MASTER IN BIOMEDECINE

The African Medicines Agency

Impacts of a new supranational health agency on clinical research and access to medicines

Mwizerwa Nkubito, Blaise

Award date:
2023

Awarding institution:
University of Namur

Faculté de Médecine

The African Medicine Agency: Impacts of a new supranational health agency on clinical research and access to medicines

Mémoire présenté pour l'obtention

du grade académique de master en sciences biomédicales

Blaise MWIZERWA NKUBITO

Janvier 2023

Université de Namur

FACULTE DE MEDECINE

Secrétariat des départements

Rue de Bruxelles 61 - 5000 NAMUR

Téléphone : + 32(0)81.72.43.22

E-mail : manon.chatillon@unamur.be - http://www.unamur.be/

The African Medicine Agency: Impacts of a new supranational health agency on clinical research and access to medicines

MWIZERWA NKUBITO Blaise

Background**:** Most African countries host only a few hundred trials per year and therefore few new medicines are marketed. Yet these countries suffer from numerous public health problems and lack accessible medicines to face them. To address these concerns the African Union (AU) established in 2019 a treaty to create a new health agency: the African Medicines Agency (AMA). Its objective is to strengthen the regulation of health products. Indeed, many African countries do not have the appropriate legal framework. This context makes access to health products complicated. In creating a continental agency, the AU's wish is to bring together the strengths of all African countries to improve their access to medicines

Aim: The aim of this work is to assess the impact that the creation of the AMA might have on clinical research and access to medicines. These effects will be assessed at the African continent level and to a lesser extent at the international level. This work will also provide an opportunity to explore the context of clinical research in Africa, which is not well represented on the world stage.

Methods: The first part of the work is based on a review of the literature to formulate hypotheses. These will enable an evaluation of the potential impacts of the agency on Africa's relations with the public and private sectors and the international scene in general. In the second part of the study, these hypotheses will be confronted with the opinions of experts gathered through interviews

Analysis: Literature and experts agree that the regulatory harmonisation objectives proposed by the AMA are necessary to allow better access to medicines. This harmonisation could stimulate the entry of industries that currently suffer from the complex regulatory context on the continent. The agency could also increase the regulatory capacity of less developed African countries and serve as an intermediary with international actors. However, this harmonisation must consider the specificities of the continent to avoid any drift to the detriment of the populations.

Conclusion: Numerous recent initiatives focused on Africa suggest that many actors anticipate the positive impacts of the agency. However, AMA is not yet fully operational and does not seem to want to focus on clinical trials first. In addition, there are disputes at a political level that are delaying the ratification of the treaty. Therefore, it is not possible to confirm any assumptions yet.

Keywords: Africa, Regulation, Harmonisation, Clinical trials, Interviews

Mémoire de master en sciences biomédicales

Janvier 2023

Thesis Supervisor: Prof. Yves Geysels

Acknowledgments

First of all, I would like to thank Professor Yves Geysels, my thesis supervisor, for his wise advice and the trust he placed in me.

Then I would like to thank my parents whose support and encouragement carried me through my studies and who taught me that there is always a way forward.

I would also like to thank my classmates, whether it was for my bachelor's or my master's degree, they made me understand that one can never succeed alone.

I would particularly like to thank Alice, Arthur, Eléa, Eléonore and Julinne and wish them all the best for the future.

Finally, I would like to thank Chloé, who always believed in me when I had the most doubts.

Table of contents

List of abbreviations

AMA	African Medicines Agency
AMRH	African Medicines Regulatory Harmonisation
ANZTPA	Australia New Zealand Therapeutic Products Authority
APEC	Asia-Pacific Economic Cooperation
ASEAN	Association Southeast Asian Nations
AU	African Union
AUDA	African Union Development Agency
AVAREF	African Vaccine Regulatory Forum
BMFG	Bill and Melinda Gates Foundation
CDC	Centre for Disease Control and Prevention
CRO	Contract Research Organisation
CT	Clinical Trial
CTA	Clinical Trial Application
CTIS	Clinical Trial Information System
EAC	East African Community
EC	Ethics Committees
ECOWAS	Economic Community of West African States
EDCTP	European and Developing Countries Clinical Trials Partnership
EMA	European Medicines Agency
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GDP	Growth Domestic Product
GHD	Global Health Diplomacy
GMP	Good Manufacturing Practices
HbD	Harmonization by doing
ICF	Informed Consent Form
ICH	International Council for Harmonisation
IMP	Investigational Medical Product
IND	Investigational New Drug

IRB	Investigational Review Boars
LMIC	Low- and middle-income countries
MA	Marketing Authorisation
NCD	Non-Contagious Diseases
NEPAD	New Partnership for Africa's Development
NGO	Non-Governmental Organisation
NIH	National Institute of Health
NRA	National Regulatory Authority
OOAS	Organisation Ouest Africaine de la Santé
PANDRH	Pan American for Drug Health Harmonization
PANHO	Pan American Health Organization
PMDA	Pharmaceuticals and Medical Devices Agency
RCORE	Regional Centres of Regulatory Excellence$
REC	Regional Economic Community
TGA	Therapeutic Goods Administration
UHC	Universal Health Coverage
WAHO	West African Health Organisation
WHO	World Health Organisation

Introduction

1 Clinical research

Clinical research is a mandatory step in the development of a new medical product. While safety of a new drug is assessed during the preclinical phases, clinical research checks how it will affect human health outcomes. Clinical research is carried out through clinical trials[1] (CT). As defined by National Institute of Health (NIH), clinical trials are "research studies performed in people that are aimed at evaluating a medical, surgical, or behavioural intervention.[2]" The main goal of this type of study is to gather scientific knowledge on the products tested. Patient studies are the best way to evaluate the efficacy, dosage, and safety of health products[3].

However, while clinical trials ensure the safety of their participants, there is no assurance that participants will derive any therapeutic benefit. Patients are aware of this limitation through the informed consent. This measure avoids therapeutic misunderstanding and is mandatory for the admissibility of the study's results by the authorities before any marketing[4]. Indeed, clinical trials are governed by very strict rules to protect the interests of the patient before those of scientific research. Experiments carried out on prisoners in the concentration camps of the Second World War were judged during the Nuremberg trials and led to a reflection on human experimentation[5]. This was followed by the Nuremberg code in 1945 and the Helsinki declaration in 1964 which led to the creation of guidelines, the Good Clinical Practices (GCP)[6]. To harmonize practices, the *International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use* (ICH) proposed a standardization of these practices under the name ICH-GCP in the late 90's[7].

Clinical studies are usually designed in 4 different phases (*Figure 1*):

- Phase I is usually conducted on a few numbers (less than 100) of healthy volunteers. The main goal of this phase is to evaluate safety and to find the correct dose.
- Phase II involves patients (100 to 300) affected by the studied disease. Indeed, the main goal is to judge effectiveness of the product
- Phase III also evaluates safety and efficacy but on a much larger (+/- 3000) and heterogeneous population.
- Phase IV is the longest and biggest phase. It concerns all the patients that will use the product after its commercialization. This phase assesses long term side effects. It is part of the pharmacovigilance process[8].

Figure 1 Clinical Trials phases[9]

Clinical trials are expensive studies. Ranging from a few million dollars for phase I to tens of millions of dollars for the more advanced phases[10]. Trials cannot be conducted without a substantial financial contribution from one or more sponsors. These sponsors, who may be private or public, will determine the nature of the trial. If their aim is to market the products of the study to make a return on investment, the trial will be a commercial one. This is particularly the case for drug studies sponsored by pharmaceutical companies. If the sponsors' intention is not monetary, the study will be non-commercial[11]. The most common motivation for these studies is global public health. A good example is the various studies financed by states and Non-Governmental Organisation (NGOs) during the Ebola epidemic that affected West Africa[12].

2 Regulation of clinical research

Adhering to GCPs ensure the ethical and scientific integrity of clinical trials. Although the ICH has proposed a harmonization of these standards, they are not law, each country is the master of its own health policy[13]. Each country must therefore have a National Regulatory Authority (NRA) as well as qualified Ethics Committees (EC)[14]. They analyse the trial requests made by the sponsors through the dossiers they submit called *Clinical Trial Application* (CTA). These dossiers contain all the information on the safety and efficacy of the test product collected during the pre-clinical studies. They also contain the entire clinical trial process and the measures that will be taken to ensure patient safety[15]. One of the most important measures is informed consent. All patients enrolled in clinical trials should be made aware of the effects of the product they are testing. They should also be made aware of how the trial will be conducted. To prove this, patients must sign an *Informed Consent Form* (ICF) that has been previously evaluated by an ethic committee[16].

A sponsor must therefore comply with all the requirements of the NRAs of a country to carry out a trial and be able to market a drug[17]. It is not uncommon for a sponsor to decide to distribute its trial in several countries at the same time. These trials are said to be multi-national. They allow a sponsor to broaden the scope of its market. It also allows to facilitate the recruitment of patients for its study while increasing the heterogeneity of panels.[18]

Despite these fundamentals, the assessment of a dossier may differ between countries. Both in the way of its organisation and in the distribution of tasks to carry it out. This situation is linked to political choices but also to questions of resources and capacity[19]. The WHO created in 2018 a benchmarking tool for national health regulatory authorities. This tool ranks the regulatory systems of the 194 member countries on a maturity scale from 1 (lowest) to 4 (highest). These levels are based on many criteria and there are many disparities around the world. In fact, according to WHO estimates, only 25% of countries reach the highest levels of maturity. Almost 75% of NRAs have a sub-optimal level of maturity and most of them are low- and middle-income countries (LMICs). This poorly developed regulatory context is unfavourable to the marketing of drugs and therefore indirectly to the conduct of clinical trials[20].

Indeed, the NRAs have as mission to regulate all health products: the investigational new drugs (IND)/investigational medical product (IMP) tested during CTs but also medicines already on the market in other countries whose manufacturers want to expand the market. These have already passed through clinical trials and are already on the market in other countries. As pharmaceutical research is an expensive process, sponsors may decide to reach new markets. To do this, they submit a dossier containing all the information about the drug, including data from the trials it has undergone[21]. Low-capacity NRAs will take time to analyse a marketing

application, which will waste the limited exploitation time that companies have on their drugs. Therefore, sponsors often avoid LMICs as new ground for their products but also as new places to conduct CTs because of their complex regulatory environment and small market. Not only, these countries have few CTs performed on their territory and therefore few new drugs emerging. But also, they have limited access to the medicines that already exist[20,22].

3 Status of Clinical Trials across the world

Clinical Trials have different status and regulation across the globe. The USA and the European Union are the leaders in terms of CTs and their regulatory systems have been used as a model to build others[23]. Understanding how they are organised therefore provides an overall understanding of how the regulation of clinical trials works around the world.

3.1 America

NRAs in the Americas are not at the same level of maturity. Some of them, such as those in Argentina, Colombia, Canada, and the United States, are considered by the WHO as references in their geographical areas. Others are at a much lower level of maturity[24].

To conduct a trial in the USA, a sponsor company must file an Investigational New Drug (IND) demand which details the nature of the medical product and the design of the study. The dossier will be reviewed and approved by the NRA of the USA: the Food and Drug Administration (FDA). The FDA will designate an Institutional Review Board (IRB) according to the type of trial and its location. This board will assess the dossier and approve it or not. Once the trial has been approved, the sponsor can proceed to recruitment. The FDA keeps an eye on the progress of the studies and compliance with GCP through inspections. The sponsor must keep up with the GCPs and it will also be responsible of post-approval pharmacovigilance. After the FDA's evaluation of the trial data, it will grant marketing approval for the product or not. This authorization is valid throughout the country. All the regulatory aspects of CTs are centralized by FDA[14].

The U.S FDA created in 1902, is a pioneer in the regulation of health products and the USA is the leader in terms of the number of clinical trials in its territory. Thus, this organization has served as a model for NRAs around the world. For example, their direct neighbour, Canada, has a similar evaluation system for CTs. Nevertheless, these similarities are less evident in the south of the continent. Indeed, as noted above, LMICs have difficulty establishing effective regulatory systems due to a lower level of maturity of their regulation authorities. Thus, Caribbean countries, some Central American countries such as Honduras and Costa Rica, as well as South American countries such as Peru and Paraguay, are having more difficulty implementing effective regulatory policies. However, there is a Pan American Health Organization (PANHO) which is helping these countries through its Pan American Network for Drug Regulatory Harmonization (PANDRH)[25].

3.2 Europe

The European Union is the second region in terms of clinical trials. However, he European regulation system for CTs involves more intermediaries than the American one. Indeed, each member country has its own national health agency which is the link between sponsors and the international regulatory body: the European Medicines Agency (EMA). In the interests of harmonisation, the EMA introduced a regulation that took effect on 31 January 2022: EU 536/2014. This regulation sets out a common procedure for all member countries. In this way, sponsors will be able to submit their dossier to a single national agency, the reporting member state. Once the reporting state has accepted the file, it will issue a clinical trial authorisation on behalf of all member countries involved in the study. The centralised submission of the dossier is made possible thanks to an online and centralised platform called the Clinical Trial Information System (CTIS). If the national EC of the reporting state grants a Clinical Trial Authorisation, the sponsor will be able to launch its trial. At the end of this trial, its data will be sent to the EMA, which will evaluate them and grant or not a Marketing Authorisation (MA) for the tested product. This MA will be effective throughout all the European Union. Once on the market, the EMA will be responsible for the pharmacovigilance of the product throughout the member countries[26].

3.3 Asia and Oceania

Health regulation across Asia is quite like in South America: not all NRAs are at the same level. However, it is important to note that some countries such as China, Singapore, Indonesia, and India have NRAs at level 3 or 4. Since 2010, the US and Japan have been working together to harmonise their regulatory approaches to clinical trials. This initiative, called Harmonization by Doing (HbD), is helping to advance the Pharmaceuticals and Medical Devices Agency (PMDA), the Japanese regulatory body[27]. This level of maturity combined with favourable policy measures for the implementation of trials on their territories make these countries emerging markets for sponsors[28]. The same is true for Central Asian countries such as Turkey and Lebanon[29]. It is important to note that some initiatives to harmonise regulatory practices do exist and they are mainly based on existing economic relationships such as the Association of Southeast Asian Nations (ASEAN) or the Asia-Pacific Economic Cooperation (APEC)[30 31].

For the Oceania countries, most clinical trials are divided between Australia and New Zealand. Both countries have a regulatory context managed by their national agencies, the Therapeutic Goods Administration (TGA) in Australia and Medsafe in New Zealand[32,33]. A joint regulatory initiative was launched in 2007 under the name Australia New Zealand Therapeutic Products Authority (ANZTPA) but was discontinued in 2014[34]. However, the two countries continue to collaborate to this day.

3.4 Africa

The regulatory context for clinical trials on the African continent is rather complex. Each member country of the African Union (AU), which includes all 54 African countries, has an NRA that handles clinical trial applications in a different way. Where one application could be sent to Europe to cover the whole territory, 54 applications would, in theory, be needed to cover the whole continent[35]. In addition to these administrative complexities, NRAs have generally low levels of maturity, 90% of them are at level 1[36]. Only a few countries, such as Tanzania, Egypt, and South Africa, have reached at least the third level of maturity with their NRAs. This context is not optimal for conducting clinical trials because the regulatory tasks take an abnormally long time. For example, it takes between 4 and 7 years longer in sub-Saharan Africa than in a high-income country for a tested drug to reach the market, which discourages sponsors[37].

The limited presence of sponsors on the continent can be demonstrated by the distribution of Contract Research Organisations (CROs) on the territory. Although clinical trials are fully funded by their sponsors, they are not necessarily in charge of their conduct. Most of the time, they will delegate this work to CROs. These companies are mandated by the pharmaceutical industry to ensure the quality and integrity of clinical trials by verifying several parameters: compliance with good clinical practices, quality control and quality assurance. These companies are therefore the real players in the field when it comes to CT's. They are responsible for ensuring the smooth running of each phase of these trials, from patient recruitment to pharmacovigilance, according to the missions that the sponsors grant them. The nature of their activities therefore requires them to be present on site and to set up their offices there[38]. This fact is directly linked to the volume of CTs worldwide: the fewer tests are carried out, the fewer CROs will be mandated and the less they will be present on site[23]. This is particularly true when observing the location of the head offices of large CROs such as PPD or IQVIA. They have dozen of agencies in the US and Europe, but only that covers the African continent.[39,40]. The apprehensions of sponsors are also demonstrated by the disparity in terms of trials among the continent. Indeed, the majority (>70%) of studies are shared between Egypt and South Africa which have maturity level 3 NRAs[41]. Still, the African continent represents only 3% of the total of CTs. Moreover, Sub-Saharan Africa accounts for an almost negligible share (<1%) of global studies[23] even though it is home to 18%[42] of the world's population and carries 25%[43] of world's disease burden.

However, the few CTs conducted are evenly distributed between phases II and III [44] but there is way less phase I studies. Moreover, there are few or no pharmacovigilance studies[37]. The subjects of these studies are most often contagious diseases that are endemic in these regions: HIV, tuberculosis, or malaria[45]. Nevertheless, Africa is also struck by Non-Contagious Diseases (NCD) such as cancer or diseases linked to nutrition disorders that are also studied[46].

4 The African Medicine Agency

4.1 Genesis of a continental agency

Aware of the flaws in the drug regulatory system on its territory, the AU mandated its development agency, the African Union Development Agency (AUDA,) formerly called NEPAD, in 2001 to find solutions. It initiated the African Medicines Regulatory Harmonisation in 2009 (AMRH)[47]. The principal goal of AMRH was to create better regulatory mechanisms among NRAs by joining their work. Firstly, focused on generic medicines, AMRH expanded its work to other fields such as CTs. Then it designated the Regional Centres of Regulatory Excellence (RCORE), institutions that would oversee specific regulatory tasks. Those NRAs, academic, scientific or research institution was designated as references for different tasks in the life cycle of medicines: from clinical trials to manufacturing or pharmacovigilance. Afterwards, AMRH launched regulatory harmonisation initiative between neighbouring countries belonging to the same Regional Economic Community (REC). Indeed, there was 8 RECs recognised by the AU existing across the continent. Although member states of those RECs do not have the same level of regulatory maturity, this initiative has already led to the implementation of harmonisation measures among 5 out of the 8 RECs[48] (*Figure 2*).

Figure 2 AMRH harmonisation plan[46]

Again, in the interests of harmonisation, the AMRH has been working on a model law: the AU Model Law on the Regulation of Medicinal Products. It was adopted in 2016 and aims to provide a legal framework for the regulation of medicines in the AU (*Figure 3*). This was developed in order to be directly integrated into the constitutions of countries that already have a solid legal framework for health products. However, it can also serve as a starting point for the construction of a legal framework for countries whose NRAs have not yet reached a sufficient level of maturity. It is through these progressive steps since 2009 that AMRH has been able to lay the foundation for what should become the AMA[47].

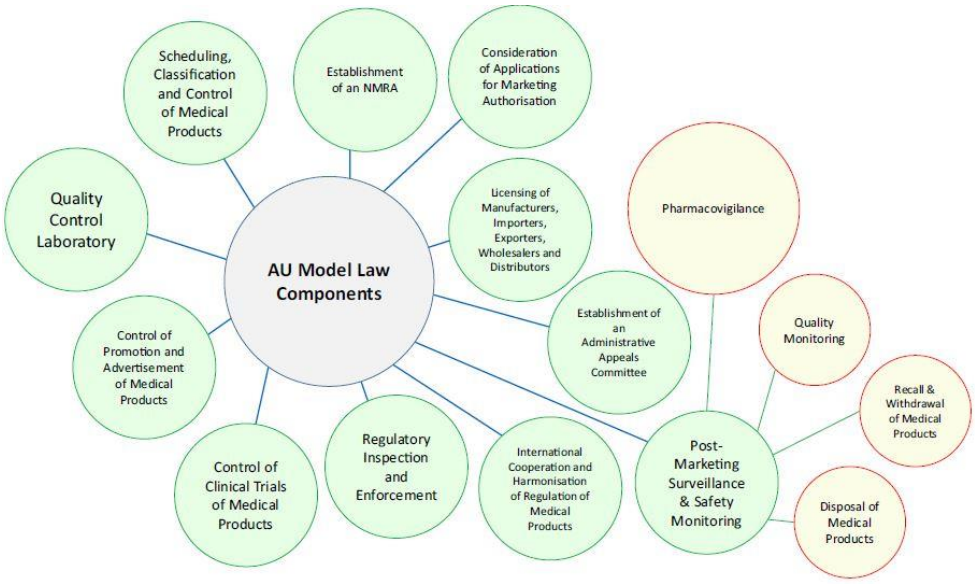

Figure 3 Key components of the AU Model Law[47]

However, AUDA is not the only organisation aware of the weaknesses of the African health system. In 2006, the WHO regional offices launched the African Vaccine Regulatory Forum (AVAREF), an initiative to improve the regulatory and ethical framework for clinical trials across Africa. Initially focused on vaccines, AVAREF will extend its activity to other interventional CTs. The forum operates as a platform for exchange between NARs, CTs and stakeholders across the continent. It works towards joint CTA assessment operations, harmonisation of practices, collaboration between countries and support to requesting countries[49]. The various epidemics that the continent has experienced have also prompted the creation of an African Centre for Disease Control and Prevention (Africa CDC) in 2017 under the leadership of the AU. The main mission of this institution is to strengthen the capacity of member states to respond rapidly to epidemics on the continent[50].

