data is a vital part of clinical studies that is to make an informed decision about the safety and efficacy of an investigational product. The generation of quality data requires a robust data quality management process (DQM) which is a continuous monitoring of clinical data collection procedures and management practices that are integrated into the entire clinical study process. This includes ensuring that data are generated, collected, handled, analyzed, and reported during the study according to SOPs and good clinical practices (GCP). Data quality management starts with a Data Monitoring Plan (DMP) specified in the study protocol and approved by the IRB, IEC, Sponsor and other regulatory authorities before the study commences. While Data Quality assurance (DQA) in clinical studies is a systematic evaluation implemented as a part of a quality control system that to ensure clinical research data quality meets the study requirements and protocol [15].

4.5.1 Data Monitoring Plan (DMP)

Study investigators are to develop a quality data monitoring plan for each key operational stage of the study that defines standards against which quality control will be conducted. Such Data Monitoring Plan to include: sampling plan; comparison of the study's case record form (CRF) to the objectives set in the study protocol; data source to be used at each operational stage; acceptable quality levels; appropriate methods for data correction; analyses; reporting of results and data quality assessment [15].

4.5.2 Data Quality Assessment

Data quality assessment is the measurement of data relative to its purpose and its ability to serve that purpose [16]. This is defined in terms of accuracy, consistency, integrity, and timeliness.

Accuracy: Accuracy of data is measured by the number of errors in a particular dataset. A typical metric to measure accuracy is the ratio of data to errors which tracks the amount of known errors (like a missing, an incomplete or a redundant entry) relative to the dataset. The specific ratio of data to error is determined by the quality management team taking into consideration the size and nature of the dataset. As a general rule, the higher the ratio, the better the accuracy.

Consistency: Consistency is defined as relevant uniformity in data across clinical investigation sites, facilities, or other assessors. Consistency specifies that two data values pulled from separate datasets should be the same and not conflict with each other.

Integrity: Integrity of data refers to the structural testing of data to ensure that the data comply with standard procedures and guidelines.

Timeliness: Timeliness corresponds to the expectation for availability and accessibility of data. This is measured by, the time between when data is expected and the moment when it is readily available for use.

4.5.3 Quality Control Activities

Data quality control comprises various activities which are shared responsibilities of the entire study team and regulatory organizations. These comprise study site audits, data entry quality control, computer system validation, quality control of statistical analysis and quality assurance of bio-specimen management among others.

4.5.3.1 Study Site Audits

Independent Ethics Committees (IECS), IRBs and other regulatory institutions should conduct study audits to evaluate a particular research study; and/or investigate reports and complaints that have been brought before them. Site audits are to be performed periodically throughout the course of a study to assess protocol and regulatory compliance, safety and welfare of participants, and to confirm that problems reported by study monitors if any have been resolved. Such reported problem may be high patient enrolment, high staff turnover and abnormal number of adverse events (AEs). Site audits also are to ensure adequate documentation of case histories, laboratory test results, Serious Adverse Events (SAEs), and informed consents.

The audit team is also to examine the timeliness of clinical tests and review of test results in addition to the timeliness and accuracy of data entered into the CRF. Investigators are to adhere to the Audit report and to be accountable for all investigational products; comments; advices; and any way forward that presented to them during the study site audit visits, and in the audit visit report.

4.5.3.2 Data Entry Quality Control

Data entry and the database quality control involve reviewing documented evidence and ensuring data accuracy and integrity by verifying that data entered was checked manually, independently, and programmatically [16]. Data entry and the database quality control is also to ensure that all data queries are resolved and that the overall database review was conducted according to SOPs.

4.5.3.3 Computer Systems Validation

Computer systems validation examines all aspects of the data handling computer systems (hardware and software) to ensure the accuracy, consistent intended performance, and the ability to discern invalid or altered records. This includes initial installation and procedures that document how changes to a computer system are justified, approved, and implemented. The validation process begins with examining user requirements, the results of the initial hardware installation qualification (IQ) tests, the operational qualification (OQ) tests, and the performance qualification (PT) tests alongside qualification and training of user personnel. Installation qualification (IQ) test is conducted to verify the installation of the software in the selected environments and its documentation while operational qualification (OQ) test is performed to verify that software will function according to its operational specifications in the selected environment. Performance qualification (PQ) test is done to verify that software consistently performs to the specification for its routine use [17].

4.5.3.4 Quality Control of Statistical Analysis

After a study's database has undergone a quality control review, it is exported into a statistical analysis system (SAS) to develop analytical programmes according to the analysis model identified on the study protocol. The database programmer is to ensure the quality control of the process is in agreement with the SAS that was developed and validated according to the SOPs.