The Covid-19 outbreak highlighted the importance of the work done by AVAREF, Africa CDC and AMRH. And it has undoubtedly accelerated discussions around the creation of an African health agency[43].

4.2 The treaty of the African Medicines Agency

During the 32nd assembly of the African union in February 2019, leaders of member states adopted a treaty establishing a continental health agency: the African medicines agency[51]. However, it is also stated that a minimum of 15 countries will have to ratify this treaty to launch the creation of the agency. This milestone was reached with the ratification of the text by Cameroon in October 2021 which set the creation of the agency one month later, in November 2021[52]. Since April 2021, the AU has appointed Michel Sidibé, former Executive Director of UNAIDS and former Malian Minister of Health, as its special envoy for the establishment of the AMA. His task is to negotiate with African countries to get the treaty ratified and he is also the agency's spokesperson on the international stage[53]. In July 2022, the AU Council votes for the East African country of Rwanda to host the AMA headquarters in its capital Kigali[54].

The AMA aims to improve regulatory capacity for medicines, provide expertise in countries that lack of regulatory framework and improve efficiency and transparency of those processes. It also aims to strengthen governance in pharmacovigilance and oversee clinical trials.

However, these missions will not impinge on the activities of local authorities, the idea being to work in collaboration with them and not above them[55]. Indeed, as its treaty establishes, the AMA is intended to be a facilitator that would allow the coordination and strengthening of the various initiatives of harmonisation of the regulation of health products. By pooling resources, which are sometimes scarce for some countries, and by supporting the efforts already made, the AMA aims to ensure the quality and accessibility of medicines in Africa.

AMA aims to be collaborative. It will work with the NRAs and RECs to bring together the strengths of each but also to avoid duplication of work. In addition, it intends to work with external partners such as diaspora members or researchers from academia to build its capacity and ensure cooperation (*Figure 4*). AMA will also be cooperative in that its teams will be limited and some of the work it does will be carried out by experts from the NRAs following an agreement by the AU member countries[52].

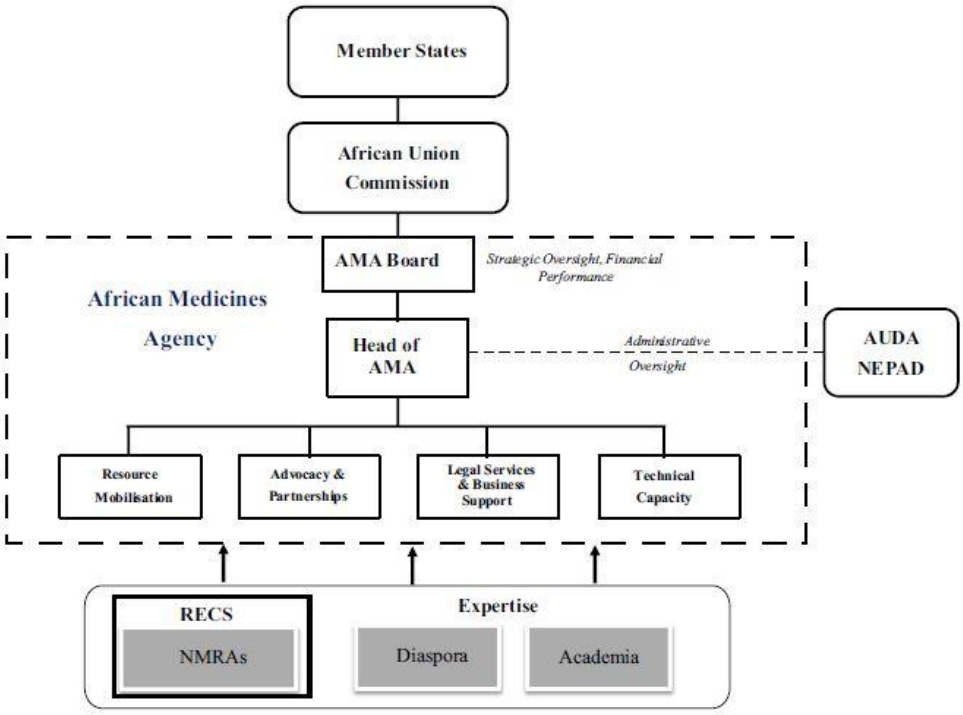

Figure 4 Proposed structure of AMA[47]

Aims of the master's thesis

The problems associated with the complexities of the regulatory system on the African continent slow down clinical research. As stated in the AMA treaty, the AU is aware of these difficulties and wants to address them. While initiatives to improve research and accessibility to health are to be welcomed, it is appropriate to question how these measures will be implemented.

The first part of this master thesis attempted to clarify the set of issues that the AMA treaty wishes to address in the future and analyse them through review of literature. This study was analysed through the prism of the different types of actors involved in research on the continent. This will allow the emergence of a series of hypotheses to be put forward on the potential impacts of the creation of the agency. These hypotheses were confronted with the opinions of experts and field actors. In this way, it was possible to set limits to the hypotheses put forward in the first part of the work.

The overall objective of this work was to draft a global picture of clinical research on the African continent, which is poorly represented on the world stage.

Methodology

The first part of the analysis was mainly based on the literature available online. It was first searched in online scientific databases PubMed, Scopus and Google Scholar using several keywords: "African medicine agency", "regulation of clinical trials in Africa", "clinical trials in Africa". As the scientific literature is still sparse, it was necessary to diversify the sources of information. The first step was to search for information on the websites of the institutions mentioned in this work: AU, AMA, WHO, AUDA, AMRH, AVAREF, Africa CDC as well as the NRAs and regulatory harmonisation initiatives. As the subject of this work is still evolving, it was necessary to keep up with recent developments in the creation of the agency. Social networks, more specifically Twitter, were a great help in this process. By following the activities of the various actors around the AMA, it has been possible to keep track of the various news. To ensure the veracity of the posts, every piece of information that was taken from them was cross-checked with other sources (scientific literature, accredited press articles or websites of recognised organisations). The few numerical data about clinical trials and population that has been put forward are taken either directly from the articles found earlier, from the databases of the Oxford University website www.ourworldindata.org or extrapolated from the information provided by the website www.clinicaltrials.gov.All the hypotheses put forward in this first part are based on a comparison of the literature with the objectives set out in the AMA treaty. The treaty is available online on the AU website and has been consulted in English and French to avoid any problems of understanding.

It was considered relevant to assess the impacts of the agency from three different perspectives:

- The private sector: This section brings together the private players in clinical research in the region, and first presents the current situation of the industry on the continent using available data and comparing it with the international situation. It then attempts to present a reflection on the potential effects of the agency's measures on the pharmaceutical industry in general and its interest towards the African market.
- The public sector: This section will focus on the position and challenges of the various institutions in charge of health and the regulation of clinical trials in AU member countries. This reflection will not be exhaustive but will rather consider the common and major problems that these countries are facing. Their resolution will be systematically assessed through the lens of the AMA.

- The international relationships: This section will address the place of the AMA on the global stage, considering the different international actors involved in African health systems: NGOs, WHO and intergovernmental agencies and their various health initiatives on the continent but also the different private non-profit actors, especially foundations that works on the continent.

The second part of this analysis was based on interviews with experts. The core of this work being related to ongoing events and recent information; it seems difficult to look after a general opinion. Indeed, the creation of the AMA is still quite confidential, even for some healthcare experts. Another way to address the subject was to contact key actors in health to understand how the AMA will affect clinical research. For the sake of objectivity, the situation has been evaluated with the help of experts coming from different background. Firstly, they differed from the region that they come from and secondly, they differed from the interests that they defend. That is why African and Occidental actors, both from private and public sectors, were interviewed.

To understand the overall situation of clinical research in Africa and the potential impacts of the agency, three distinct topics were addressed:

- Pharmacoeconomics: The objectives of those questions were to understand how the economic model of the AMA could impact healthcare regulation in general but more specifically clinical trials regulation.
- Policies: Policies are the basis for new regulation. A global harmonisation of regulation as wanted by the AMA implies changes in policy
- Ethics: Ethics is at the basis of good clinical practices. It implies that modifications in regulation of CTs could lead to changes in ethic policy.

It also seemed relevant to contact professionals directly involved in trials, whether they are clinicians or trial coordinators due to their practical perception of the specificities linked to conducting CTs in Africa.

For each of those area of interest, a battery of questions has been prepared in advance to ensure consistency in the way people of interest are interviewed (Appendix 2). Each question is motivated by the thoughts generated by the documentary research done beforehand. The interviews started with several common questions to understand the expertise of the key person and his/her knowledge of the situation. Then, depending on the field they cover, the questions were different.

The questionnaires were submitted to Prof. Y. Geysels for approval and then, the process of recruiting the first experts began. They included colleagues and acquaintances working on Africa, members of the academic staff of the University of Namur and members of the Institute of Tropical Medicine in Antwerp. Further recruitment was done through a "tree system". Each person recruited was invited to mention other experts who could answer the questionnaire and who could be contacted.

The inclusion and exclusion criteria were as follows: those contacted had to have expertise in minimum one of the three areas mentioned above and have worked in some way with an African country. Knowledge of events related to the creation of the AMA was not mandatory. To ensure that these criteria were met, each speaker was contacted by email beforehand to explain the interview request. A short abstract (Appendix 1) was attached to this email explaining the context of the work. The email specified that the interview could be conducted face-to-face or via video conference and in English or French, depending on their preference.

If they sent a favourable response to the request, they received the questionnaire that best suited their choice. The idea behind sending the questionnaire in advance was to give them time to construct nuanced answers and they were given the opportunity to ask questions about the questionnaire if they had any queries.

Except for one stakeholder who could not make time for the interview and therefore sent back his completed questionnaire by email, all stakeholders were interviewed in person. Whether by videoconference or face-to-face, each interview was recorded and later transcribed (Appendix 3) in the language in which it was conducted to avoid any translation problems. The interviews themselves followed a semi-directive mode[56], the questions of the questionnaires were all asked but the answers were free, it was sometimes necessary to direct the conversation to follow the initial thread. Some interviewees also raised issues outside the initial context of their questionnaires, but which related to other areas of study. These responses were nevertheless considered. At the end, eight experts responded: four of them were specialised in ethics, one was a clinical trials coordinator, one was an expert in pharmacoeconomic and two were specialised in policymaking. All these stakeholders have been anonymised so as not to associate their opinions with those of the institutions they work with.

Analysis

1 Literature review

1.1 Impact on the private sector

The African Union stated that the AMA main mission would be to promote harmonisation of health product regulation and scientific guidelines. Combined with the coordination of existing initiatives, such as the Regional Economic Communities, these harmonisation measures aim to provide African populations with access to safe, effective, and affordable medicines[52]. Indeed, the continent holds macabre records, such as the highest infant mortality rate, which could certainly be curbed by better access to medicines[57]. However, this is a very difficult task for LMICs whose NRAs are often unable to carry out the regulatory work necessary to bring certain medicines to market. This lack of capacity increases administrative delays and drives industry away to other regions[37]. There is little manufacturing industry on the continent which forces countries to depend on others for their production of health products. This reality was particularly felt during the COVID-19 pandemic. The continent has had a severe shortage of vaccines and to date has not been able to join the WHO's vaccination plans[58] . The same applies to research and development of new drugs because few clinical trials are carried out in the region.

However, the African continent is home to more than 1.4 billion people in a territory almost three times the size of Europe, and with a median age of around 20 years, the population is the youngest on earth[59]. However, the continent has several endemic infectious diseases such as malaria, tuberculosis, and HIV[43]. Looking at the situation pragmatically, it appears to be fertile ground for the pharmaceutical industry. there is a need to be fulfilled. The main obstacle to this collaboration would therefore be a question of regulation, according to the African Union, and the authors working on the issue tend to agree.

Thus, Dansie *et al*[60]., established, in a survey of industry players in 2019, that the harmonisation initiatives led by the AMRH in the RECs were a good way forward. By breaking down regulatory barriers and creating a free trade area in terms for health products, the AMRH has made the East African community a more open market for the industry. The East African Community (EAC) has extended its free trade economic partnerships to health products and has

also proposed common measures to regulate the circulation of medicines. Countries with fewer resources, such as Rwanda, Burundi, and southern Sudan, have been able to benefit from the momentum created with their neighbours. On the other hand, their neighbours with more resources with regulatory systems that are better able to deal with marketing applications, for example, have been able to offer a larger market to investors by relying on their neighbours' collaboration. Although the industry still complains about long delays and notes administrative problems, particularly in relation to the import-export of medicines outside the EAC, it welcomes the initiative.

AMA has on its agenda the idea of working in collaboration with existing bodies and does not want to deconstruct existing initiatives. Insofar as it would help the RECs, it could help them to close their current loopholes and meet their accessibility objectives. It could open the market by inviting its members to coordinate their procedures and adapt their measures for marketing authorisation, manufacturing, importation and exportation of health products.[61] The political position of the AMA would allow it to guide the national policy of each of its member states. After the reservations that the industry seems to have about the results of harmonisation in the EAC, it might be appropriate to work more closely with the private sector. Such collaboration would allow to be most aware of the industry's wishes regarding regulation and to act accordingly[60].

It is true that the AMA treaty does not explicitly state that the agency will establish relationships with industry, but they seem necessary to achieve the agency's accessibility objectives. On further analysis of the structure, objectives, and future operation of the AMA, there is similarities in its operation to the EMA[46]. A supranational health policy agency that coordinates and facilitates exchanges between its members while not impinging on the role of their national authorities. The EMA's attitude towards companies is described in a 2016 press release. To ensure that its population has access to essential medicines, Europe offers incentives to companies: more flexible legislation for certain diseases, market exclusivity, tax benefits, etc. All these measures are taken with a view to stimulating innovation and ensuring accessibility to new medicines. These incentives have been discussed with the industry to be relevant. The same could be done for the AMA[62].

In the same press statement, the Council of Europe notes the importance of balance in such incentive decisions. Indeed, if they are too permissive, they will not leave room for negotiation with the member states. This concern is even more valid on the African continent and its LMICs. On one hand, the industry has the power to respond to pressing demand, and on another hand, small countries have little negotiating leverage because they need what is on offer. To ensure that these collaborations are fair, the AMA should also mediate with the pharmaceutical companies. This can only be done if the agency ensures its independence. The AMA treaty seems to take these considerations into account, as it subjects the members of its technical committee to a declaration of conflicts of interest[52].

The agency should ensure a degree of independence and transparency from industry so that their collaborations serve its purposes. Beyond a question of justice, the transparency that the agency should demonstrate could facilitate the work of the industry on the ground. The COVID crisis has revealed that beyond the accessibility of health products, the continent suffers from a complicated history of clinical research. Past incidents and abuses, particularly in clinical trials, have undermined the trust of the African population in the pharmaceutical industry and health institutions[63]. This mistrust has created a climate of doubt that has given way to falsified and poor-quality medicines[64]. By creating a climate of trust and transparency it would be possible to restore this trust, which would be beneficial for all.

Another consequence of the population's lack of trust in the pharmaceutical industry is the use of so-called "traditional" medicines. These medicines, which are most often of plant origin, are used by the population because they are more accessible than manufactured medicines and have a positive connotation due to their long-standing use[65]. These traditional medicines meet the needs of the population that are sometimes not even met by the industry because of the lack of affordable or just existing medicines. The case of *artemisia annua* antimalarial teas is an example. In the absence of affordable medicines, African doctors prescribe these herbal teas, whose main plant is the active ingredient in common antimalarial drugs[66]. Unfortunately, not all traditional medicines are equally effective and sometimes even dangerous[67]. The industry must therefore be aware of this alternative reality and if it wishes to expand in the country, it must take this into account. The AMA has an agenda to regulate and standardise traditional medicines while fighting dangerous and falsified products. This supports the idea that for a proper set-up in the region, industry must work hand in hand with the agency.

1.2 Impact on African countries

Africa has high burden of infectious and non-infectious diseases and unfortunately its health system is struggling to contain them. The continent suffers from a lack of production units and poor supply chains, which increases the price of raw materials. These problems, combined with failures in price regulation, leave room for alternative medicines that are often counterfeit due to the lack of a proper patent policy. This also forces the continent to import most of its medicines[58]. In addition, there is a lack of infrastructure and qualified personnel due to a lack of funding in the sector. However, it would be wrong to consider Africa as a single block, as each country handles the situation differently. This can be seen by comparing them from the point of view of research and access to medicines.

Simpkin *et al* in 2019 [68], set out the trends in research and development on the continent. Where most high-income countries invest at least 2% of Growth Domestic Product (GDP), the African average was around 0,4% in 2016. This disparity in investment is not only seen on an intercontinental scale but also within the African continent itself. Thus, where South Africa, Nigeria or Egypt invest almost 1% of their GDP in research, Algeria or Cape Verde invest less than 0.1%. The consequences of these disparities can be seen in the capacity of each country to carry out research. In 2014, the African average of researchers per million inhabitants was 198, well below the 4000 in the USA but also below the Egyptian average of 878. These African researchers are mostly from the 21 largest universities on the continent which are shared between only 7 countries: South Africa, Uganda, Ghana, Kenya, Egypt, Morocco, and Nigeria. These seven countries are, not surprisingly, the leaders in clinical research on the continent This context and these constraints are synonymous with an overall lack of capacity for research on the continent which leads to a lack of attractiveness for companies. In terms of access to medicines, the continent exports between 70% and 90% of the medicines it consumes. However, there are some 400 local manufacturers who export mainly to the south and east of the continent. However, most medicines come from China and India, countries that have 10 and 30 times more production units than Africa respectively. The few African production units are in the same regions that invest more in research and have NRAs with higher levels of maturity[58].

Even if these obstacles have a strong political root: relative but common political instability in Africa, corruption, high taxation of health products, lack of intellectual property laws and above all a lack of legal framework for research[69], there is still a question mark over the economic dimension of the situation. While some countries have the resources to improve their health systems, others have far fewer.

In the AMA treaty, the African Union leaders clearly state that the agency will be supranational but that it will not override the decisions of national agencies. It will act as a facilitator and coordinator to provide political guidance to its member states (*Figure 7*). This could solve the political dimension of the problems that is plaguing Africa. By providing a better-defined framework for regulators, the agency could facilitate the work of regulators in terms of taxation and patents. With a better-defined framework, it would also leave less room for corruption. However, there is no indication that the agency will have the financial means to support changes in its least wealthy members.

Similar initiatives already exist through structures such as the RECs. It would therefore be interesting to study the effects of the RECs on the countries that make them up to identify improvements and limitations[46]. In this way, the effects and usefulness of a larger scale coalition could be assessed. As the East African community (EAC) was the first to implement harmonisation initiatives in drug regulation, it will provide the most information[36]. The EAC, which is made up of six countries: Burundi, Kenya, Rwanda, Southern Sudan, Tanzania, and Uganda, launched its health harmonisation initiative in 2012. Through a series of working groups, some members have been given leadership responsibilities for certain issues. For example, Tanzania is responsible for drug evaluation and registration, Kenya for quality management, Rwanda for information management and Uganda for good manufacturing practices (GMP). The other members, who have less capacity, were supported by their neighbours in a healthy collaboration. The tasks of regulation are shared according to the capacities of each, and the personnel to carry out these tasks is also shared. In theory, this system is beneficial for everyone and benefits the populations of each of the countries concerned[36]. However, as Ndomondo-Sigonda *et al.* point out, in practice the EAC has some problems with its funding and more specifically with its management[70].

Firstly, although in this partnership everyone is supposed to contribute according to their capacity, countries like Burundi can only contribute with difficulty. Indeed, where each of the EAC members enjoys heterogeneous funding from the country's treasury, private investments and various international donations, Burundi can only rely on its own funds[70]. The small country does not attract investors due to its little population [68]. As a result, it is unable to meet the costs of all that this collaboration requires. Since 2012, Burundi has trained 4 pharmacists in drug quality control but due to lack of funds, it has not been able to pay them properly and they have left for other organisations or companies[36].

Secondly, the funding allocated to EAC missions does not always correspond to their real costs. Some budgets are released for projects that do not require so much and, reversely, some services offered by national agencies are not properly invoiced. There is therefore a lack of clarity about the costs of these activities, which are still new for some countries[70]. These loopholes are undoubtedly opportunities for corruption[69].

Finally, in stark contrast to Burundi, countries such as Uganda rely almost entirely (>98%) on private funds to finance their missions[70]. Considering the sensitivity of the tasks of national agencies (drug export policy, regulation of drugs and their clinical trials, etc.), it is problematic that they are dependent on companies that will mainly defend their interests.

It is now necessary to determine whether AMA could have known about these flaws. By acting as the primary intermediary with international actors, AMA could address the lack of heterogeneity in terms of funding sources for some small countries. By acting as a go-between, AMA could redistribute the various grants and donations to the countries that need them most. This system makes even more sense when linked to the second problem mentioned above related to poor cost estimation. Some agencies, such as the Ghana FDA, are overwhelmed by

donations and do not know what to do with them when some of their neighbours are desperately short of funds[68].

The AMA, in addition to redistributing its funds according to the needs of each of its stakeholders, aims to propose draft legal frameworks for each of the issues concerning the regulation of medicines as the AU Model Law. Although it does not have the power to incorporate these draft laws into the constitutions of its members, it does have the capacity to mandate teams to work on the development of these. Indeed, one of the main sources of these legal uncertainties is the lack of qualified personnel to work on them[71]. Ideally, therefore, in guiding the policy of its members, the agency should promote the training of qualified personnel in the countries it will support. This could be done by subsidising infrastructure and schools or by facilitating training in neighbouring countries if the first option is not feasible[68].

In practice, there is no certainty about what the agency will do as its executive bodies do not yet exist and it has not yet presented any concrete actions. However, the AMA treaty gives some indication of its ambitions. The second paragraph of its 29th article states that the member states of the agency will establish the calendar and focal points for its activities. It will be necessary to wait to see all this take shape.

1.3 Impact on international relationships

The AMA treaty sets out in its 30th article the range of actors with which the agency will be prepared to collaborate. It turns out that it does not contain any restrictions and leaves the possibility for the agency's executives to judge the merits of the relationships it establishes. However, the article specifies that it will maintain privileged contacts with the WHO, the Africa CDC, and the RECs. The same applies to the various United Nations organisations and NGOs already working on the continent.

The AMA is modelled on the EMA[46], so the two agencies will undoubtedly have a close relationship if only to set up its operations. In February 2022, the European Union announced its support of 100 million euros for the AMA's regulatory tasks[72]. This support also extends to the various associations and NGOs working in the wake of the EMA, such as the European & Developing Countries Clinical Trials Partnership (EDCTP)[45].

Beyond Europe, numerous links have been created in recent years with Asia, so much so that China has become the second largest importer of medicines into Africa. India also maintains privileged relations with the continent[58]. As both countries have also undergone major reforms in their health systems to improve access to medicines, they could be key allies for AMA. China has been running a public health campaign against malaria since 2010 and announced zero cases in 2017. It therefore offered to share its experience internationally, particularly in Africa, where the disease is a widespread health problem[73,74].

The agency could also count on the collaboration of the United States, which in 2020 will celebrate 20 years of official partnerships to support public health in Africa. Over $100 billion distributed to support health services in sub-Saharan Africa[75]. Private initiatives in the United States, however, have been around longer. An initiative like United Support of Artists for Africa (USA for Africa) and its song "We are the World" has raised more than 100,000,000$ “to help ease the pain of poverty in Africa”[76]. The Bill and Melinda Gates Foundation (BMGF) can also be mentioned for the various funds it raises for Africa. It has also contributed to the 100 million allocated by the EU to AMA[77]. These types of private initiatives bring a considerable financial windfall to the continent but are less explicit about their actions than public initiatives.

This foreign financial mass that has fuelled research in Africa for decades has given rise to reflection by some authors. Indeed, Taylor-Robinson *et al.* denounce a situation of dependence of African countries which, in the absence of infrastructure and a correct framework, relies entirely on donations. In the case of clinical research, for example, this context destabilises the relationship between African researchers and patients about foreign researchers and their substantial resources. Negotiations would therefore be biased, and African refusals would be difficult to accept. Authors associate this complicated relationship with a neo-colonial drift in research. This type of drift can only be avoided by having strong ethics committees reviewing research proposals[78]. While it is true that a single African country may lack clout in the face of ambitious investors, support from a supranational agency such as the AMA could make a difference. The agency would thus act as a buffer to bring weight to negotiations with foreign actors.

Chattu *et al.* stated in 2021[43] that the real role of the AMA will not be to take the place of other institutions already in place (RECs, NRAs...) and start from scratch but rather a global health diplomacy (GHD) role. A role of intermediary and negotiation that some states alone could not assume.

1.4 Comparative analysis

Although the creation of the AMA has been officially initiated, it has so far, no concrete action. The literature on the agency is therefore sparse and based mainly on supposition. There are many hypotheses about its functioning and impacts. It therefore seemed appropriate to compare these hypotheses with the opinions of professionals working in the African context. The impact of AMA is examined from three angles: regulatory, ethical, and economic. To give it a more concrete aspect around which to analyse the situation, the reflection was focused on the impacts that the agency could have on clinical research, more specifically.

1.4.1 Preamble

Each of the interlocutors who intervened in this reflection defended different interests and points of view. However, they all argued that coordination on health issues on the continent would be beneficial and even necessary. In this sense, they are in line with the available literature. However, they are not all certain about the feasibility of AMA's objectives. Some are positive about the future of the agency, while others have more reservations. What is unanimous, however, is that the continent is currently suffering from a lack of accessibility and regulation of health products and that this problem must be addressed. On this point, all agree that solutions will be found through collaborations. Opinions on the nature of these collaborations differ. Some consider partnerships with industry; others fear its influence. Some talk about links with other international agencies, others advocate approaches within the continent itself. This comparative analysis will be based on the reflections of these discussions and will explain the divergent and convergent opinions through three key themes in clinical research.

1.4.2 Regulatory and policies

All experts seem to agree that harmonisation of regulation is needed. Sharing practices and networking expertise should help to improve access to health care. The various initiatives that took place in recent years in Africa lead them to believe that harmonisation is possible.

It should be possible to build on the foundations laid by the RECs. It would also be possible to evaluate the progress of the different regulatory agencies using the new tools available, such as the WHO benchmarking tool. It would be beneficial because it would create a network of expertise that would benefit everyone. In this way, it would be possible to avoid duplicating efforts and each country could learn from the past and future experiences of other members to strengthen its expertise. All this with the aim of saving time in the process. These changes could attract the industry to a more accessible market, provided that the agreements reached by the AMA also strengthen the regulation of non-African relationships.

A proposed model for this regulatory collaboration would be that of the EMA. The procedures would be similar throughout the country and the AMA would be responsible for centralisation. However, it was pointed out that the economic situation in Africa is very different from the situation in Europe and that this system might not be feasible. There are many disparities in terms of resources on the continent and an "equal sharing of tasks" could be complicated to implement. An alternative model proposed by one of the experts would be a model with three levels of competence: continental, regional and national. As pharmaceuticals are very diverse in nature, they require different efforts when it comes to assessing and regulating them. A model like this would therefore call for a higher level of expertise when resources are lacking. A simple generic drug whose molecule is already known and evaluated in a neighbouring country could be treated at a national level in a country like Burundi. On the other hand, a monoclonal antibody or a vaccine that requires more steps should be evaluated on another level with the help of other countries or the agency directly.

Another proposal made by an expert could be added to the latter and would apply more to clinical trials and their experimental products. It would be an accreditation system that the Agency would grant to sites that follow its standards and requirements. This would ensure the validity of the data that emerges and make it easier for countries with fewer resources to evaluate it. While this system is initially proposed for testing sites, it could be extended to drug production sites, storage sites, etc. It would then be a matter of setting up standards specific to the continent. Ideally, these standards should be in line with the ICH standards, but it is imperative to consider the specificities of the continent because, according to several experts, international guidelines do not take them into account. Among these specificities, there is that of traditional medicines for example. These medicines are on the agency's agenda and must be regulated because local people will not stop using them.

The last thing the experts highlighted was the presence of competent people on the continent and the importance of health regulators. They argued that the lack of experts in public institutions is mainly due to a lack of opportunities. The best trained and most competent people find work in international institutions if they do not have a place to practice. Networking of expertise and harmonisation that would strengthen the institutions would therefore be a way of bringing in competent people. In the end, all experts agree that the changes the AMA is proposing can only come from political choices and that it is therefore the politicians who must initiate the process.

The question remains, however, that the majority of experts interviewed, while agreeing that research and access to medicines would be improved on the continent if the AMA was established, did not talk at all about initiatives from Africa itself. Whether it is clinical research or the pharmaceutical industry in general, the projects are initiated by foreign actors. This raises the question that emerged during the literature review: "What would be the place of African actors in projects that are not initiated or funded by them? One expert mentioned, for example, that some trial sites do not have the funding to operate when they do not have ongoing projects. They are therefore extremely dependent on the funding and trials they are allocated.

Some mentioned the imbalance that this situation causes in the interviews. It can give rise to certain abuses against which ethics committees have an important role to play. The AMA must therefore consider the ethical dimension that these objectives imply.

1.4.3 Ethics

Ethics committees are not new in Africa. The various research-related incidents in the 1990s[63] initiated the establishment of ethics committees on the continent. However, once again, they do not all have the same means. There are good training programmes to train competent professionals in research and health ethics. Some ECs even find themselves in charge of tasks normally carried out by NRAs due to the lack of sufficiently competent authorities. However, due to lack of resources, some ethics committees work on a voluntary basis or are totally dependent on external funding. Some speakers emphasised that this situation depends only on policy makers. The AMA, if it wants to ensure proper ethics review within its member countries, should promote the role of ECs to be funded by their governments. At present, the ECs are experiencing the same problems as the regulatory bodies, because without adequate funding, competent workers flee to other institutions to exploit their skills. A political will to re-emphasise the importance of their work would bring ethics specialists back into the institutions. In order to function properly, the regulatory agency and the ethics committee must work closely together and what is good for one must, to some extent, be good for the other. If AMA wants to strengthen the NARs, it cannot forget in its policy to do the same for the ECs.

Harmonisation of the regulatory bodies implies the same approach within the ethics bodies. Indeed, the ethical evaluation of research cannot be dissociated from scientific evaluation[7]. Therefore, if one party does not follow these harmonisation steps, the agency would be exposed to problems in its evaluation processes in the future. Considering a multi-site, multi-country clinical trial, for example, it would be complicated to provide a CTA in a reasonable time if the ECs do not agree among themselves. It appears that this situation has already been taken into account in the harmonisation initiatives in the field of health within the RECs. For example, the Economic Community of West African States (ECOWAS), through its health organisation (OOAS/WAHO)[79], has put in place a harmonisation of ethics committees within its territory. This approach could, as with the NAR, be a starting point for a global harmonisation of ethics on the continent.

Nevertheless, these harmonisation initiatives should not obscure the disparity of resources on the continent. As with the NRAs, it would be illusory to think that overnight all ethics committees will operate at the same level. Harmonisation can therefore only be possible if it considers the capacities of each member state and creates a network where more vulnerable actors can rely on actors with more capacity. It would not be advantageous to ask a small country with little capacity to do the same work as a more advantaged country.

This harmonisation must also consider the same specificities of the territory. Although ethics is basically universal, it is context specific. Relying on international guidelines is therefore essential but not sufficient. These guidelines are often composed for countries where access to health care is easier than in Africa for example. They also do not consider the place of the individual within his or her community, where this place is sometimes very important in certain African countries. These specificities are common to many LMICs and there are specific guidelines[80,81] for these particular contexts that the AMA must take into account if it starts harmonising ECs too. As for regulatory issues, one expert proposed harmonisation at different levels to take these specificities into account. Indeed, the continent is a mosaic of different cultures and communities, if only by comparing the linguistic blocks: Portuguese-speaking, Arabic-speaking, French-speaking or English-speaking. It could therefore be necessary to set

up regional and central ethics offices in addition to local ECs. In this way, each problem could be addressed by an interlocutor who is closest to the issue.

Consistency between regulators and ECs is essential to leave no loopholes in the evaluation of files. In a research context that involves many essential actors, this cohesion would make it possible to establish strong bodies and a framework that would be able to prevent abuses. In this way, the member countries of the AMA would be able to properly evaluate and refuse research that, at best, would not benefit researchers and populations, and at worst, would totally exploit them. The latter practice, known as ethics dumping[82,83], is the practice of exporting unethical research practices from a privileged environment, both intellectually and financially, to a less privileged environment. This process can be intentional in the case of researchers exploiting the legal ambiguity of research ethics in certain countries/communities or unintentional in the case of a lack of training of researchers. This dumping can therefore directly harm local populations by injuring them, making them sick or killing them, but also by despoiling their resources without their informed consent. To avoid these abuses, AMA must be firm and defend its members to avoid double standards. The risk, as one of the experts points out, is that some countries may be attracted by the lucrative aspect of certain research and lighten their evaluations. However, the lack of resources remains a real problem on the continent. As mentioned earlier, the agency itself will need funding. It has already received funding from various international bodies. As the agency's missions are important, it must maintain a certain independence and impartiality in its policy. As one of the speakers said, the origin of the funding will certainly influence its choices.

1.4.4 Pharmacoeconomics

It is certain that the various objectives of the AMA will require substantial resources to be put in place. The agency will need to rely on external investors as some African states are already struggling with their contribution to the AU and will find it difficult to add to their contribution to the AMA. It is therefore legitimate to ask how the agency will finance its activities as this is likely to have an impact on its functioning. According to one of the speakers, at first sight, the agency will have to rely on the support of private or public contributors such as the BMFG or the EU for example[62,77]. Then in the long term it will have to migrate to a more independent model based on contributions from countries but also from industries wishing to work on the territory. As for the question of whether this will influence the agency's decisions, it probably will to some extent, but it should not impact on the quality of the research. Indeed, neither private nor public contributors have any interest in poor regulation of research and medicines. According to the expert, in this context everyone stands to gain as long as the relationships are made in full transparency. The industry is aware that Africa is a market to be explored and the continent needs better access to health products. However, that such an investment will not be made from pure altruism on the part of the private sector and that the sector will have to find its own way. This suggests that the incentive system mentioned above is a possibility.

As for the place of a future African market in relation to other global players, he said that it would not have a negative influence on existing markets and would rather benefit the people of the continent by boosting the development of local infrastructure. This opinion may be debated, as a certain relocation of research to less expensive countries, particularly in Asia or Eastern Europe, has been observed in recent years[84]. This "migration of research" could also take place towards Africa, but everything will depend on the policy that AMA will adopt. An opening to all types of research or a focus on certain specific issues.

1.4.5 Limitations

Although this work has tried through its method to avoid bias, it still shows some limitations.

The first is due to the Belgian socio-cultural context in which this work was written. Belgium is a high-income country with a highly mature NRA. Furthermore, 6 of the 8 experts interviewed come from similar backgrounds. In the end, only two of the experts interviewed had direct experience of an African health care context. The relationship to health and research is strongly linked to the socio-cultural context and this analysis would have been very different if this work had been written in Africa or in another context. Furthermore, although the continent suffers from health-related problems overall, this is not true at all levels. There are a number of preconceived notions that the West has about Africa that skew the way in which health issues are understood.

The second limitation of this work is indirectly related to this reality. Africa in this work has been several times considered as a homogeneous block. Even if the disparities that exist on the continent have been noted, certain generalisations have been made to facilitate the analysis and to fit it into the format that this work requires. Some inaccuracies therefore remain, as the situation differs significantly between the 54 countries that make up the continent. A more detailed analysis would have required more information and data, as well as a range of other skills that are outside the scope of a master's degree in biomedical sciences. A geopolitical or economic analysis of the situation could be considered

The final and most important limitation of this work is the subject matter, which implies a number of biases. The whole work is based on a study of an agency that is still in the planning stage. Since its launch at the end of 2021, the AMA is still in the start-up phase and has only received ratifications from about 20 countries. Moreover, the agency is not yet making much of a splash abroad and is still poorly or not known to public, even among health professionals. This reality has also highlighted that there is currently much less interest in the African continent in terms of research and health. This context has created a series of difficulties and biases in this work.

There is lack of literature and data available about Africa. Whether from NGOs, companies, or international organisations, it has been difficult to find usable data for quantitative analysis. The few papers available on AMA were all in the same direction and based on the same literature. In the absence of a quantitative analysis, it was decided to carry out a qualitative analysis with the help of experts, but this approach also suffers from the lack of information available on the agency.

First of all, the experts recruited were chosen among people working or had worked in Africa. This condition already considerably reduced the number of people who could be recruited. Moreover, most of the experts contacted had a high level of expertise and many responsibilities. Of the fifteen or so people who were contacted, only ten or so responded to the recruitment emails and only eight people responded positively. The refusals were often motivated by a lack of availability and the few participants also had very limited availability. These constraints partly explain the small sample size.

Only 8 experts responded to the interviews, with such a small sample it is necessary to understand their position and what could induce bias.

- One of the experts was unaware of the creation of the agency, while the other seven will see their work directly affected by the agency's decisions.

- The pharmacoeconomic expert works for the pharmaceutical industry. Even if his opinion does not commit his company, it is guided by his position. The view on the impact of the agency is therefore partial.
- One of the experts in policy and regulation is the author of leading articles on the agency. His views are therefore already partly reflected in the literature.
- The sample of experts is, by chance, mainly composed of ethics experts. This must have influenced the analysis
- Some of the experts are colleagues, which could influence the convergence of some opinions.

As the interviews progressed, new elements came to light. So much so that they were brought forward in the final interviews to confront the experts' point of view. The semi-directive mode implies an interaction between the interviewer and the respondent and therefore a risk of orienting some answers. However, the questionnaires were all identical to avoid too much rambling.

Conclusion and perspectives

At the jubilee of the creation of the African Union, the heads of its member states solemnly declared their wish to see "an integrated, prosperous and peaceful Africa, driven by its own citizens, representing a dynamic force in the international arena*"* in 2063[85]. This objective, soberly called Agenda 2063, is a direct descendant of the discussions that led to the creation of the African Medicines Agency. A well-functioning health system is part of the AU's aspirations. Indeed, as the WHO states, universal health coverage (UHC) is a sine qua non and an indicator of a sustainable and prosperous socio-economic environment[86]. By seeking to harmonise and regulate health products and clinical research on the continent, the AMA is the daughter of this agenda.

Indeed, the complex regulatory climate on the African continent is an obstacle to research and access to medicines. Procedures are long and difficult and regulatory offices lack both human and financial resources. Harmonisation of this context therefore appears to all parties, private and public, as a necessary step. Harmonising regulation to facilitate trade and provide safe and effective medicines on the continent. Harmonisation initiatives have been attempted in the past through other organisations and on a smaller scale. Although not all have been successful, they have had an impact on clinical research and access to medicines at their scale. The AMA therefore appears to be the convergence of these initiatives. A project that could build on the foundations of its predecessors.

The agency could have a large impact on research at several levels: with its member states of course, but also with industry and other regulatory agencies around the world. Assessing this impact is still complicated as the agency is still in its infancy, but it is possible to make some assumptions based on the literature. By homogenising its regulatory context, the African continent could become an exploitable market for the pharmaceutical industry. A territory where it would be possible to carry out clinical research but also a place where production units or laboratories could be set up. Freed from constraints, manufacturers could expand on the continent. This situation could have a direct impact on access to medicines, making it simpler and more indirectly bringing a significant financial windfall to the continent. More directly linked to this harmonisation, the member countries of the agency could communicate more easily in terms of regulation and feed off each other's experiences. Finally, the creation of the agency puts a new international interlocutor on the map, which could facilitate relations with partners outside the continent.

All authors discussing the agency see it as a boon to the continent and support its creation. Discussions about the AMA therefore seem enthusiastic, and the project looks promising on paper. Nevertheless, with such a large project, it is legitimate to have some reservations and to stop and ask questions about its realization and impact. Given the limited literature available, this study has sought solutions from the field. Actors who were questioned on subjects concerning clinical research but also on the potential concrete actions they envisage for the agency.

The first thing that emerges from these exchanges is the relative confidentiality of AMA. It is still only known to those working in the field, but this situation is set to change as its treaty is ratified by African countries. All experts agree on the usefulness of regulatory harmonisation and the benefits it could bring to the continent. Directly by strengthening and capacifying the regulatory structures of member countries but also by facilitating their exchanges. The

industries themselves are only asking for a favourable context to set up and are ready to participate to put it in place. Better regulation saves them time and money.

Just in the inspirations it draws from the EMA, the AMA is already showing that it will interact with many international actors. For funding, of course, but also as a model for building its policy. This reality highlights the fact that beyond its harmonisation missions, the agency will have to pay attention to its interactions with these actors. It must adopt a policy that is in line with international standards, but it must be aware of the specificities of its continent and its situation:

- A policy that gives importance to vulnerable communities and succeeds in dealing with the disparities and differences within the continent, notably by resituating the place of ethics committees in clinical research in Africa to prevent abuses such as ethic dumping.
- A policy ready to legislate the case of traditional medicines and fight substandard and falsified medicines. Something that the AMA treaty already establishes.
- A strong but transparent policy that will not leave room for corruption and can make Africa a territory where quality research can be done.