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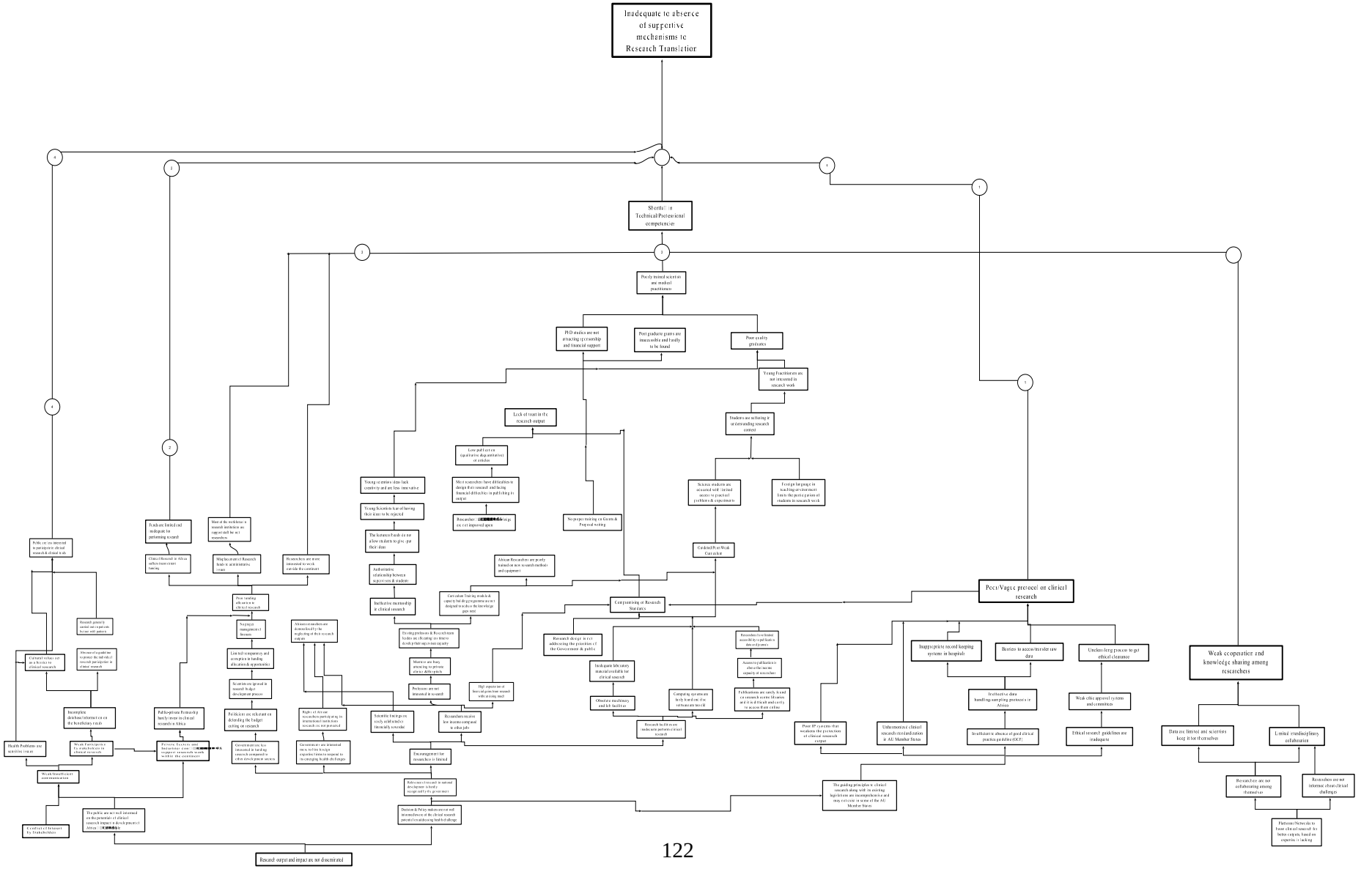
ANNEXES

ANNEX 1: PROBLEM TREE



ANNEX II QUESTIONNAIRE

UNESCO-MARS SUMMIT 2017 Breakaway Session
Clinical Research Translation from Bench to Bedside
an
Analytical Data on the Problem Inventory

Following the evolving challenge which is Lack of Clinical Research Translation Output in Africa to the inadequate to absence of supportive mechanisms to Research Translation, the African Union Scientific, Technical and Research Commission conducted a consultation through a round table discussion with African Scientists that are involved in the health research sector. The output of this consultation results in identifying four (4) gaps which are: ***Poor/Vague protocol on clinical research*** ; ***Funds are limited and inadequate for performing research***; ***Shortfall in technical/professional competencies***; ***Public are less interested to participate in clinical research and clinical trials***. In this regard and to improve the consultation and participation of stakeholders a questionnaire was developed.