Under these conditions, Africa could fully benefit from a possible new status as a player in clinical research. It would seem that it is not only African countries that benefit from this situation. Indeed, a number of foreign industries and players, notably from Asia, have made the move towards the continent, with partnerships planned for the coming years[87]. Michel Sidibé, for example, was speaking at a summit held by IQVIA in Kenya in late 2022[88].

However, the AMA is not yet operational, and it should not be forgotten that only about 20 of the 54 countries have ratified its treaty. Political issues related to the governance of the agency would block the accession of some countries. Without these agreements, it will only be possible to speak of the agency in the conditional. Nevertheless, some actors are annoyed by the slow progress of these steps because it delays the setting up of a precise calendar It should also be remembered that the agency's main mission seems to be the regulation of medicines already in circulation. In a recent paper, Michel Sidibé stressed the importance of clinical research to create new products in a territory plagued by endemic diseases and with a young population whose genetic profile could help and improve global clinical research[89]. However, CTs are likely to be in the final stages of the agency's considerations.

It is certain that the agency will draw inspiration from its counterparts around the world to build itself. However, the creation of AMA may be an opportunity for the world to learn from Africa. Indeed, prior to the COVID crisis, the continent faced an Ebola outbreak which gave rise to the Africa CDC. It put in place a series of epidemic control measures that were used against COVID and proved effective. These measures at least partly explain the few cases that the continent has seen[90]. This experience accumulated over the years is not to be overlooked at a time when pandemics are likely to become increasingly common[91].

What is certain, however, is that if the AMA succeeds in achieving its goals, the work of thousands of researchers and scientists on the continent over the years could be highlighted and perhaps given a greater voice on the world stage.

References

1. Food and Drug Administration, F. The Drug Development Process, Step 3: Clinical Research. *FDA* https://www.fda.gov/patients/drug-development-process/step-3-clinical-research (2019).
2. The Basics. *National Institutes of Health (NIH)* https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics (2015).
3. What Are Clinical Trials and Studies? | National Institute on Aging. https://www.nia.nih.gov/health/what-are-clinical-trials-and-studies.
4. Philips-Nootens, S. Le malentendu thérapeutique : un défi pour le consentement en recherche clinique. in *Revue de droit. Université de Sherbrooke* vol. 36 133 (Université de Sherbrooke. Faculté de droit, 2005).
5. Shuster, E. Fifty Years Later: The Significance of the Nuremberg Code. *N. Engl. J. Med.* **337**, 1436–1440 (1997).
6. Riis, P. Thirty Years of Bioethics: The Helsinki Declaration 1964-2003. *New Rev. Bioeth.* **1**, 15–25 (2003).
7. ICH harmonised guideline integrated addendum to ICH E6(R1): Guideline for Good Clinical Practice ICH E6(R2) ICH Consensus Guideline. *ICHGCP* https://ichgcp.net/home.
8. Learn About Clinical Studies - ClinicalTrials.gov. https://www.clinicaltrials.gov/ct2/about-studies/learn#WhatIs.
9. Clinical Trial Phases | CERN Foundation. https://www.cern-foundation.org/education/clinical-trials/clinical-trial-phases.
10. Martin, L., Hutchens, M., Hawkins, C. & Radnov, A. How much do clinical trials cost? *Nat. Rev. Drug Discov.* **16**, 381–382 (2017).
11. National Institute of Pharmacy and Nutrition. Non-commercial clinical trials. *Országos Gyógyszerészeti és Élelmezés-egészségügyi Intézet* https://ogyei.gov.hu/non_commercial_clinical_trials.
12. Shuchman, M. NGOs push for decentralised Ebola treatment in DR Congo. *The Lancet* **393**, 2110–2111 (2019).
13. Good Clinical Practice (GCP) » Office of Clinical Research (OCR) » Clinical and Translational Science Institute » University of Florida. https://clinicalresearch.ctsi.ufl.edu/study-management/prn/regulatory-assistance/good-clinical-practice/.
14. Clinical Research Regulation For United States | ClinRegs. https://clinregs.niaid.nih.gov/country/united-states#scope_of_assessment.
15. Swissmedic 2019, © Copyright. Clinical Trial Application. https://www.swissmedic.ch/swissmedic/en/home/humanarzneimittel/clinical-trials/klinische-versuche-mit-arzneimitteln/gesuch-zur-bewilligung-eines-klinischen-versuchs.html.
16. Commissioner, O. of the. Informed Consent. *U.S. Food and Drug Administration* https://www.fda.gov/regulatory-information/search-fda-guidance-documents/informed-consent (2020).
17. Apply for a licence to market a medicine in the UK. *GOV.UK* https://www.gov.uk/guidance/apply-for-a-licence-to-market-a-medicine-in-the-uk.
18. EMA. Call to pool research resources into large multi-centre, multi-arm clinical trials generate sound evidence on COVID-19 treatments. *European Medicines Agency* https://www.ema.europa.eu/en/news/call-pool-research-resources-large-multi-centre-multi-arm-clinical-trials-generate-sound-evidence (2020).

19. Comparison: Canada and United States | ClinRegs. https://clinregs.niaid.nih.gov/country/canada/united-states#regulatory_authority.

20. Guzman, J., O'Connell, E., Kikule, K. & Hafner, T. The WHO Global Benchmarking Tool: a game changer for strengthening national regulatory capacity. *BMJ Glob. Health* **5**, e003181 (2020).

21. EMA. National competent authorities (human). *European Medicines Agency* https://www.ema.europa.eu/en/partners-networks/eu-partners/eu-member-states/national-competent-authorities-human (2018).

22. Leisinger, K. M., Garabedian, L. F. & Wagner, A. K. Improving Access to Medicines in Low- and Middle-Income Countries: Corporate Responsibilities in Context. *South. Med Rev.* **5**, 3–8 (2012).

23. ClinicalTrials.gov. Studies on Map - World. https://clinicaltrials.gov/ct2/search/map.

24. List of Stringent Regulatory Authorities - Americas (AMRO/PAHO). https://www.who.int/initiatives/who-listed-authority-reg-authorities/SRAs-amro-paho.

25. The Pan American Network for Drug Regulatory Harmonization (PANDRH) - PAHO/WHO | Pan American Health Organization. https://www.paho.org/en/pan-american-network-drug-regulatory-harmonization-pandrh.

26. Clinical trials - Regulation EU No 536/2014. https://ec.europa.eu/health/medicinal-products/clinical-trials/clinical-trials-regulation-eu-no-5362014_en.

27. Health, C. for D. and R. US/Japan Regulatory Collaboration. *FDA* https://www.fda.gov/medical-devices/cdrh-international-programs/usjapan-regulatory-collaboration (2022).

28. Ali, S., Egunsola, O., Babar, Z. D. & Hasan, S. Clinical trials in Asia: A World Health Organization database study. *Perspect. Clin. Res.* **10**, 121 (2019).

29. ClinicalTrials.gov. Studies on Map - Middle East. https://clinicaltrials.gov/ct2/search/map/click?map.x=444&map.y=175&mapw=726.

30. ASEAN Health Ministers, Economic Ministers adopt ASEAN Pharmaceutical Regulatory Policy. *ASEAN Main Portal* https://asean.org/asean-health-ministers-economic-ministers-adopt-asean-pharmaceutical-regulatory-policy/ (2022).

31. Asia-Pacific Economic Cooperation. *APEC* http://www.apec.org.

32. Administration (TGA), T. G. Therapeutic Goods Administration (TGA) | Australian Government Department of Health. *Therapeutic Goods Administration (TGA)* https://www.tga.gov.au/therapeutic-goods-administration-tga (2021).

33. Medsafe Home Page. https://www.medsafe.govt.nz/index.asp.

34. Oceania Regulator ANZTPA Shut Down by Australia and New Zealand. https://www.raps.org/regulatory-focus™/news-articles/2014/11/oceania-regulator-anztpa-shut-down-by-australia-and-new-zealand.

35. Solarin, O., Mohammed, S. I., Ndlovu, N., Vanderpuye, V. & Olaiya, V. Partnerships and Collaborations: The Right Alliances for Clinical Trials in Africa. *JCO Glob. Oncol.* 954–958 (2020) doi:10.1200/JGO.19.00194.

36. Ncube, B. M., Dube, A. & Ward, K. Medicines Regulatory Science Expertise in Africa: Workforce Capacity Development and Harmonisation Activities Towards the Establishment of the African Medicines Agency. *Pharm. Med.* **36**, 83–97 (2022).

37. Ndomondo-Sigonda, M., Miot, J., Naidoo, S., Dodoo, A. & Kaale, E. Medicines Regulation in Africa: Current State and Opportunities. *Pharm. Med.* **31**, 383–397 (2017).

38. Corcoran, B. What is a contract research organization (CRO)? *MED Institute* https://medinstitute.com/blog/what-is-a-contract-research-organization-cro/ (2022).

39. Locations. *PPD Inc* https://www.ppd.com/who-we-are/locations/.

40. Locations. https://www.iqvia.com/locations.

41. ClinicalTrials.gov. Studies on Map - Africa. https://clinicaltrials.gov/ct2/search/map/click?map.x=744&map.y=357&mapw=1325.

42. Africa Population 2022 (Demographics, Maps, Graphs). https://worldpopulationreview.com/continents/africa-population.

43. Chattu, V. K. *et al.* Politics of disease control in Africa and the critical role of global health diplomacy: A systematic review. *Health Promot. Perspect.* **11**, 20–31 (2021).

44. Edem, B. *et al.* Trends in clinical trial registration in sub-Saharan Africa between 2010 and 2020: a cross-sectional review of three clinical trial registries. *Trials* **22**, 472 (2021).

45. Makanga, M. European & Developing Countries Clinical Trials Partnership. *Impact* **2017**, 12–13 (2017).

46. Chattu, V. K. *et al.* Advancing African Medicines Agency through Global Health Diplomacy for an Equitable Pan-African Universal Health Coverage: A Scoping Review. *Int. J. Environ. Res. Public. Health* **18**, 11758 (2021).

47. Ncube, B. M., Dube, A. & Ward, K. Establishment of the African Medicines Agency: progress, challenges and regulatory readiness. *J. Pharm. Policy Pract.* **14**, 29 (2021).

48. Ndomondo-Sigonda, M. & Ambali, A. The African Medicines Regulatory Harmonization Initiative: Rationale and Benefits. *Clin. Pharmacol. Ther.* **89**, 176–178 (2011).

49. Akanmori, B. D. Presentation of AVAREF and its emergency joint-review process. (2020).

50. Home. *Africa CDC* https://africacdc.org/.

51. Zarocostas, J. Health ministers adopt African Medicines Agency treaty. *The Lancet* **391**, 2310 (2018).

52. Treaty for the Establishment of the African Medicines Agency (AMA) | African Union. https://au.int/en/treaties/treaty-establishment-african-medicines-agency.

53. African Union Congratulates Honourable Michel Sidibé, from the Republic of Mali on his Appointment as African Medicines Agency Envoy | African Union. https://au.int/en/pressreleases/20210401/african-union-congratulates-honourable-michel-sidibe-republic-mali-his.

54. African Union Selects Rwanda to Host African Medicines Agency, Grants Africa CDC Autonomous Status - Health Policy Watch. https://healthpolicy-watch.news/au-rwanda-african-medicines-agency/ (2022).

55. African Medicines Agency (AMA) | AUDA-NEPAD. https://www.nepad.org/microsite/african-medicines-agency-ama.

56. Imbert, G. L'entretien semi-directif : à la frontière de la santé publique et de l'anthropologie : *Rech. Soins Infirm.* **N° 102**, 23–34 (2010).

57. Newborn Mortality. https://www.who.int/news-room/fact-sheets/detail/levels-and-trends-in-child-mortality-report-2021.

58. Holtz, L. Figure of the week: Africa's trade in pharmaceuticals. *Brookings* https://www.brookings.edu/blog/africa-in-focus/2021/12/09/figure-of-the-week-africas-trade-in-pharmaceuticals/ (2021).

59. Population of Africa (2022) - Worldometer. https://www.worldometers.info/world-population/africa-population/.

60. Dansie, L. S., Odoch, W. D. & Årdal, C. Industrial perceptions of medicines regulatory harmonization in the East African Community. *PLOS ONE* **14**, e0218617 (2019).

61. Evaluating the sub-Saharan African pharmaceutical market | McKinsey. https://www.mckinsey.com/industries/public-and-social-sector/our-insights/should-sub-saharan-africa-make-its-own-drugs.

62. Council conclusions on strengthening the balance in the pharmaceutical systems in the EU and its Member States. https://www.consilium.europa.eu/en/press/press-releases/2016/06/17/epsco-conclusions-balance-pharmaceutical-system/.

63. Annan, B. A. and F. What do Pfizer's 1996 drug trials in Nigeria teach us about vaccine hesitancy? *Brookings* https://www.brookings.edu/blog/africa-in-focus/2021/12/03/what-do-pfizers-1996-drug-trials-in-nigeria-teach-us-about-vaccine-hesitancy/ (2021).

64. Adebisi, Y. A. *et al.* Revisiting the issue of access to medicines in Africa: Challenges and recommendations. *Public Health Chall.* **1**, e9 (2022).

65. Abdullahi, A. A. Trends and Challenges of Traditional Medicine in Africa. *Afr. J. Tradit. Complement. Altern. Med.* **8**, 115–123 (2011).

66. de Ridder, S., van der Kooy, F. & Verpoorte, R. Artemisia annua as a self-reliant treatment for malaria in developing countries. *J. Ethnopharmacol.* **120**, 302–314 (2008).

67. Byard, R. W., Musgrave, I., Maker, G. & Bunce, M. What risks do herbal products pose to the Australian community? *Med. J. Aust.* **206**, 86–90 (2017).

68. Simpkin, V., Namubiru-Mwaura, E., Clarke, L. & Mossialos, E. Investing in health R&D: where we are, what limits us, and how to make progress in Africa. *BMJ Glob. Health* **4**, e001047 (2019).

69. Zola Matuvanga, T. *et al.* Setting-up an Ebola vaccine trial in a remote area of the Democratic Republic of the Congo: Challenges, mitigations, and lessons learned. *Vaccine* S0264410X22005448 (2022) doi: 10.1016/j.vaccine.2022.04.094.

70. Ndomondo-Sigonda, M. *et al.* National medicines regulatory authorities financial sustainability in the East African Community. *PLOS ONE* **15**, e0236332 (2020).

71. Nabyonga-Orem, J., Asamani, J. A. & Makanga, M. The state of health research governance in Africa: what do we know and how can we improve? *Health Res. Policy Syst.* **19**, 11 (2021).

72. African medicines regulators receive boost of 100 million. *European Commission - European Commission* https://ec.europa.eu/commission/presscorner/detail/en/IP_22_993.

73. Chen, J.-H., Fen, J. & Zhou, X.-N. From 30 million to zero malaria cases in China: lessons learned for China–Africa collaboration in malaria elimination. *Infect. Dis. Poverty* **10**, 51, s40249-021-00839-y (2021).

74. Lin, S. *et al.* China's health assistance to Africa: opportunism or altruism? *Glob. Health* **12**, 83 (2016).

75. Tbilisi, U. S. E. 20 years of aid: America's ongoing support for Africa's public health [video] (July 15). *U.S. Embassy in Georgia* https://ge.usembassy.gov/20-years-of-aid-americas-ongoing-support-for-africas-public-health-video-july-15/ (2020).

76. Home. *USA For Africa* https://usaforafrica.org/.

77. Ahead of EU–AU Summit, African Medicines Regulators Receive Boost of More Than 100 Million Euros from Team Europe and The Bill & Melinda Gates Foundation. *Bill & Melinda Gates Foundation* https://www.gatesfoundation.org/ideas/media-center/press-releases/2022/02/100-million-euros-donated-to-fund-african-medicines-agency.

78. Taylor-Robinson, S. D., Spearman, C. W. & Suliman, A. A. A. Why is there a paucity of clinical trials in Africa? *QJM Int. J. Med.* **114**, 357–358 (2021).

79. Inaju-Challydoff, D. L'Organisation Ouest-Africaine de la Sante (OOAS). | Economic Community of West African States (ECOWAS). *—D'une CEDEAO des Etats à une CEDEAO des peuples* https://ecowas.int/institutions/west-africa-health-organisation-waho/?lang=fr.

80. Emanuel, E. J., Wendler, D. & Grady, C. What makes clinical research ethical? *JAMA* **283**, 2701–2711 (2000).

81. TRUST. Global Code of Conduct for Research in Resource-Poor Settings. *Global Code of Conduct* https://www.globalcodeofconduct.org/ (2018).

82. Schroeder, D. 'Ethics dumping' – the dark side of international research. *The Conversation* http://theconversation.com/ethics-dumping-the-dark-side-of-international-research-88675.

83. *Ethics Dumping: Case Studies from North-South Research Collaborations*. (Springer International Publishing, 2018). doi:10.1007/978-3-319-64731-9.

84. Cooper, M. Experimental Labour—Offshoring Clinical Trials to China. *East Asian Sci. Technol. Soc. Int. J.* **2**, 73–92 (2008).

85. Agenda 2063: The Africa We Want. | African Union. https://au.int/en/agenda2063/overview.

86. Universal health coverage (UHC). https://www.who.int/news-room/fact-sheets/detail/universal-health-coverage-(uhc).

87. Bartlett, K. China Paving 'Health Silk Road' in Africa. *VOA* https://www.voanews.com/a/china-paving-health-silk-road-in-africa/6780782.html.

88. IQVIA Africa Health Summit. https://www.iqvia.com/locations/middle-east-and-africa/events/2022/09/iqvia-africa-health-summit.

89. Hwenda, L., Sidibe, M. & Makanga, M. The African Medicines Agency: the key to unlocking clinical research in Africa. *Lancet Glob. Health* S2214109X22002431 (2022) doi:10.1016/S2214-109X(22)00243-1.

90. Happi, C. T. & Nkengasong, J. N. Two years of COVID-19 in Africa: lessons for the world. *Nature* **601**, 22–25 (2022).

91. Poorolajal, J. The global pandemics are getting more frequent and severe. *J. Res. Health Sci.* **21**, e00502–e00502 (2021).

APPENDICES

APPENDIX 1

This short abstract was sent with the recruiting emails to introduce the subject

The African Medicine Agency: analysis of regulatory impact on clinical trials

Clinical trials are still the safest way to assess the efficacy and safety of health products before they reach the market. They play a key role in determining the fate of medicines. Following some historical abuses, clinical research is highly regulated and is under the supervision of different national and supranational bodies such as the FDA or the EMA. These two major agencies oversee thousands of trials every year, some of which result in new drugs. Clinical research thus makes it possible to provide safe medicines to the population according to its needs. However, when it comes to clinical trials, not all countries are on the same page. Most African countries host only a few hundred trials per year and therefore very few new medicines are marketed. Yet these countries suffer from numerous public health problems and lack accessible medicines for the various diseases that plague them. To address these concerns, in February 2019, the African Union (AU) and its member states concluded 10 years of negotiations by establishing a treaty announcing the creation of a continental health agency: the African Medicines Agency (AMA). In November 2021, following the ratification of this treaty by the minimum of 15 member states, the AMA project was launched. The launch was undoubtedly delayed by the health situation that hit the world in 2020. The Covid-19 pandemic, preceded by an Ebola outbreak a few years earlier, underlined the extent to which the continent needed to get its health system in order. Indeed, many African countries do not have the capacity to provide a proper health system because they simply do not have the legal framework to cover its activities. From importing/exporting medicines, to placing them on the market or manufacturing them, the rules differ between countries, where they exist. This context makes access to health products complicated. However, some countries, such as South Africa, stand out for their well-established legal framework and better-than-average health system. making it the leader in clinical research in Sub-Saharan Africa. In creating a continental agency, the AU's wish was to bring together the strengths of all African countries to sustainably improve their global capacity to carry out scientific research. As the AMA is still in its infancy, it remains to be seen how it will influence the regulation of clinical research.

APPENDIX 2

These are the standard questionnaires sent after the recruitment phase

The African Medicine Agency: analysis of regulatory impact on clinical trials

Key people interview: Ethics experts

- Present yourself: What are your areas of expertise? Are you familiar with clinical trials? With their regulation?
- Are you aware of the situation of CTs across Africa? Have you worked from near or far in/with this context?
- Are you aware of the creation of the African Medicine Agency? Do you know its objectives?
- Health Ethics Committees are rather new across Africa and are even inexistant in some countries. However, EC are essential to set new rules concerning healthcare, especially CTs. How do you think AMA will handle this reality?
- Does global harmonization in regulation means global ethic harmonization? What standards will be used to set up the ethical context of member countries (ICH-GCP)?
- Do cultural differences between member states and/or occidental countries will impact those modifications?
- The AMA claims to be only led by African actors but its initiative involves number of international actors. Atrocities that have happened in the past during North-South studies show how a good ethic context is vital. How could the AMA make sure of that? What should be its ethic model?
- Do you want to add something that has not been covered by our interview?
- Would you be available for further questions in the context of this work?
- Do you know anybody that could interested to participate in this work?

The African Medicine Agency: analysis of regulatory impact on clinical trials

Key people interview: clinicians and clinical trials coordinators

- Present yourself: What are your areas of expertise? Are you familiar with clinical trials? With their regulation?
- Are you aware of the situation of CTs across Africa? Have you worked from near or far in/with this context?
- Are you aware of the creation of the African Medicine Agency? Do you know its objectives?
- According to you and your experience what are the difficulties linked to conducting CTs in African countries?
- Now that you know the objectives of the AMA, how do you think it will impact your work? In a positive or in a negative way?
- Do you want to add something that has not been covered by our interview?
- Would you be available for further questions in the context of this work?
- Do you know anybody that could interested to participate in this work?

The African Medicine Agency: analysis of regulatory impact on clinical trials

Key people interview: Pharmacoeconomics experts

- Present yourself: What are your areas of expertise? Are you familiar with clinical trials? With their regulation?
- Are you aware of the situation of CTs across Africa? Have you worked from near or far in/with this context?
- Are you aware of the creation of the African Medicine Agency? Do you know its objectives?
- Do you think that AMA will be able to finance its objectives? Indeed, for several programs and initiatives, African countries had to rely on external partners (NGO, NATO, EMA, charities…). Will it be the same in this case or the actual African climate will allow a little more independency?
- There are several actors that are involved in the creation of the agency such as the Gates foundation. Could this economic leverage allow them to impact regulation? At what level, in what form, via what agreements could they do so?
- The regulatory harmonization projects of the agency will have a definite impact on the economy of the member states. Will it be positive? Is this a win-win operation?
- The AMA is supposed to make regulatory context more open for international collaborations. Could a new open market for clinical trials impact the economy of occidental countries. What could be the impact on the economy of a leader in CTs such as Belgium?
- Do you want to add something that has not been covered by our interview?
- Would you be available for further questions in the context of this work?
- Do you know anybody that could interested to participate in this work?

The African Medicine Agency: analysis of regulatory impact on clinical trials

Key people interview: Policy experts

- Present yourself: What are your areas of expertise? Are you familiar with clinical trials? With their regulation?
- Are you aware of the situation of CTs across Africa? Have you worked from near or far in/with this context?
- Are you aware of the creation of the African Medicine Agency? Do you know its objectives?
- We know there are lots of disparities across Africa in term of policy making and healthcare regulation. Several initiatives have been made in the past and were not that ambitious. Do you think that the agency will be able to encounter its objectives of global policy harmonization?
- On which basis the AMA will establish its policy? Is it possible that it will be inspired/influenced by foreign policies (FDA/EMA…)? The AMA claims to be only led by African actors but we're aware of the lack of policymakers on the continent. How could it remedy this problem?
- The regulatory harmonization projects of the agency imply a major change in policies across member states. Will it be positive? Is this a win-win operation?
- The AMA is supposed to make regulatory context more open for international collaborations. Could new healthcare policies in Africa impact occidental countries. What could be the impact on the policy of a leader in CTs such as Belgium?
- Do you want to add something that has not been covered by our interview?
- Would you be available for further questions in the context of this work?
- Do you know anybody that could interested to participate in this work?

APPENDIX3

Answered questionnaires; the underlined sections are interventions from the interviewer

Key people interview: Ethics expert

Present yourself: What are your areas of expertise? Are you familiar with clinical trials? With their regulation ?

J'ai une formation de médecin, l'essentiel de ma carrière s'est déroulé dans l'industrie pharmaceutique. J'ai toujours travaillé sur les maladies infectieuses, en commençant par les antibiotiques et puis je suis passé du côté des vaccins. Les derniers postes que j'ai eus étaient dans une équipe qu'on appelle « Access to Medicine ». Il concernait essentiellement les maladies liées à la pauvreté : le paludisme, la tuberculose, la leishmaniose et la santé mentale ce qui était assez intéressant. Depuis 5 ans, je travaille pour une ONG fondée par Médecins sans frontière et par des partenaires académiques du Sud. Elle développé des médicaments qui n'existe pas car ils n'ont aucune raison économique d'exister. Nous travaillons essentiellement sur les maladies tropicales négligées mais aussi sur le VIH pédiatrique et l'hépatite C. Je suis aussi membre d'un comité d'éthique sur le sujet de du recrutement des volontaires sains dans la recherche biomédicale. La recherche au sud est un sujet qui m'intéresse. Nous savons notamment qu'en Inde il y a de véritables usines à volontaires sains. La réglementation n'étant pas aussi rigoureuse que dans d'autres pays. J'ai beaucoup travaillé dans des pays à ressources limitées : En Afrique en Amérique du Sud, En Asie... J'ai été sponsor d'essais cliniques essentiellement dans le domaine des vaccins. Je me suis éloigné des essais cliniques depuis 7 ou 8 ans donc ce n'est plus mon souci quotidien. Mais avec l'angle de l'éthique on touche un certain nombre de points qui je pense sont pertinents pour vous.

Are you aware of the situation of CTs across Africa? Have you worked from near or far in/with this context?
Answered in question 1

Are you aware of the creation of the African Medicine Agency? Do you know its objectives?

Oui mais de façon assez large. Dans ma carrière les agences réglementaires ont été des partenaires critiques dans nos activités. Quand on développe un vaccin ou un médicament on veut répondre aux exigences d'agence afin de le valider et de le mettre sur le marché. Je sais que cette en agence est en discussion depuis un moment et qu'elle a été créée. Mais très honnêtement je ne suis pas tout à fait au fait des détails de son fonctionnement et de ses missions.
Alors je vais vous préciser les objectifs : l'harmonisation globale de la régulation de la santé en Afrique. L'idée étant de créer un cadre légal qui permettrait une uniformité. Et les missions qui sont données en priorité par l'agence sont : les médicaments génériques mais également les médicaments de mauvaise qualité. Tout ça pour s'assurer que l'accès aux médicaments soit possible pour toute personne sur le continent. Je travaille dans le cadre des essais cliniques parce que c'est ma spécialisation. Un papier est sorti récemment sur ce sujet et sur l'importance que donne l'agence aux essais cliniques mais ce n'est pas leur priorité. Donc ce qu'il faut retenir ce sont les mots uniformité, harmonisation.

Health Ethics Committees are rather new across Africa and are even inexistant in some countries. However, EC are essential to set new rules concerning healthcare, especially CTs. How do you think AMA will handle this reality?

C'est une problématique qui est complexe parce qu'effectivement dans pas mal de pays à ressources limitées, les autorités délèguent de grosses responsabilités aux communautés d'éthique. En leur disant que c'est à eux d'assurer le bon déroulement des essais cliniques. Comme première approche ça fonctionne car ces pays ont des ressources limitées et ne peuvent pas implanter tout de suite une administration centrale qui surveillera les essais. Mais le problème c'est de s'assurer que les comités d'éthique sont suffisamment équipés pour effectuer leur travail. En termes de ressources humaines mais aussi de moyens de fonctionner. Très souvent il fonctionne de manière gratuite avec très peu de subsides ce qui est très compliqué parce qu'ils font un travail qui prend du temps. C'est une question de moyens donc. Ensuite il y a le fait que les autorités nationales devraient à terme ne pas se reposer uniquement sur les comités d'éthique mais mettre en place des systèmes d'audit, de surveillance, de contrôle. Parce que déléguer aux comités d'éthique le bon déroulé d'un essai ou la véracité des données qui sort de cet essai, c'est illusoire. La plupart des comités d'éthique n'ont pas les moyens ou ne se sentent pas nécessairement légitime d'inspecter de but en blanc un investigateur. Une option serait que l'agence de médecine africaine dise qu'elle se permet le droit de mener des audits, des inspections sur les essais cliniques qui se déroule sur le continent. On pourrait aussi imaginer, en allant encore plus loin, les essais ne sont licites que dans les sites qui ont été accrédités par l'agence. Afin de s'assurer que le personnel est correctement qualifié, qu'il y a les infrastructures nécessaires pour assurer la qualité des études, la sécurité des patients et cetera. Ce sont des discussions que nous avons autour des essais concernant les volontaires sains. Une recommandation que nous faisons c'est de dire qu'il faut accréditer des sites. Les sites qui mettent en place des essais cliniques doivent répondre à un certain cahier des charges. Qui est la responsabilité non pas des comités d'éthique mais des agences gouvernementales. Les sites qui ne respectent pas ces réglementations ne verront pas leur donner reçu par l'agence. C'est quelque chose de majeur. Car si l'agence dit :« nous n'acceptons de recevoir des données venant uniquement de sites correctement accrédités ». Je pense que les gens vont se mettre en ordre de bataille. Ils il faut tout de même prendre en compte les limites en termes de temps et d'argent etc... Mais ça peut être une direction dans laquelle l'agence voudrait aller. Car pour certains types d'essai clinique ce sont déjà des exigences appliquer En Europe et aux États-Unis.

Donc décharger le travail qui n'est pas directement celui des comités d'éthiques. Et avoir un système d'accréditation qui permettra d'assurer que le cahier des charges est respecté.

Does global harmonization in regulation means global ethic harmonization? What standards will be used to set up the ethical context of member countries (ICH-GCP)?

Idéalement je pense qu'on ne devrait pas accepter de double standard. Les standards doivent être équivalent partout dans le monde car sinon on s'expose au risque qu'on appelle le dumping éthique. Ce serait donc l'idée que les choses interdites dans certains pays, nous les ferions dans des pays du Sud. Ce n'est pas acceptable bien sûr. Il faut que les agence d'enregistrement sois suffisamment exigeante là-dessus pour éviter ça. Après il ne faut pas calquer nécessairement l'ensemble de l'approche du monde occidental sur l'ensemble du monde. Il faut aussi que chaque région débatte de ses spécificités. Mais quand même les grands principes doivent rester les mêmes. Pour les essais cliniques : et le consentement libre éclairé et individuel ce n'est pas

négociable. Qui font que les standards soient négociés au niveau local par exemple qu'est-ce qu'une juste rémunération selon le temps que les personnes passent dans l'essai. Mais néanmoins les principes doivent rester les mêmes je pense. Parce que le risque c'est que les essais cliniques étant un business, certains pays relâchent leurs exigences pour attirer les investigateurs.

Do cultural differences between member states and/or occidental countries will impact those modifications?

Je ne serai pas vous dire comme ça de manière générale. Mais il est évident qu'il faut tenir compte des particularités de chaque pays et discuter de la façon dont certains grands principes intangibles peuvent être appliqués de manière très concrète dans les pays. Je sais que nous avons eu souvent des discussions autour des essais cliniques notamment sur la question de la contraception pour les femmes. Ce n'est pas depuis Paris où Genève que nous déciderons ce qu'il doit se passer. Il faut poser la question et en parler avec des acteurs de terrain. En leur demandant comment ces demandes devraient être traitée dans leur contexte. Une fois que les grands principes sont posés après on peut voir. En définitive en termes d'éthique, je vais me répéter, il faut faire attention à deux choses : le double standard et le dumping éthique. Une des questions sur laquelle on planche dans mon groupe de travail c'est celle des vulnérabilités. Il faut faire attention lorsqu'on met en place des essais cliniques aux populations qui sont potentiellement vulnérables. Par leur niveau économique, d'éducation. Il faut faire attention aussi à la vulnérabilité potentielle des comités d'éthique, des systèmes de santé, des investigateurs locaux. C'est très compliqué parce que quand vous arrivez avec la promesse d'un énorme investissement, c'est très compliqué pour les gens de dire non. En anticipant ça, il faut éviter de mettre les gens dans une situation comme celle-là. Il ne faut pas abuser de leur vulnérabilité. On a effectué un travail comme celui-là avec une initiative qui s'appelle TRUST. Ce sont de grands principes qui consiste à dire que à chaque fois qu'on veut travailler, au nord ou au sud, il faut repérer à l'avance des vulnérabilités essentielles. Faisons en sorte de ne pas abuser de la vulnérabilité encore une fois. Non seulement c'est le des patients mais également celle des systèmes de santé... Quand on arrive dans un endroit reculé avec un budget de de dizaines de millions, quelle est la capacité des gens à refuser ?

The AMA claims to be only led by African actors but its initiative involves number of international actors. Atrocities that have happened in the past during North-South studies show how a good ethic context is vital. How could the AMA make sure of that? What should be its ethic model?

Il y a beaucoup de guidelines qui existent mais je crois que la meilleure chose que l'agence pourrait faire c'est d'être en contact avec les Agence des autres pays, continent afin de créer une communauté. De façon à créer un dialogue et de partager des bonnes pratiques. Également l'agence devrait faire en sorte que l'Afrique devienne, pour les agences pharmaceutiques, un marché attractif. C'est autre chose que l'éthique dont on parle là mais le gros problème de l'Afrique actuellement c'est qu'il y a autant d'agences que de pays. Les marchés sont totalement fragmentés, chaque pays à ses propres exigences et tout ça crée de petits marchés qui valent peu de choses aux yeux de l'industrie. Par exemple si je mets en place une fabrication au Kenya et que la réglementation de l'Éthiopie qui est à côté est différente je ne pourrais pas y accéder. À la différence de l'Europe par exemple qui me permet si j'enregistre mon médicament au niveau européen de le faire parvenir aux 27 pays. Je suis certain que l'agence a été aussi créée pour ça. C'est très lié à l'attractivité du continent afin de réaliser des essais cliniques mais aussi simplement pour le marché pharmaceutique. Si l'Afrique s'organise pour assurer que les

échanges entre pays soient fluides. Brutalement, les regards de l'industrie, des CROs vont changer. Il est important que cette agence dialogue avec les autres grandes agences et en fasse partie. Tout ça créerait un écosystème qui ferait de l'Afrique au marché attractif mais également un endroit où on fait de la bonne recherche clinique, fondamentale...

Do you want to add something that has not been covered by our interview?

Il y a une dimension dont on n'a pas parlé c'est celle de l'anticipation des pandémies et des épidémies. Et là c'est un contexte dans lequel l'agence africaine devrait jouer un rôle proéminent. On l'a vu avec Ebola, le COVID, la variole du singe…

Would you be available for further questions in the context of this work?
/
Do you know anybody that could interested to participate in this work?
/

Key people interview : Ethics expert

Merci pour le moment que vous m'accordez. Le but de ce questionnaire était d'avoir des avis divergents. En parlant avec des experts dans différents domaines, j'ai un avis plus nuancé sur le sujet. Le but en vous laissant le questionnaire à l'avance était de vous laisser aussi former un avis plus nuancé

Present yourself: What are your areas of expertise? Are you familiar with clinical trials? With their regulation ?

Je suis prof d'éthique des soins de santé et dans ce cadre-là j'enseigne aussi l'éthique de la recherche sur l'être humain. Même si ce n'est pas directement ma spécialité, c'est plus quelque chose que j'enseigne. C'est une spécialité qui demande d'être à jour. Votre sollicitation a aussi attrait, je pense, au fait que j'ai participé à une grande recherche financée par le gouvernement américain pendant 12 ans. Elle était financée par le NIH via Fogarty un organisme de l'état américain qui finance la recherche à l'étranger, principalement en Afrique, plus précisément en Afrique subsaharienne. Il est important de le préciser parce qu'il y a une série de différences entre les pays sur le continent, le Congo n'est pas l'Algérie par exemple. Dans ce cadre-là, j'ai accumulé une série d'expériences en éthique de la recherche et j'ai enseigné l'éthique de la recherche à l'étranger (Congo, Madagascar…). Je connais un peu l'état de la recherche dans ces pays-là, je ne connais pas la situation des autres pays.

Vous apportez une nuance qui est essentielle. Je parle de l'Afrique comme un tout mais il ne faut pas oublier que l'Afrique, c'est 54 pays et ce qui est vrai pour certains d'entre eux ne l'est pas pour les autres

Are you aware of the situation of CTs across Africa? Have you worked from near or far in/with this context?

Le but de l'étude à laquelle j'ai participé était de former et d'augmenter la capacité des chercheurs sur place en matière d'éthique de la recherche parce que précisément les chercheurs dans les pays d'Afrique subsaharienne n'ont aucune connaissance en éthique de la recherche avec le risque évidemment que les firmes pharmaceutiques profitent de cette ignorance là pour faire des recherches qu'ils n'auraient peut-être pas faites dans des pays plus riches avec des moyens financiers plus élevés et donc aussi des infrastructures en éthique plus développée. Donc oui je connais un peu l'état de la recherche en matière de sciences de la vie. Finalement, il y a peu de recherches et plus précisément en fait il y a peu de recherches indépendantes. La plupart des recherches qui sont effectuées dans les pays que j'ai fréquentés. C'étaient des recherches dont le promoteur était occidental. Et qui avait besoin, sur place, d'un relais parce qu'il fallait des connaissances spécifiques sur le pays où la région ou bien il y avait des problèmes de langues, des tas de problèmes comme ceux-ci. On s'adresse à ces chercheurs mais souvent comme à des subalternes. Et les chercheurs que je connaissais s'en plaignaient. A la fois, ils étaient contents qu'on vienne les chercher et qu'ils puissent faire des publications avec leurs noms dans les grands journaux mais, en même temps ils se rendaient bien compte qu'ils ne seraient jamais premiers auteurs et que souvent on leur demandait de faire des tâches ingrates. Au total il y a peu de recherches et souvent ces recherches sont commanditées par des occidentaux et principalement les États-Unis qui sont les plus gros consommateurs de partenariats avec l'Afrique. Donc là il y a un gros problème et le gros problème que j'ai également constaté qui est notamment visible en Afrique de l'Ouest c'est que les organes de contrôle de ces recherches sont très peu développés. D'une part il y a peu de lois qui régulent la recherche sur l'être humain, contrairement à ce qui se passe dans les pays occidentaux où le contrôle est assez fort. Et les contrôles des comités d'éthiques existent souvent mais ne sont pas toujours suffisamment sérieux dans les analyses qu'ils font. Ces 2 éléments conjugués font qu'il y a des choses parfois questionnables qui passent même si les recherches qui sont faites en

partenariat avec un pays occidental sont analysés par les comités de ces pays occidentaux. On a donc la collaboration de 2 communautés d'éthiques, un occidental et un africain. Avec des difficultés que si l'un dit oui le comité d'éthique des pays qui accueille la recherche va avoir du mal à dire non. Par exemple si Harvard dit oui, à Lubumbashi, on aura du mal à dire non.

Dans les premiers documents que j'avais lu pour la première partie de mon mémoire j'étais tombé sur un document qui parlait notamment de néocolonialisme de la recherche avec des termes parfois que je n'aurais pas utilisé exactement mais il y a une certaine situation qui créé un déséquilibre dans la collaboration qui bénéficie plus à côté qu'à l'autre. Un expert d'une précédente interview me précisait qu'il y a des situations où on a des médicaments qui sont testés dans ces pays mais qui ne bénéficieront jamais à la population sur place.

Cet expert a eu une bonne idée de vous mettre le point sur ça. Et de dire que c'est du néocolonialisme selon moi c'est le terme. Je ne sais pas si dans le cadre de votre travail ce que vous pouvez l'utiliser dans tous les cas référencez-le correctement mais pour moi je le défendrai. C'est du néocolonialisme déguisé bien sûr

Are you aware of the creation of the African Medicine Agency? Do you know its objectives?