This questionnaire has been specifically designed by the African Union Scientific, Technical and Research Commission, covering the four (4) gaps identified as the major resultant causes of **"*Inadequate to absence of supportive mechanisms to research translation*"** in Africa. This analytical data gathering is targeted towards achieving a comprehensive fact/data based analysis of the problem from Clinicians, Clinical Researchers, Bio-scientists among others. This is to bridge the gap of clinical research translation from Bench to Bedside in Africa, proffering solutions through an African Inclusive Strategy, building upon dynamic translation models and strategic implementation analysis within major research translation pillars and sub pillars cutting across stakeholders in the dimensions of Mechanisms; Systems and Physical Infrastructure.

This questionnaire is divided in to four (4) sections**.** Kindly avail, your opinions and narrations (elaborations) where requested below.

Privacy Statement

Kindly be informed that all personal information and opinions shared in this questionnaire shall be used solely for the purpose of the analytical data research. Therefore the AU-STRC stands firm on the nondisclosure and misuse policy in accordance to best practices / standards.

Personal Details

Name: ----------

Age Group: 25 – 30 ; 30 -35; 35 – 40; 40 – 45; 45 – 50; 50 – 60 ; Above 60

Scientific Domain ----------

Area of Specialization ----------

Institution ----------

Country ----------Email: ----------

Telephone ----------Mobile ----------

INSTRUCTION

Please kindly respond to the following questions with a rating scale of 1 – 6 where (1) – Very Poor, (2) – Poor, (3) – Average, (4) – Good , (5) – Very Good , (6) – Cannot Answer. Rate your responses on the problems identified in this section.

SECTION 1

POOR/VAGUE PROTOCOL ON CLINICAL RESEARCH

Official procedures or rules governing clinical research in the continent is pertinent to achieving good governance in research translation and proffering solution against the challenge of unharmonized clinical research and standardization in AU Member States.

1. **Do you have a clinical research guiding principle in your country?**

   Yes ☐ **No** ☐

1.1. Do you have a Research Ethic Committee in your distinguished Country?

Yes ☐ **No** ☐

1.2. Does your country have a weak ethic approval system?

Totally Agree ☐ **Agree** ☐ ☐ ☐ ☐ **Totally disagree**

1.3. Is the existing ethical research guideline adequate to perform clinical research?

☐ ☐ ☐ ☐ ☐

1.4. Are the recording systems in your National/Private Hospitals well-kept and handled?

Yes ☐ **No** ☐

1.5. Is the accessibility to health record easily accessible in your country?

Yes ☐ **No** ☐

End of Section 1

SECTION 2

FUNDS ARE LIMITED AND INADEQUATE FOR PERFORMING RESEARCH

This is another challenging factor globally and more worrisome in Africa. It is identified as a fundamental supportive mechanism lacking in Africa's clinical research. Clinical research development requires consistent and dedicated financial backing from the private sector as well as the government.

1. Has there been a collaborative support to clinical research by the Private sector and Industries investing directly in clinical research in your country? Yes / No; If yes,
   Elaborate how the public – private partnership has enhanced clinical research in your country.

2. Often times the place / importance of clinical research is misconstrued hence the less interest of government in funding research and politicians are reluctant on defending the budget cutting on research. How much is this applicable to your country? (Scale of 1 – 6)

3. The demoralization of scientists due to the fact that their findings are not being financially rewarded and are rarely celebrated, as well as being ignored in research budget development

process predisposes researchers to be more interested to work outside the continent. Does this apply to your country? Yes/NO

4. Poor funding allocation to clinical research over the years has led to inconsistent funding to clinical research in Africa. Has this been the case of your country? Yes/No

5. Is the relevance/potential of research on addressing health challenges and improvement of national development recognised by decision and policy makers in your country ? Yes/No

End of SECTION 2

SECTION 3

SHORTFALL IN TECHNICAL/PROFESSIONAL COMPETTENCIES

An evaluation of Africa's infrastructural capabilities revealed that facilities in Africa are grossly inadequate. Machinery and laboratory facilities are obsolete, laboratory materials are insufficient. Such paucity of technical resources affects the students negatively by limited access to practical and experiments, thereby limiting their understanding and overall output.