Bonne question et j'ai un peu honte de dire que non je ne le savais pas. Je ne la connaissais pas et puis je me suis renseigné pour cette interview et honnêtement j'aurais pu vous dire oui mais je ne la connais pas je dirais même que ça m'a un peu surpris parce que c'est contraire à tout ce que je pensais savoir. C'est à dire il y a encore 2-3 ans d'ici avant le COVID j'étais au Bénin pour un colloque qui réunissait des chercheurs de la région et on avait évoqué plusieurs choses en matière de recherche et à ce moment-là en aucun cas on a évoqué la possibilité d'une agence telle qu'elle celle-là. En précisant d'ailleurs que c'était un problème qu'il n'y ait pas de centralisation. Il y a 3 ans qui sont passés et je ne me suis pas tenu au courant ce n'est pas spécialité première mais j'ai été étonné. Donc non je ne savais pas

Vous n'êtes pas la première personne me à me dire ça. Et vous parlez de la COVID et c'est un des accélérateurs pour l'agence. Le fait qu'une pandémie comme celle-là soit arrivée a mis en lumière les failles du système de santé en Afrique notamment maintenant on a très peu de personnes qui sont vaccinées contre le COVID en Afrique. Ça a fait accélérer les démarches mais ça fait une dizaine d'années que les gens travaillent dessus. Il fallait un minimum de 15 pays pour lancer la démarche afin de créer l'agence de manière officielle on a eu les 15 pays et je ne vais pas vous cacher que le nombre augmente très difficilement. Les pays qui se portaient bien sans ont du mal à signer et évidemment ceux qui ont plus de mal ont tendance à signer. Pour en revenir au grand public c'est vrai qu'il y a très peu de gens qui sont au courant de la création de cette agence. Et les objectifs si vous ne les connaissez pas sont les suivant : créer une harmonisation en Afrique. Les objectifs premiers n'étaient pas dirigés vers la recherche clinique mais plutôt vers le libre échange des médicaments et la régulation de ceux-ci. Afin d'éviter les médicaments toxiques falsifiés et aussi stimuler la production de médicaments sur le territoire africain. Créer un marché qui serait propice aux entreprises pharmaceutiques. Des grands objectifs avec pour des instants pas trop de détails et le but de mon travail c'est de partir de ces objectifs pour voir s'ils sont réalisables. Les essais cliniques sont un peu une préoccupation annexe mais ça me paraissait intéressant à aborder.

J'ai été consulté moi aussi les objectifs que vous donnez et la question des essais cliniques est à peine évoquée parce qu'ils disent : Coordonner les examens conjoints de demandes de réalisation d'essais cliniques. Je ne pense pas il y a plus et je vous avoue que je ne comprends pas bien ce que signifie. Il faudrait préciser ce qu'on entend parce que c'est un peu vague on

voit bien que c'est un niveau très pratique de gestion du médicament manufacturé et pas vraiment de l'amont. Ce que je trouve problématique.

Health Ethics Committees are rather new across Africa and are even inexistant in some countries. However, EC are essential to set new rules concerning healthcare, especially CT's. How do you think AMA will handle this reality?

C'est une bonne question parce que sur place beaucoup de pays n'ont pas les moyens de faire en sorte que leur comité d'éthique soit bien formé. Même s'il y a de l'argent, quand on s'adresse à un comité d'éthique local on se rend compte que leur travail est rémunéré par certaines firmes pharmaceutiques. Il y a une certaine manne financière qui pourrait être utilisée. Je trouve que ça vaudrait la peine qu'on centralise le travail et que à l'intérieur de cette nouvelle agence l'agence africaine médicament il y ait des subdivisions régionales Afrique de l'Ouest, Afrique central, Maghreb… par exemple. Et que ce soit en relais possible pour les différents comités d'éthiques régionaux nationaux et qu'évidemment l'agence puisse engager des personnes compétentes qui travaillent sur ces questions-là et qu'on ait un comité d'éthique central auquel ils pourraient faire appel. Et là ça permettrait vraiment de faire du bon travail parce que faire de l'éthique de la recherche ça demande une formation conséquente. Il y a des législations, des textes internationaux à respecter il y a des tas d'éléments qu'il faut avoir en tête. Si on fait ça peut-être qu'on échappera en partie à une certaine corruption locale. Il faut voir cependant comment cette agence-à va être financée parce que si elle est financée par les firmes pharmaceutiques uniquement ou par certains pays occidentaux et cetera ça va être compliqué.

Vous parliez de compétences de personnes compétentes. C'est une des choses qui a été évoquée par tous les participants qui ont été interviewés. Certains doutent de la capacité des pays africains à former et à avoir des personnes formées pour ce genre de questions (éthiques ou autres). Et le premier expert dont je vous parlais tantôt me disait que c'était plutôt l'inverse il n'y a pas de contexte dans lequel ces personnes formées pourraient travailler et utiliser leurs compétences et donc elles vont plutôt travailler dans le privé. Est-ce que vous allez plutôt dans ce sens-là ou bien vous avez une autre opinion ?

Je pense que c'est tout à fait pertinent parce qu'il y a des centres de formation tout à fait performant notamment en Afrique du Sud où on peut facilement se former et aussi dans d'autres pays souvent anglophones. On peut y avoir une formation de qualité mais la question est de savoir : quelqu'un qui fait son cursus en sciences biomédicales par exemple et qui fait un master spécialisé en éthique de la recherche : qu'est-ce qu'il pourra faire de cela ? Effectivement s'il est vraiment bon il finira par être engagé par un ministère ou par l'OMS ou une autre un autre organisme international mais il ne fera pas bénéficier les jeunes de son pays de ses compétences. Donc effectivement il y a des formations en éthique qui existent un peu partout en Afrique mais qu'est-ce qu'on fait avec ça ? Il faut des capacités de formation mais il faut aussi que les gens qui se lancent dans ces études-là aient une certaine assurance sur ce qui se trouveront à la fin de leurs études. Sinon il y aura des universitaires en plus qui ne pourront pas trouver de travail et qui partiront.

C'est un des points d'honneur que j'avais : c'est de travailler avec des experts qui venaient d'autre part que la Belgique globalement. Parce que je craignais d'avoir un seul son de cloche.

Comme vous le disiez au début il y a très peu de personnes qui sont au courant de l'initiative de l'agence africaine du médicament. Et même si ce n'est pas spécialement volontaire il y a toujours une espèce de condescendance par rapport à des initiatives qui sont faites « avec 3 bouts de bois ». On aurait tendance à penser qu'il n'y a juste pas de personne compétente alors que ce n'est pas le cas, on n'en parle juste pas

Ce n'est sûrement pas le cas non. Mais les gens qui sont vraiment compétents sont repris par des agences internationales et donc il y a une fuite du cerveau c'est une réalité. Ou alors ils sont sur place mais sont engagés par des ONG internationales et ils perdent pied par rapport à la situation sur place. Et pour l'agence il y a des doutes parce qu'encore maintenant il n'y a pas encore de site internet officiel il y a un hébergement sur le site de l'Union africaine. Mais il y a un doute qui s'installe dans l'esprit de chacun c'est presque la première chose qu'on fait de créer un site internet. Quelqu'un qui veut faire un organisme comme ça c'est de mettre en lumière via un site pour attirer des gens compétents qui pourraient proposer leur candidature et en fait ça n'existe pas.

Je suis rendu compte de la difficulté de trouver des informations fiables quand je me suis retrouvé en chercher sur Twitter.

Does global harmonization in regulation means global ethic harmonization? What standards will be used to set up the ethical context of member countries (ICH-GCP)?

Idéalement si on veut être tout à fait sérieux il faut repartir de repères qui sont les plus universels et puis à partir de ça on pourrait travailler pour prendre en compte les spécificités locales. Je cite plutôt des repères d'ordre éthique vous citez plutôt des repères d'ordre scientifique et méthodologique mais la question c'est savoir si l'éthique est pareille à Kigali ou à Washington. Moi je dirais oui et non c'est-à-dire : oui au départ parce qu'il faut partir d'une réalité qui est que tous les êtres humains sont pareils mais non il y a certaines spécificités et donc il faut travailler sur celles-ci. On est tous pareils on a tous les mêmes besoins mais il y a des besoins spécifiques, des réalités spécifiques qui doivent être prises en compte. C'est comme ça aussi que l'agence pourrait être reconnue parce qu'on se rendrait compte qu'ils sont au courant des normes mais ils y travaillent pour voir s'il n'y a pas nécessité de les adapter. Il y a des éléments qui doivent être pris en compte, les éléments religieux mais également l'élément du développement économique. Mais tout dépend de là où on part je ne suis pas pour dire que l'éthique doit être différente nécessairement selon la région du monde où on est mais elle peut être à la fois commune et spécifique c'est paradoxal. Elle peut être commune mais avec des spécificités. De la même façon que l'on peut dire que tous les êtres humains aiment leurs enfants dans toutes les cultures on voit que les parents protègent leurs enfants mais en même temps il y a une façon de faire qui peut être particulière. On sera toujours dans une situation où les enfants sont un bien précieux que l'on protège mais on peut les protéger de plein de façons différentes. Et je pense qu'en matière de médicaments c'est probablement ça aussi on est on est semblable mais avec des spécificités

Do cultural differences between member states and/or occidental countries will impact those modifications?

C'est sûr qu'il y a une réalité où sur ce continent il y a des cultures différentes qui se côtoient : les blocs anglophones, les blocs francophones, les blocs de langue arabe. Une façon de résoudre cette multitude de cultures c'est les bureaux régionaux qui permettraient d'éviter ceci point si on crée différents bureaux régionaux qui relaient avec une structure centrale on évite de tomber dans quelque chose ou une seule voie voudrait faire de la limite et n'aurait plus de

force du tout. C'est le risque quand on essaie de concilier toutes les cultures on ne dit plus rien finalement. Moi je crois que c'est possible. Surtout ce qui est intéressant c'est qu'on essaye que les différents blocs aient leurs voix vraiment. On sait par exemple que toute l'Afrique francophone est en train de perdre du terrain par exemple, au Rwanda le français est en train de perdre pied et le l'anglais est devenu la langue principale, le pays a d'ailleurs reçu des fonds américains grâce à ça. Il y a des efforts à faire mais moi j'y crois. Je crois que c'est l'occasion ou jamais de créer quelque chose de solide qui aidera vraiment l'Afrique parce que le médicament en Afrique c'est vraiment un problème majeur.

The AMA claims to be only led by African actors but its initiative involves number of international actors. Atrocities that have happened in the past during North-South studies show how a good ethic context is vital. How could the AMA make sure of that? What should be its ethic model?

Sur les collaborations nord-sud au niveau de la recherche la littérature regorge de guidelines. Il suffit d'aller les pêcher par exemple du côté des États-Unis il y a un homme qui s'appelle Emanuel qui a publié des guidelines qui permettent de réguler la recherche qui vient du Nord et qui va se faire dans un pays du Sud. Par exemple il faut que le médicament sur lequel on travaille puisse profiter aux communautés locales. C'est un repère essentiel. Quand on mobilise des ressources humaines localement il faut qu'il y ait un retour sinon c'est l'exploitation ça revient à la colonisation. On prend et puis on s'en va. Au niveau des ressources elles existent théoriquement il suffit d'aller les pêcher. Le tout maintenant c'est qu'il y ait des gens compétents qui sache que ces guidelines existent et sache qu'il ne faut pas tout reprendre de 0. Il va falloir malgré tout que l'agence soit très solide pour éviter que l'on soit dans des rapports déséquilibrés entre un Nord qui sait qui a les cerveaux et l'argent et un sud qui serait traitée comme un petit enfant.

Do you want to add something that has not been covered by our interview?

Une des choses qui m'avait aussi marqué dans les objectifs de l'agence point ce sont des médicaments traditionnels. Parce que ça serait une spécificité africaine. Il existe en Europe ou en Amérique du Nord des médecines traditionnelles mais c'est beaucoup moins qu'en Afrique. Il y a une série de médicaments en Afrique qui sont standardisées et traditionnels. Ils sont amendés par les grosses industries Pharma qui les ont approuvées et donc ils ont été testés au point de vue stabilité et cetera et ça pourrait être fantastique de les réguler. Et il y a une série de choses sur lesquelles il y a encore polémique notamment chez nous comme l'Artemisia pour la malaria. Et l'agence pourrait défendre une approche plus africaine du médicament. Sur place beaucoup de gens se soignent avec des médicaments traditionnels. Bien sûr ils iront la pharmacie pour des médicaments spécifiques mais au fond à la maison ils utiliseront des remèdes traditionnels. Et donc c'est quitte ou double parce que parfois c'est vraiment efficace mais parfois c'est n'importe quoi voire même toxique et donc il y a quelque chose à faire là il y a une vraie culture du médicament traditionnel.

Would you be available for further questions in the context of this work?

/

Do you know anybody that could interested to participate in this work?

/

Key people interview: Ethics expert

Present yourself: What are your areas of expertise? Are you familiar with clinical trials? With their regulation ?

Je suis d'origine béninoise. Je suis enseignant en santé publique mais aussi en bioéthique plus généralement et plus particulièrement en éthique de la recherche. Ça fait une quinzaine d'années que je travaille dans ce domaine au Bénin. J'ai travaillé dans d'autres pays africain également. J'ai contribué à renforcer la capacité des comités d'éthique mais aussi des chercheurs en éthique de la recherche.

Are you aware of the situation of CTs across Africa? Have you worked from near or far in/with this context?

Je n'ai pas eu de revue récente mais il y a une douzaine d'années j'avais essayé de faire une analyse de la situation de la recherche et de son encadrement. En Afrique, surtout de l'Ouest. Ce qui est ressorti est vieux certes mais étant dans plusieurs comité d'éthique moi-même, je peux dire que des essais cliniques ont lieu sur le continent et ceux-ci sont mieux encadrés depuis une dizaine d'années. Et ce plus que d'autres recherches sur le continent. Cela est peut-être une surprise pour vous je n'en sais rien parce que c'est le contraire qui est véhiculé. Si vous comparez les essais cliniques à d'autres recherches biomédicales vous verrez que du fait des sponsors et des obligations au niveau de la réglementation internationale, les essais cliniques sont les mieux encadrés. On pourrait ajouter que les essais sur les thérapies dite traditionnelles le sont un peu moins. Mais globalement les essais cliniques sont bien encadrés. J'ai participé à un programme qui avait pour but de recenser les essais cliniques et à ma grande surprise il y en a très peu. Il faut déconstruire l'idée reçue que l'Afrique est un terrain à essais cliniques. Je ne nie pas les enjeux, je fais partie des gens qui pendant longtemps ont travaillés à l'éthique et à l'encadrement de la recherche en Afrique en m'appuyant sur les scandales qui ont eu lieu dans les années nonantes. Mais les choses se sont améliorées. Et moi mon discours c'est la comparaison avec les pratiques de nos pays pour nos propres recherches ou des recherches avec des niveaux de risques où on contourne la réglementation

Are you aware of the creation of the African Medicine Agency? Do you know its objectives?

Bien évidemment. Moi au Bénin à travers les projets que j'ai en commun avec l'agence béninoise de régulation on a eu connaissance de la création de l'agence africaine du médicament. Le contrôle la qualité des médicaments. Je ne connais pas les instances et autres mais je sais que c'est récent.

Health Ethics Committees are rather new across Africa and are even inexistant in some countries. However, EC are essential to set new rules concerning healthcare, especially CT's. How do you think AMA will handle this reality?

Vous m'excusez mais j'ai envie de rectifier 2 choses : je peux comprendre que la justification de votre étude s'est appuyée peut-être sur ça mais je vais rectifier vous allez voir et vous pourrez l'intégrer si vous le souhaitez. Les comités d'éthique ne sont pas du tout nouveaux en Afrique à moins que dans ce terme nouveau vous y voyez là connotation « plus récent que dans les pays développé » si c'est cela oui. Dans les pays développés depuis les années septante - quatre-vingt il y a eu un certain élan, une généralisation de ces comités. Mais en Afrique, et je peux vous donner 2 simples exemples, ça fait plus de 20 ans que les comités sont fonctionnels. Avec

aujourd'hui un niveau de capacité qui n'a rien à envier celui des pays développés. D'ailleurs quand on dit « on va aller les renforcer », c'est erroné. L'éthique c'est se mettre ensemble pour réfléchir et personne n'a besoin de d'aide pour réfléchir. Les gens n'ont pas besoin d'être aidé pour être renforcés. C'est la limite de l'idée de partager ces pratiques. Je vous donne 2 exemples. Le premier : c'est le réseau des comités nationaux d'éthiques de la recherche qui a été porté par l'OOAS (Organisation Ouest Africaine de la Santé) qui existe depuis bientôt une décennie. Les comités nationaux existent depuis plus de 20 ans dans tous les pays. Nous avons dans certains pays des lois comme au Bénin par exemple qui sont le niveau de réglementation le plus élevé y compris si vous les comparez avec les pays développés. Et en matière de recherche, certains pays comme les nôtres sont au moins aussi avancés que les pays développés. Mais je reconnais que nous rencontrons des difficultés, c'est peut-être là que vous pourrez recontextualiser. J'ai travaillé un peu partout en Afrique et les pays africains foisonnent de communautés d'éthique. Nous avions fait par exemple une étude pour le Cameroun qui recensait une trentaine de comités d'éthique mais dans les faits il y en avait une dizaine de fonctionnels et c'est peut-être sur ce point que vous pourriez rebondir. Mais les comités d'éthique ne sont pas nouveaux en Afrique. Le problème que nous avons et qui persiste depuis que j'ai commencé à travailler : c'est que les politiques n'ont pas réellement prévu la pertinence de l'éthique aussi bien dans la recherche que dans la santé publique. Nous souffrons un peu de ça. Si vous allez dans n'importe quel pays, les institutions financent les comités d'éthique. Dans nos pays la plupart des comités, à quelques exceptions près, n'ont pas de moyens. Si vous listez les difficultés, vous pourriez préciser que les gens rencontrent des difficultés à ne serait-ce qu'indemniser les déplacements des travailleurs. Il en va de même pour la formation continue des chercheurs pour être au fait des nouveaux enjeux si on prend les essais cliniques par exemple. Les problèmes viennent donc d'un manque de conscience des décideurs, des autorités.

Je ne suis pas quelqu'un qui demande des ressources financières même si c'est le nerf de la guerre. Mais si l'agence peut recentrer la place des comités d'éthique dans la réglementation de la recherche et en particulier des essais cliniques ça serait déjà ça. Je vois plus ça comme un rôle de plaidoyer. Si l'agence dit : « nous reconnaissons les comités d'éthique et les États doivent le raccorder de la considération », ce serait bien. Et pour ce qui est de l'harmonisation nous avons tenté avec l'OOAS une démarche d'harmonisation des pratiques en Afrique de l'Ouest. Et ce n'est pas mauvais en ce qui concerne les essais cliniques. On espère une rigueur dans l'encadrement et que ce niveau soit partagé. Les comités n'ont pas les mêmes niveaux de rigueur en termes d'évaluation, de suivi et autres. Il serait intéressant que, surtout concernant les essais cliniques, qu'au-delà des normes que nous utilisons liées aux bonnes pratiques, qu'il y ait considération de certaines spécificités. Je vais vous donner un exemple. Au Bénin, comme je vous l'ai dit, nous avons une loi qui a intégré un aspect qui n'existe nulle part : chaque chercheur qui mène un essai clinique au Bénin doit s'acquitter d'une assurances responsabilité civile. Dans les pays développés les centres de recherche, les chercheurs sont assurés mais dans notre pays les chercheurs ne sont pas assurés contre la responsabilité civile cela veut dire que lorsqu'il arrive un accident au cours d'un essai qui n'est pas lié à un médicament il n'y a pas de couverture. Voilà des choses qui sont liées à ce contexte que l'agence pourrait mettre en avant

Je vais essayer de paraphraser ce que vous dites. Donc selon vous l'agence en tant que telle n'a pas à améliorer la situation des comités d'éthique étant donné que ces comités sont très compétents et s'en sortent déjà très bien mais sa mission serait de recentrer leurs objectifs. Viser une harmonisation globale des pratiques pour faciliter certaines démarches je suppose. Et les comités d'éthiques n'auraient donc pas besoin d'un appui de l'agence en tant que tel c'est ça ?

Je ne dirai jamais ça. Je l'ai dit précédemment les comités ont besoin de l'agence. L'agence en tant que telle et financé par les États j'imagine ? Et je ne sais pas jusqu'à quel point l'agence a des ressources pour dire d'appuyer les comités en termes de ressources financières. Mais l'agence peut appuyer en faisant un plaidoyer sur la place des comités éthiques. L'agence pourrait également travailler à renforcer les capacités de ces comités. Elle pourra gagner dans chaque pays des sessions d'échange par exemple. Parce que les enjeux évoluent tout le temps. Il y a quelques années on ne parlait pas d'intelligence artificielle par exemple. L'agence peut travailler à renforcer les capacités. Là où je vais encore plus son rôle, c'est travailler à mieux faire appliquer les bonnes pratiques cliniques et prendre en compte les spécificités liées à notre contexte. Je vous parlais tantôt de la loi sur la responsabilité civile qui est une bonne pratique mais qui n'existe que chez moi.

Does global harmonization in regulation means global ethic harmonization? What standards will be used to set up the ethical context of member countries (ICH-GCP)?

Oui bien sûr ce serait une bonne base mais l'essentiel serait de prendre en compte les spécificités. Par exemple pour ce qui est du consentement éclairé il y a du travail qui est fait à l'international pour prendre en compte nos difficultés.

Do cultural differences between member states and/or occidental countries will impact those modifications?

Oui, je l'ai dit. Le contexte de soin n'est pas le même. La place de la recherche n'est pas la même. Il faut se poser la question de comment la recherche est perçue, celle du consentement éclairé…Définitivement, il faut prendre en compte ces réalités. Nos pays sont aussi très différents entre eux. Quand je vais en conférence internationale je me rends compte que certains collègues d'autres pays n'ont pas conscience de comment fonctionne certaines recherches spécifiques. Je sais que l'idée n'est pas forcément d'avoir le même niveau partout mais il y a un écart qui peut tout à fait être comblé dans nos pays. Et d'un pays à un autre le contexte de soin n'est pas le même. Il y a aussi des réalités socioculturelles qui doivent être envisagées. Je ne peux pas ignorer la communauté parce qu'elle fait partie intégrante de la vie de tout un chacun.

The AMA claims to be only led by African actors but its initiative involves number of international actors. Atrocities that have happened in the past during North-South studies show how a good ethic context is vital. How could the AMA make sure of that? What should be its ethic model?

Et vous savez comment les comités d'éthique ont été créés ? En Afrique j'entends. C'est souvent à la suite de scandales. Au Bénin par exemple c'était après une étude sur le VH qui n'avait pas respecté les bonnes pratiques cliniques. Ce qui arrive souvent dans les pays francophones d'Afrique, c'est un peu différent pour les pays anglophones, c'est que les comités d'éthique sont créés et financés par des initiatives du Nord et sous les standards du Nord. Ce qu'il faudrait c'est que ces comités soit créé pour nous, pour notre contexte et que nous soyons conscients de cette réalité. Si tous les chercheurs avaient une base sur laquelle travailler, une base légale, locale, aucun chercheur du Nord ne viendrait travailler en dehors de ce cadre. Il faudrait, c'est peut-être utopique, je désire obtenir un cadre adapté à nos réalités soutenue par les décideurs. Qu'il comprenne qu'il faut autant qu'on développe les universités, les laboratoires mais

également un cadre éthique pour former et aussi faire appliquer les normes qui existent. La plupart du temps nous ne faisons que copier les normes et comme tout le monde quand en pratique ce n'est pas à jour nous ne remettons pas ça en cause. Je suis partant pour qu'il y ait un cadre développé à partir de nos réalités, venant de notre initiative.

Do you want to add something that has not been covered by our interview?

Peut-être un enjeu qui n'est pas abordé c'est la collaboration entre les comités. Comme vous le savez les essais cliniques sont souvent multisites, multi pays. Et s'il y a un problème peut-être que l'harmonisation aiderait à le régler. Aujourd'hui le chercheur soumet dans 3 ou 4 différents pays avec des évaluations différentes d'un pays à un autre et une ligne du temps différente. Peut-être que l'harmonisation pourrait corriger ce problème et que l'agence pourrait jouer un rôle pour qu'un projet soit évalué principalement dans un seul pays. C'est un sujet que nous avions commencé à aborder quand nous avons créé la coalition des comités d'éthiques d'Afrique de l'Ouest.

Would you be available for further questions in the context of this work?

/

Do you know anybody that could interested to participate in this work?

/

Key people interview: Ethics expert

Present yourself: What are your areas of expertise? Are you familiar with clinical trials? With their regulation?

I'm American and I came to Belgium in the 80's. I have a bachelor and a master's in philosophy. I started working with the European forum for the GCP in the early 90s. I shared a working group that created the first European guidelines for ethics committees. I became familiar with Europe. We did that in the context of the European directive for good clinical practices. I became really familiar with clinical research with the pharma industry but also with the academic world. I then worked with the UN and went to Africa. I've also worked with WHO to set up guidelines for ECs in Asia and West Pacific. […] I've been to Africa quite a few times in quite a few countries. I worked there for European projects in Ethiopia, Gambia and Ghana

Are you aware of the situation of CTs across Africa? Have you worked from near or far in/with this context?

Yes

I've also worked with the African Union

Are you aware of the creation of the African Medicine Agency? Do you know its objectives?

Yes, as a part of the AU. I think Kigali is actually a perfect to put their HQ. It makes a lot of sense to me. I've visited National agencies when I worked in Africa. I think they want to be a kind of EMA in Africa. I don't think it will be an EMA because you don't have the same political and economic union that you have in the EU, but coordination is the right word yes.

Health Ethics Committees are rather new across Africa and are even inexistant in some countries. However, EC are essential to set new rules concerning healthcare, especially CT's. How do you think AMA will handle this reality?

I don't think there's a lack of ECs. Some countries maybe (Congo…). I think most countries that I can think of have a rather well-established EC. I think that there is a big problem with the support of ECs in the countries but that varies from country to country.

Almost all countries have ECs but there is disparities in their capacities. How could they manage that?

What Africa could use is a coordination across the different ECs. If the AMA was to involve itself in a sort of capacity building in ECs that would be a good thing. Because the variation between ECs is not only between countries but also within countries. So, you cases where you have some good EC in a country and some that are poorly supported and really struggling. Even though, those people are extremely dedicated. The weakness in Africa has been more than the ECs. I think people make a big mistake thinking that because a country is less wealthy that it doesn't have capacity. That's just not the case. It's not because of less national incomes that the ECs are less good, they're not. The real weakness are national regulatory agencies. The relationship between NRAs and ECs is very important. Europe went on a pathway to make closer relationship between ECs and NRAs. The other big challenge is that healthcare is a national concern. It means that from the perspective of the government, agencies such as EMA or FDA comes under the auspices of the government because healthcare is an economic concern too. That's why we don't have European ECs. We will see that with the AMA. It will remain in Africa even more than in Europe. There's a big concern on local health from national

authorities. Which is quite understandable because they're paying the bills and they organize health within the country.

Does global harmonization in regulation means global ethic harmonization? What standards will be used to set up the ethical context of member countries (ICH-GCP)?

ICH-GCP is a very good starting point but it's very thin about ethics. That could be a task for the AMA to establish a guideline for ethics review in Africa. The WHO is also very involved with this and wants to govern ethics in the world. But again, ECs are linked to research and research are linked to public policies and that's a national concern. What is good is to bring the relationship so that those committees get to know one another and get confidence in one another and in regulatory authorities. This is much more important than the guidelines in a certain sense

Do cultural differences between member states and/or occidental countries will impact those modifications?

No, I don't think so. They might impact decision making by regulatory authorities or by the ECs. But I've never seen any SOPs (Standard Operating Procedures) or guidelines in an African context. How many cultural differences you could find in a country? How could you put it in a guideline? What sense it would make? We live a culture that think we should divide people by culture.

The AMA claims to be only led by African actors but its initiative involves number of international actors. Atrocities that have happened in the past during North-South studies show how a good ethic context is vital. How could the AMA make sure of that? What should be its ethic model?

Atrocities will continue to happen. But you're right we want good policy in order to diminish the risks of those atrocities. That's why we have ECs and their regulatory oversight. I think it will depend on money where it comes from. Going back to your question about culture; It's not so much about culture but about independence in decision making.

Do you want to add something that has not been covered by our interview?

/

Would you be available for further questions in the context of this work?

/

Do you know anybody that could interested to participate in this work?

/

Key people interview: Clinical trials experts

Present yourself: What are your areas of expertise? Are you familiar with clinical trials? With their regulation?

I*'m a pharmacist by training and initially I worked in clinical research department for a pharma company in Europe. I was a CTs coordinator. Then I left and I went to work in the humanitarian sector with different NGOs in the field at HQ level. At that period, I worked much more on issues related to access to medicines and QA of medicines. Since XXXX, I've been working at XXX. I was at first, the head of the CT unit. We were coordinating CTs, but it was really different than in pharma companies. It was smaller at XXX because we were working only in collaboration with research institutions with the Global South, mainly sub-Saharan Africa. It was interesting to see the differences in what you can do in term of standards depending on the resources you have. Since XXXX, I'm working in research and teaching policy support for equitable access to quality assured medicines. So, it's not about CTs but they're still issues that are relevant with the AMA. I found your proposal to have a chat interesting because we've been ourselves wondering what will happen with this agency. Many people are talking about it as something that already exist but it's not the case.*

Are you aware of the situation of CTs across Africa? Have you worked from near or far in/with this context?

Answered in first question

Are you aware of the creation of the African Medicine Agency? Do you know its objectives?

For me it's really something that could be revolutionary. It could be the African version of the EMA. At the moment in Africa, we've very scattered situation with regulatory authorities with a very low level in capacity. We've Nigeria, Ghana et Tanzania who reached the maturity level 3 for medicines regulation, but I don't think CTs are included. You have Egypt which have reach level 3 for vaccine. You've countries in EAC that are doing an effort of harmonization. But still, they have Sudan and DRC in the group which bring the level quite down. But everything is a little bit scattered. […] I think initially the idea for AMA and was not really to bring standards up but to be able to rely on each other opinion in order to speed up the market. For Africa that would mean that if we have to harmonize so that we can then use mutual alliance etc… then everybody has to reach a certain level. It would be something revolutionary and great because you would improve standards, harmonize. Regulatory Authorities (RA) would work relying on each other opinion and would avoid duplicating forces. So that's all very wonderful but I was already anticipating, I have the impression is talking as if it was already existing and it is not. They're serious holes there. South Africa didn't sign it yet, Nigeria neither. I've talk recently to the director of an African RA, and he/she really seemed to have big doubts because they have serious reservations about the governors of the AMA as it is proposed now. And particularly, it seems that high level governors are at a political level. So, a purely political model could decide to hire and fire the director of a body that should be technical and not political. So, if these big countries do not buy in then it will not be an African medicine authority. Also, the next consideration is that the HQ is now put in Kigali and of course Kagame really wants to promote its country, but Rwanda almost not have pharma industry. The last consideration is that most of the countries that have signed the treaty are in the west of Africa and they're less well-regulated than in the East and south. The one who could benefit more are

signing in and the one who could share what they already know shy away. I think it's a fantastic initiative but there's a perception that is much more advanced than in practice.

According to you and your experience what are the difficulties linked to conducting CTs in African countries?

Firstly, we have the resources that often come from outside. They're very good examples: even if poor countries managed to develop institute and agencies and build capacity, they have much less core fundings. My institute has somebody to pay the costs of a CT unit even between two big studies. Our colleague in the South completely depends on external funding so they need to have a project ongoing all the time otherwise they can't pay people. They have a number of context where they don't have the capacity or the infrastructure. The more you go the bush, the less you have the infrastructure, the trained staff etc… But I did my PhD on that (which is a little bit old) and we've seen that everybody keeps on using ICH-GCP and everybody forgot WHO GCP. GCP are really build for the context of rich countries. The way they talk of informed consent completely ignore the issue of population that are illiterate. And the fact that in most African countries, people do not have health insurance. For them being included in a CT will be a way to get access to free care for a given period. So, by definition, the freedom to decide is not the same. This is completely not considerate. Something that I found scandalous is that the ICH-GCP when they look at actors in research, they talk about investigators, sponsors, monitors, and EC completely ignore the communities and patient's association. Including them should be important everywhere but even more in communities that are not yet familiar with research… There's a very good ethics guideline, the guideline SCIOMS (2016). They talked a lot about the engagement of the community, the benefit sharing If you look there's a lot of medicines, for let's say cancer, in lot of phases III that are done in SA or Kenya. Then it's very likely that those medicines come to the market for a price that is out of reach for Kenya or SA. So, there you're missing an international regulation. WHO made an annex to the Helsinki declaration in 2016, the declaration of Taipei. It's a very good regulation giving you ethics guidelines for management of biobanks for research. After the Ebola outbreak in West Africa, they were many that were sent to the USA without any approval from the countries. All those things which now are important to make clinical research fair in Africa. Most important thing is, I would say, communities' engagement and benefits sharing not only at a patient level but at a community level.

I would hope that once they can start working with CTs they will have an innovative look and not just copy paste ICH-GCP and EMA regulations, they must adapt them. With African colleagues we've sent them some input and comments and they've never replied to us and clearly, they didn't take that into account. All these revisions were purely on technical aspect. So, when it comes to QA, there's perfect guidelines. I think the issue of communities should be also important in Europe. Perhaps it would be more difficult to establish who's the community but they're patient's association. Who wouldn't involve patients in the co-design of CTs? They're maybe also representative of communities/patients' associations in Africa also with whom you could discuss. Priorities.

There is a global code of conduct for CTs conducted in the global South from the TRACE project. It's just a code of conduct but I think there's good stuff there. They've been written to face problems such as Ethics dumping.

Now that you know the objectives of the AMA, how do you think it will impact your work? In a positive or in a negative way?

Answered in 4

Do you want to add something that has not been covered by our interview?

Concerning the link between AMA and CTs, I've had the perception that CTs regulation may be the last one to come unless it's a political priority

Would you be available for further questions in the context of this work?

/

Do you know anybody that could interested to participate in this work?

/

Key people interview: Pharmacoeconomics expert - The expert did not have time for the interview and sent back his completed questionnaire

Present yourself: What are your areas of expertise? Are you familiar with clinical trials? With their regulation?

- *I am supporting countries in Europe Middle East Africa (EMEA) in their engagement with information partners like WHS, pharmacies, hospitals, …*
- *I actively contributed to the creation of XXX, an association linked to medicine distribution in Africa, and I am still a board member. In that context I also visited a selection of African countries.*
- *I have some notion about clinical trials and how they are operated without knowing the precise regulations.*

Are you aware of the situation of CTs across Africa? Have you worked from near or far in/with this context?

I never worked in this context, but I am aware that the involvement of Africa in Clinical Trials is rather low and surely not in proportion to the size and share of the population. Besides that, the genomic profile is so much different from other continents and even very diverse amongst the African population that more dedicated trials are an absolutely necessity.

Are you aware of the creation of the African Medicine Agency? Do you know its objectives?

- *Yes, I am aware of their creation and the stage they are in now.*
- *Based on previous exposures from key stakeholders a few aspects that are high on the agenda are:*
    - *Fight against Falsified Medicines*
    - *An increased level of access to products*
    - *A central products registration system*
    - *Have more African patients involved in clinical trials*

Do you think that AMA will be able to finance its objectives? Indeed, for several programs and initiatives, African countries had to rely on external partners (NGO, NATO, EMA, charities…). Will it be the same in this case or the actual African climate will allow a little more independency?

- *For sure the AMA will need the financial support and funding from donor organisations and other countries to be able to get installed and develop its role. BMGF is already a strong contributor at this stage, but more will have to follow*
- *Already now several countries don't pay their contributions to the African Union; increasing their budget to also support now the AMA will be a challenge. As such alternative financing models will have to be developed through (for the time being) donor support, while moving towards a more independent model based on contributions from pharma for product registrations, fees for Falsified Medicines tracking, distribution licenses and increasing contributions from the member states.*

There are several actors that are involved in the creation of the agency such as the Gates foundation. Could this economic leverage allow them to impact regulation? At what level, in what form, via what agreements could they do so?

- *On one side they will aim for the independency of the agency by allowing them to build their own regulations*

- *On the other side they are not going to put their money in a bucket without a bottom and would build in milestones to be achieved before making the next package of support available. Not sure they will be intervening in how precisely certain regulations and organizational aspects are handled as long as they are set-up in a professional and transparent way.*
- *Off course they will provide their expertise and experience where required, what might indirectly effectively influence some models.*

The regulatory harmonization projects of the agency will have a definite impact on the economy of the member states. Will it be positive? Is this a win-win operation?

- *Everything that leads to a stronger collaboration should be seen as a benefit for all states. Some countries might already have a good regulatory framework but access to medicines, counterfeit, production, distribution and trade are very common topics which can only be solved by a central authority.*
- *Besides that, such central authority, implementing solid and trustworthy control mechanisms, should be a good partner for many healthcare stakeholders amongst whom surely the pharma industry.*

The AMA is supposed to make regulatory context more open for international collaborations. Could a new open market for clinical trials impact the economy of occidental countries. What could be the impact on the economy of a leader in CT's such as Belgium?

- *I don't think that an increased share of African citizens in clinical trials will have a negative impact of the way these trials are done in western countries; they will still have to provide their quota of patients in case selected for that particular trial.*
- *I only see a benefit for the African countries through an increase of the patients to be involved and the development of a stronger clinical trial infrastructure*.

Do you want to add something that has not been covered by our interview?

- *Whatever will be done and organized in Africa to improve the access to medicines, the critical bottle neck will remain affordability. Who is going to pay for a higher use of medicines? It would be absolutely justified to go in that direction, but already today many citizens cannot benefit from a healthcare coverage plan.*
- *A pragmatic approach will be needed from the beginning; big philosophical discussions and concept building will find many fathers, but the implementation and respect at all management levels will be the long-term challenge.*

Would you be available for further questions in the context of this work?

/

Do you know anybody that could interested to participate in this work?

/

Key people interview: Policy expert

Present yourself: What are your areas of expertise? Are you familiar with clinical trials? With their regulation?

I am currently working at a local pharmacy manufacturing company in Zimbabwe we manufacture generic product for Zimbabwe market. I have an undergraduate degree in pharmacy from Zimbabwe and I continued my studies with a master's in pharmacy at the university of XXX. There I was looking at the implementation of the AU model law in medical products regulation and the establishment of the African medicine agency. So really my area of expertise I have got to do with pharmacy and pharmaceutical products and medicines regulation harmonization in the African context. In terms of clinical trials, I do not know much about clinical trials or the current landscape in Africa. However, I have a general understanding of how the process goes.

Are you aware of the situation of CTs across Africa? Have you worked from near or far in/with this context?

In my work I have been quite far from the context of clinical as well across Africa. However, I know a few initiatives that work towards clinical trials in Africa specifically the AVAREF initiative I know they have done a lot of work in terms of trials in Africa. And also, there was a recent publication from Michel Sidibe on the African medicine agency, and they were also looking at the CTs in Africa

Are you aware of the creation of the African Medicine Agency? Do you know its objectives?

So, the African medicine agency have several objectives and I the main one in term of its main aim is to be sure that African people have got access to quality, safe, affordable and efficacious medical products specifically for diseases that affect Africa disproportionately. They also want to upscale the regulatory capacity that we have in Africa: human resources, medicine regulatory harmonization and regulation space in general. They will also be looking at clinical trials, oversight of vaccine production as well as medical product regulation. Those are the main key objectives. And an oversight of the regional regulation initiatives

We know there are a lot of disparities across Africa in term of policy making and healthcare regulation. Several initiatives have been made in the past and were not that ambitious. Do you think that the agency will be able to encounter its objectives of global policy harmonization?

Yes, I think that they will be able to lead the objective. The reason I'm saying that is because NEPAD has been existing for over 10 years. During those 10 years, you have 5 regional economic communities who conducted medicines regulation initiative out of 8 region blocks. You have lessons that have been learned from those initiatives (from EAC…). Now when it comes to the AMA, when we want to now transition to a regional to a continental level, you can pool together the resources, the expertise and the lessons that have been learned over the last decade. It's going to be easier because it's different than starting from 0. The AMA is going to use the existing regional harmonization initiative as the foundation for its establishment. By that virtue, I think it's going to be quite easier for the agency to meet its objectives.

And secondly, when it comes to political will, you see the COVID-19 pandemic played a key role in launching the AMA and getting countries to ratify the treaty. The pandemic showed all the gap that existed in the African healthcare space. If we have had an agency as the AMA during the pandemic, certainly it would have been able to better handle the pandemic. The pandemic actually ended up being a facilitator of insuring the establishment of the AMA. There was a lot political will, not only from governments in Africa but also key stakeholders,

continentally and internationally (WHO, EU, BMG Foundation) who raised over 100M $ for the agency. With financial backing, political will and good will and also with just a place to start from (the regional initiatives), I think the agency is a good place to actually meets its objectives.

On which basis the AMA will establish its policy? Is it possible that it will be inspired/influenced by foreign policies (FDA/EMA…)? The AMA claims to be only led by African actors but we're aware of the lack of policymakers on the continent. How could it remedy this problem?