1. How will you rate the interdisciplinary collaboration, data and knowledge sharing among researchers in your country? Scale of (1 – 6) if answer is to the negative, give a brief outline on the obstacles to their collaboration.

2. Platforms/Networks to boost clinical research for better outputs, based on expertise is lacking in most African countries since researchers are not well informed on the challenges of clinical research. Has this been the case in your country? Yes/NO .

3. Research as a highly ethic based domain, requires a lot of stable players for it to achieve a global best standard. How has inadequate laboratory materials, obsolete machinery/lab facilities , fairly found computing systems and out dated softwares led to compromise of research standards in your country? Scaleof 1 – 6

4. How accessible are publication data and journals in research library to researchers in your country? In the scale of 1 – 6 (the accessibility)

5. If publication data and journal are available in research libraries in your country, are they affordable? Yes/No

6. As foreign language stands as a barrier to the active participation of students in research in most African countries, has research context been well understood by researchers in your country? In the scale of 1 - 6. how well do researchers in your country understand research context?

7. So far, based on infrastructural gaps of inadequate research facilities to perform clinical research along with outdated/weak /poor curriculum, how would you classify the quality of most graduates from your country? (In scale of 1-3 of which POOR 1 , FAIR 2, GOOD 3.)

8. In the case of an emerging health challenge in your country, how does the government respond to the challenge? Give a brief narration.

9. How will you rate the interest of Professors, Mentors, Research Team Leaders in research and allocation of time in building their supervisee capacity in research? Scale of (1 – 6) – *FOR STUDENTS *

10. How would you describe/rate the existing relationship between Supervisors, Lecturers, Heads and students? In the Scale of (1-6) Authoritative – Encouraging- *FOR STUDENTS*

11. Is the capacity of researchers in your country periodically built in the areas of Grants and proposal writing, new research methods and equipment, Research designs, technics of qualitative and quantitative articles? Yes/No

END OF SECTION 3

SECTION 4

PUBLIC ARE LESS INTERESTED TO PARTICIPATE IN CLINICAL RESEARCH AND CLINICAL TRIALS

The role of the public in the advancement of clinical research in Africa cannot be disregarded. As research output and impact are not disseminated, the African public is ignorant of the potentials and effects of clinical research in improving their quality of life. This is caused by insufficient communication due to conflict of interest among stakeholders, the government, industry and the researchers themselves.

1. How will you rate the level of communication between stakeholders and the level to which the public are informed on the potentials of clinical research impact in development of the country's lifestyle? Scale of 1- 6 (1is weakest)

2. The weak participation by stakeholders in clinical research in most African countries has brought about incomplete database/information on the beneficiary needs and reality is that health problems are sensitive issues, has your country broken the barriers of cultural values to clinical research? Yes/No

3. It is mostly observed that research is often carried out on patients but not with patients as there is the absence of guideline to protect the individual research participation in clinical trials in most parts of Africa. Are the patients across communities in your countries carried along and properly guided on the event of any clinical trial? Yes/NO.

END OF SECTION 4

Thank you for availing all the answers to this questionnaire. And for being a part the sources to this époque document that will bridge the gap of research translation from bench to bedside in Africa.

The health research translation protocol is an indispensable part for health care development in Africa, especially that most of the research publication in the continent is in health and related fields. However, there is dearth of taking the research output from the "bench to the bedside" and this has been a significant challenge to Scientists, Entrepreneurs, Enterprise and the Governments.

This publication presents scientists and researchers a roadmap to the creation of mechanisms to support research translation from "bench to the bedside"; and among others, guidelines for improved clinical research practice for AU Member States. The publication provides useful direction on the necessary impetus on research translation.

Dr. E. Osagie Ehanire, MD, FWACS
Minister of Health
Federal Republic of Nigeria

The African Union Scientific, Technical and Research Commission is herein saluted for a very timely document entitled "Research Translation from the Bench to the Bedside".

In this document, the health challenges in Africa are aptly articulated, with due emphasis being given to the growing chronic and non-communicable diseases burden in Africa. This emerging and now correctly acknowledged threat of NCDs in Africa is proving to be a concern to all stakeholders in health including health research and funding bodies such as our own – the South African Medical Research Council (SAMRC).

This book is to be recommended for a read by stakeholders that are interested in having meaningful input into improving health for Africa and to health researchers in Africa at large.

Dr. Thabi Maitin, PhD
Division Manager, Research Capacity Development,
South African Medical Research Council

African Union
Scientific Technical Research Commission