In terms of the establishment of the agency, it's definitely going to be influenced by existing institution such as the FDA and the EMA. I know for a fact that in one of the documents that was written about the AMA, they staged that part of the establishment of AMA will be based on a model that is similar to what is used in Europe. There is some learning from what already exists in other continent. There isn't really any point to reinvent when you have system in place that works. What you need to do is to learn from those continents and adapt what they have to the African context. Because our context is slightly different from theirs. in terms of the claims of the African medicine agency to be only led by African actors: We're way of a lack of policy makers on the continent. If we look at the existing regional harmonization initiatives (RHI) they all report that they have challenges when it comes to human resources. We have instances where the national regulatory authorities (NRA) or the RHI train people and those people will leave the agency because they can be paid better either by the pharma industry or by multilateral organizations. So, we have challenges in terms of remuneration and the regulatory sciences field. The challenge is in job descriptions that are not quite detailed for what exactly the role entail. In term of training programs, we don't have a lot of postgraduate training programs in Africa that look at regulatory affairs and regulatory sciences so that's also a barrier for people that should be upscaled. And also, just the number of people that are employed by NRA is not a lot. You find that in some countries, you have even 8 reviewers and some reviewer could be responsible for reviewing the entire dossier without any former specialization when they look at the clinical or non-clinical aspect of it. This multiskilling of one person is also a sour problem. But still, bearing that in mind they are initiatives in place to try and upscale the regulatory workforce and improve regulatory capacity on the continent. So, the regulatory harmonization initiative themselves are one of the keyways that regulators are actually getting upscales over the last ten years. So, these harmonization initiatives that actually have training programs. You'll find that for example in EAC. You can have a country like Tanzania which has got an NRA that operates at WHO maturity level 3 being twinned with a smaller NRA that doesn't have a lot of capacity. By having those countries twinned together, you have staff between the two agencies rotating, working and learning from the other institution. Also, by them working together, you know you get to upscale the other authority. So, they're a lot of different twinning arrangements in such initiatives that exists within the regulatory combination initiative that exist in South. That one the keyway people are getting upscaled. The second is through your stringent RA. So, you're looking at Swiss Medic in Switzerland, they're looking at the EMA which has got some procedures, you're also looking at the FDA which has the tentative approval pathway. Those process have been keys in actually upscaling African regulators. You have these two RA in Switzerland as well as in the EU regulating and looking at Marketing Authorization Application (MAA) for medical products thar are going to be used in Africa. And while they're doing this, they work with WHO and African regulators in that process of dossier assessment and evaluations in GMP inspection and that actually also upscale the African regulators. They can also learn from that process as well. So, both these initiatives: the regulatory harmonization initiative as well as the stringent

RA are helping to upscale African regulators so that we policymakers on the continent that actually know what they're doing. Obviously one of the WHO key mandate is actually to train people especially when it comes to pharmaceutical quality assurance and regulation. So, WHO has the WHO prequalification program that also involves African regulators as well. African regulators can participate in this program and improve their regulatory capacity and upscale their human resources. These 3 initiatives have been helping to actually improve the regulatory capacity and expertise in Africa. I think when the agency is actually built, because it will also be doing expertise for NRA. For now, there is 4 NRAs at maturity level 3 (Nigeria, Ghana, Egypt, Tanzania). If we have that kind of agencies and their expertise and capacity, they can contribute to the AMA and ensure that it will operate quite well. And we have the regional centre of regulatory excellence as well that have been established some years back and they also work to upscale the HR and regulatory capacity in Africa. All of these initiatives are going to make sure that we have expertise. I've no doubt they're going to be able to find people to work in the agency. Also, some people who are African and work outside of Africa might be interested of coming back home to work as well.

The regulatory harmonization projects of the agency imply a major change in policies across member states. Will it be positive? Is this a win-win operation?

Yes, I think it will be a win-win for everyone: for the continent and for the NRA themselves. As I mentioned, most NRAs have a number of challenges that they face. They've got backlogs, limited HR, limited technical capacities, low fundings as well because they do not receive money from the government. When it comes to harmonization they will benefits because they'll be able to get products on the market quicker through work sharing initiative and collaboration. You'll find that you reduce things such as duplication of efforts, the timeline of approval of MP. This is very important especially for this context. It definitely is a win for NRA. Through collaboration, they are not only upscaling themselves, but they're also will be able to dedicate their limited HR for other things that are more important, that only they can control like pharmacovigilance for their own market. At the end of the day, we must remember that all of this is to ensure that African people get access to qualitative, sure, efficacious and affordable MP. They're some publication saying that sometimes it takes even as much as 4 to 7 years for African people to get access to medicines. I think the agency being created will be a very important institution reducing some of these timelines.

The AMA is supposed to make regulatory context more open for international collaborations. Could new healthcare policies in Africa impact occidental countries. What could be the impact on the policy of a leader in CT's such as Belgium?

I think it will influence international collaborations because if you have a continental agency that brings together 55 African countries and a population of over 1.3 billion people you essentially create one big market for a number of different things. So, for CTs for example, it means that you have access to more people to participate to clinical trials and Africa also has quite diverse demographic and genetics as well. When you'll have the agency in place you will have this situation where you have access to a much bigger context. You could go through one agency for it to register your CT and get marketing authorization as well for your MP. And have access to 55 countries and 1.3 billion of people that essentially operate as one entity. The one main challenge that exists right now is that you've got countries that sort of operates in silo which makes everything more time consuming. […] I think it has an impact on international collaborations. It'll be easier to collaborate with one entity: the AMA than trying to come up with collaborations with number of different countries or number of NHRI. In term of the impact on western policies: I think it will have an impact but not to a great extent. It also depends on what exactly it's been looked at. But I think this impact we'll be really in Africa not so much impact in other foreign jurisdictions.

Do you want to add something that has not been covered by our interview?

The AMA will be hosted in Rwanda which I think it's going to be quite great. Geographically, Rwanda is quite central for a lot of people. And not only that, but they've also shown a real political will and leadership as well. We know that things are going to move there.

Would you be available for further questions in the context of this work?

/

Do you know anybody that could interested to participate in this work?

/

Key people interview: Policy expert

Present yourself: What are your areas of expertise? Are you familiar with clinical trials? With their regulation ?

Je suis pharmacien de santé publique et ma carrière a été principalement d'accompagner, d'appuyer des pays à faible et moyens revenus dans le développement du système pharmaceutique. J'ai d'abord commencé par travailler dans le système pharmaceutique principalement dans 3 pays africains : au Tchad au Sénégal et au Cameroun. Là j'ai travaillé à tous les niveaux de la pyramide sanitaire, du niveau le plus périphérique au niveau le plus central. Dans les systèmes pharmaceutiques, d'organisation, des systèmes d'approvisionnement en médicaments, d'assurance de la qualité et des achats : c'est très vaste. En fait tout ce qui peut envelopper une politique pharmaceutique dans un pays. Donc ça a été la première partie de ma carrière après ça je suis rentré en Europe et j'ai travaillé pour des organisations internationales. Là j'ai pu travailler sur les questions d'accès au traitement. Sur l'accès aux produits contre le sida et pour la tuberculose et aussi beaucoup sur la question d'accès aux médicaments contre la tuberculose mais aussi aux maladies non transmissibles. Nous regardions aussi tout ce qui était maladies respiratoires : l'asthme, les bronchites chroniques... De là après je suis parti à l'OMS au département médicaments essentiels et produit de santé à Genève où j'ai géré 2 programmes qui visait à appuyer la révision et la mise en œuvre des politiques pharmaceutiques dans les pays africains. Au total c'était 19 pays et je travaillais avec les conseillers pharmaceutiques régionaux et pays à la mise en œuvre d'activités concrètes dans ce domaine. Je travaillais entre autres au renforcement des systèmes réglementaires et à renforcer et développer les systèmes réglementaires dans les pays. Ensuite je suis partie aux nations unies où j'ai géré une équipe qui apportait de l'appui dans l'approvisionnement en produit de santé pour les programmes du fond mondial. On était aussi présent dans 19 pays. Nous apportions aussi du conseil au renforcement des chaînes d'approvisionnement et des systèmes réglementaires aussi. Donc comment utiliser l'argent donné par le Fond mondial non seulement pour acheter des produits mais également renforcer des systèmes. Nous fournissons des ressources pour aider à ça. Depuis X ans maintenant je suis consultante indépendante pour des organisations internationales et des bailleurs de fonds qui sont la Commission européenne, la commission allemande, la coopération française… Ils interviennent depuis quelques temps, un an/un an et demi de manière assez appuyée sur le renforcement des systèmes de réglementation des pays africains. […] Je travaille aussi pour le secrétariat de l'AMRH.

Are you aware of the situation of CTs across Africa? Have you worked from near or far in/with this context?

Directement je dirais non, j'ai une connaissance mais je n'ai pas travaillé directement. Je sais juste que dans le cadre de l'AMA, il y a le comité AVAREF qui accompagné l'évaluation des essais cliniques entre autres ceux des vaccins. Maintenant ça s'est étendu aux autres médicaments. Ils accompagnent les pays dans l'acceptation des essais cliniques. C'est tout ce que je sais. Je n'ai pas d'expertise dans ce domaine-là.

Are you aware of the creation of the African Medicine Agency? Do you know its objectives?

Vous êtes tout à fait consciente de la création de l'agence africaine du médicament vous connaissez également ces objectifs je ne reviendrai donc pas dessus étant donné que vous les connaissez

We know there are lots of disparities across Africa in term of policy making and healthcare regulation. Several initiatives have been made in the past and were not that ambitious. Do you think that the agency will be able to encounter its objectives of global policy harmonization?

Pour moi c'est un agenda ambitieux et compliqué à mettre en œuvre. Mais il est indispensable. Même s'il y a effectivement une grande disparité au niveau des autorités d'un pays à l'autre je vois bien grâce aux évaluations faites par l'OMS. Ils ont mis en place cet outil de benchmarking des autorités qui est maintenant utilisé dans beaucoup de pays pour évaluer à quel niveau sont des autorités. On voit bien que sur le continent africain il est encore très peu d'autorités qui sont à un niveau de fonctionnalité qui soit acceptable. Il s'agit d'un outil à 4 niveaux : le un est un niveau auquel ce n'est pas encore opérationnel c'est très balbutiant, et le niveau 4 est un niveau extrêmement performant. L'objectif pour les pays est d'atteindre au moins un niveau 3. À ce jour nous avons quelques pays qui ont atteint le niveau 3 : Le Ghana la Tanzanie l'Égypte, l'Afrique du Sud et le Nigeria. Il s'est passé des choses donc. Et moi qui travaille dans ce domaine depuis 30 ans je dois avouer que dans les 5 dernières années j'ai eu l'impression qu'il y a vraiment des choses qui se passaient. Avant j'ai eu l'impression qu'il ne se passait rien, ça ne donnait pas de résultats. C'est aussi parce qu'avant on ne savait pas ce qu'on attendait de ces autorités. Maintenant avec cet outil de benchmarking, on a un guide extrêmement clair de ce qui est attendu des autorités. Cela permet de les évaluer et également ça leur permet de s'autoévaluer. Il permet de donner un chemin de ce qu'il faut mettre en place pour arriver au niveau de fonctionnalités minimum qui est le niveau 3. Ça c'est extrêmement important parce que maintenant on sait ce qu'on a tenté ces autorités. Ce qui apparaît clairement pour moi aussi c'est que les niveaux sont très disparates et que probablement il faut que ces autorités arrêtent de vouloir toutes se développer de manière individuelle. Il faut qu'elles apprennent à travailler ensemble, à mutualiser leurs efforts et à collaborer beaucoup plus. C'est pour ça qu'une initiative d'harmonisation a vu le jour sous le secrétariat de l'AUDA- NEPAD en Afrique du Sud. Cette initiative, qui existe depuis quelques années au niveau des communautés économiques régionales a permis de définir des guidelines d'enregistrement et d'inspection des produits et établissements communes. Elle a permis des évaluations et des inspections conjointes. Pour moi c'était un excellent départ. L'objectif maintenant c'est de se dire : « c'est très bien que les pays se mettent ensemble mais comment aller plus loin dans cette harmonisation ?» L'objectif étant d'avoir une réglementation pharmaceutique qui soit structurée à 3 niveaux : continental, régional et national. Pour moi le niveau continental doit permettre aussi de faire monter l'expertise. Il y a des produits qui vont être introduits dans l'ensemble des pays mais qui sont extrêmement sophistiqués et qui demandent une expertise plus poussée pour être évalué aussi bien sur la partie qualité que clinique. Pour avoir une évaluation de qualité, il est probablement mieux de mutualiser les efforts à un niveau continental afin d'être sûr d'avoir une bonne expertise et que les résultats de cette évaluation puissent être repris par les pays afin d'accélérer l'enregistrement. C'est évident qu'avec la disparité de niveau qu'il y a devant les autorités, si on veut vraiment changer et sécuriser plus les produits qui circulent en Afrique, il n'est probablement pas opportun de développer toutes les autorités, même si elles doivent monter en capacité.

Je relisais d'ailleurs le traité pour l'agence africaine du médicament parce que je travaillais sur quel produit serait prioritaire pour une évaluation continentale. Et j'ai retrouvé dans l'article du traité qu'il mentionnait les médicaments pour les essais cliniques. C'est donc quelque chose qui est à considérer. Pourquoi chaque pays devrait évaluer les produits expérimentaux sachant qu'un essai clinique est souvent fait dans plusieurs pays ? Autant faire une évaluation à un niveau central qui pourra servir aux pays participants.

C'est ce qui arrive en Europe actuellement avec la nouvelle régulation.

Exactement oui. Moi je vois une vraie plus-value. Les pays veulent absolument être souverains garder la main sur tout ce qu'ils font mais on se rend compte que même les pays occidentaux n'arrivent pas à faire face, à effectuer correctement le travail pour évaluer les produits qui arrivent sur le marché et qu'eux-mêmes recherche à partager ce travail avec d'autres. On

imagine que des autorités en Afrique qui n'ont même pas les ressources humaines où financière en place devrait absolument travailler plus les unes avec les autres. L'objectif maintenant c'est de déterminer quel produit nous laisserons au niveau national ou bien que nous laissions au niveau régional ou encore au niveau continental. C'est un travail que nous avons actuellement. Nous discutons avec les communautés économiques régionales pour comprendre comment ils choisissent les produits à évaluer à leur niveau et où il voit des difficultés supplémentaires qui nécessiteraient de monter de catégorie à un niveau continental. Pour moi cela fait plus de sens afin d'accélérer l'acceptation des produits et surtout garantir que cette évaluation est faite correctement. Le problème aujourd'hui c'est qu'il y a plein d'autorités qui ne sont pas à un niveau de fonctionnalité acceptable et autorisent des produits sous standard ou falsifié. Mutualiser les efforts c'est aussi renforcer l'expertise et ça permet aux personnes qui font ce travail de se former les uns les autres. Bénéficier de l'expertise de chacun et faire grimper l'expertise à un autre niveau.

Vous parlez de médicaments falsifiés et je sais qu'il y a également ce grand débat en Afrique que l'AMA devra traiter celui des médicaments traditionnels entre autres. Je sais que certains pays sont plus touchés par ce genre de soucis que d'autres. Et c'est vrai qu'avoir des experts qui auront l'habitude de travailler avec ce genre de situation serait une plus-value dans ce cadre de formation mutuelle. C'est clair que chaque pays à sa spécialité qui pourrait tout à fait aider pour la suite.

Oui voilà c'est ça l'objectif aussi, une mutualisation de ressources, d'expertise. Pour un objectif de mise à disposition des produits plus rapidement.

On which basis the AMA will establish its policy? Is it possible that it will be inspired/influenced by foreign policies (FDA/EMA…)? The AMA claims to be only led by African actors but we're aware of the lack of policymakers on the continent. How could it remedy this problem?

Ce que vous dites est tout à fait juste. Ce que je vois en étant au secrétariat de l'AMRH, Il y avait un groupe de personnes qui travaillait sur la loi modèle (AU Model Law). Ils ont également des responsables de NRA, celles qui sont les plus développées, qui ont une capacité à contribuer à la mise en place de l'agence et à définir la structure et tout ce qui doit être mis en place. Moi je suis assez confiante. Je pense que le rôle que l'agence européenne joue aujourd'hui par rapport à l'agenda général c'est juste de partager leur expérience. En dehors de ça c'est vraiment aux leaders de cette agence de s'entourer de personnes qualifiées qui vont comme en Europe construire quelque chose. Le fait de consulter des structures plus développées dans ce domaine-là peut leur éviter de perdre du temps et de faire des erreurs importantes. En même temps il y aura sans doute des erreurs et dans tout ce qu'on construit c'est normal qu'il y ait des erreurs, des moments on n'aura pas pris la bonne décision. Mais moi je suis confiant qu'il y aura des gens suffisamment compétents. Il y a de l'expertise, il y a des gens qui sont intelligents pour mettre en place cette agence. Le seul souci que j'ai peut-être c'est comment on va laisser suffisamment de place aux gens expérimentés d'un point de vue légal et réglementaire afin de ne pas être bloquée par un agenda politique qui influencerait la prise de décision vers quelque chose qui pourrait ne pas être un succès.

Vous n'êtes pas la première personne à me soulever ce point. On m'a dit que parfois on a cet agenda politique qui est en arrière-plan et on se pose des questions sur le fondement de certaines décisions que l'agence ferait. Et une autre chose que vous dites aussi c'est qu'il y a des personnes compétentes. Je parlais de statistiques tantôt pour être très factuel, il y a effectivement peu de policymakers sur le continent en tant que tel. Mais il y a une donnée qu'on aurait tort de négliger en parlant de cette statistique c'est qu'il y a énormément de gens qui

partent du continent parce qu'il il n'y a pas de cadre dans lequel ils pourraient exercer leurs compétences. Un autre expert que j'ai contacté disait qu'avec une agence du médicament africaine on aurait un retour de ces personnes qui pourraient être enfin exploiter pour leurs compétences. Ce ne serait donc pas tellement un manque de ressources en tant que tel mais plutôt un manque d'opportunités.

Oui c'est ce cadre qui permettrait aux personnes qui ont des compétences de vraiment faire leur activité de manière libre aussi. Moi je suis entièrement d'accord avec vous. J'ai plein de collègues africains que je croise dans les réunions à l'internationale dans différentes agences, qui sont dans ces structures là et qui ont des choses à apporter à ce qui se met en place ; à limite beaucoup plus que moi. Moi j'ai une carrière durant laquelle j'ai travaillé avec plus souvent l'Afrique que mon propre pays finalement. Mais ce que je dis toujours et dans les cours que je donne aussi :« le temps pour des gens comme nous d'accompagner ces pays-là, il arrive à une fin ». Maintenant ce sont les collègues de ces pays qui ont été formés et qui sont peut-être allés se faire une expérience ailleurs. C'est à eux de revenir et de mettre en place les systèmes qu'il vous faut. Je pense que c'est essentiel quoi. En 30 ans de carrière, j'ai travaillé avec des gens qui ont énormément de capacité, qui ont beaucoup plus de diplômes que moi, et qui, dans un environnement de travail correct, auraient la capacité d'utiliser leurs talents.

The regulatory harmonization projects of the agency imply a major change in policies across member states. Will it be positive? Is this a win-win operation?

Oui moi je pense que ce serait bénéfique à tout le monde car ça mutualise les efforts et ça permet d'avoir un résultat plus satisfaisant. Mais également ça va faire monter l'expertise et aider ceux qui sont un peu à la traîne à augmenter leur niveau d'expertise. Également ça créera un réseau de gens qui pourra susciter une entraide. Dans ma carrière je n'arrête pas de dire qu'il y a ce que j'ai appris à l'université, les expériences que j'ai fait sur le terrain mais également et c'est la chose la plus importante : c'est le réseau. Ces gens autour de moi qui m'ont aidé à faire face à des situations et à trouver la meilleure solution. La mise en réseau ne peut être que bénéfique à tous. Ça les positionnerait aussi sur la scène internationale comme des interlocuteurs qui seront de plus en plus pris au sérieux par les autres autorités de réglementation à l'international Mais également auprès des producteurs de produits santé qui arrêtez de considérer que lorsqu'ils travaillent avec le continent africain, ils peuvent se permettre d'apporter tout et n'importe quoi.

Cela rejoint tout à fait ma question suivante. Créer une agence continentale cela va créer des contacts à l'internationale. Ce serait une vitrine pour montrer ce qui se passe sur place

The AMA is supposed to make regulatory context more open for international collaborations. Could new healthcare policies in Africa impact occidental countries. What could be the impact on the policy of a leader in CT's such as Belgium?

Quand je suis en contact avec des fabricant ils me disent toujours que pour un marché ils ont besoin d'avoir une visibilité sur la demande mais également ils ont besoin de savoir qu'ils pourront introduire leurs produits plus facilement et que les exigences réglementaires pour les introduire seront harmonisées au maximum entre les pays. Afin que quand ils soumettent un dossier pour un produit ou un essai, elle soit traitée dans un délai raisonnable et que ça incite à le faire. Pour moi si on a une agence du médicament qui coordonne une vraie harmonisation des réglementations et qui montre qu'il y a plus d'efficacité dans la réglementation, ça montre un signal très clair au producteur qu'ils ont maintenant un interlocuteur pour pénétrer sur ce marché. Ça fera aussi que les besoins de l'Afrique seront mieux pris en compte par les

producteurs. Aujourd'hui souvent les producteurs visent les marchés plus lucratifs où la demande est très claire et le continent africain n'en fait pas partie. Je pense que ce sera bénéfique pour l'évolution économique du marché pharmaceutique en Afrique.

Donc créer un terrain propice qui serait une garantie pour ces producteurs.

Do you want to add something that has not been covered by our interview?

/

Would you be available for further questions in the context of this work?

/

Do you know anybody that could interested to participate in this work?

/