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Speaking exclusively to PharmaBoardroom, Medicines for Africaâ??s Lenias Hwenda gives a comprehensive overview of the African Medicines Agency, why such a regulatory body was needed, how it differs from the European Medicines Agency, and its progress thus far. Hwenda also examines how the AMA stands to impact Africaâ??s clinical trial footprint and the role that the pharma industry can play in building a more robust regulatory ecosystem in the continent to ultimately bring better medicines to African patients in a more timely manner.

What is the African Medicines Agency?

The African Medicines Agency (AMA) is a specialised agency of the African Union (AU) whose purpose is to provide leadership in improving the regulatory environment for the development of Africaâ??s pharmaceutical sector. It entered into force on 5 November 2021 and it will be based in the Rwandan capital of Kigali. Its responsibility will include the development of common regulatory standards and harmonised legislation for medicines across Africaâ??s 54 countries. Modelled on the European Medicines Agency (EMA), the AMAâ??s functions will include regulating the development of pharmaceutical production in Africa, and the evaluation, inspection, coordination and sharing of information about medical products authorised for the African market.

Why did African countries want to create the AMA?

Fundamentally, the desire for the AMA came from the need to address several critical issues that affect the timely availability of medicines to African patients and the quality of those medicines, of which I will highlight three.

The first source of motivation was a need to create an enabling environment for local pharmaceutical manufacturing motivated by the challenge that the Africa region has a very high burden of disease (17 percent of the global population and 25 percent of the global disease burden) and it meets its medical needs by importing 99 percent of its vaccines and 95 percent of pharmaceuticals for 1.3 billion people. African countries found this an untenable situation. It kept the regionâ??s medicines supply chains extremely vulnerable to disruption and shortages that limit availability of medicines. Hence, there was a need to increase medicines availability and supply chain security through the production of medical products on the continent. And to manufacture quality, safe and effective medical products you require a regulatory environment capable of effectively overseeing quality production.

The second source of motivation for the creation of AMA was the need to reduce the timelines and cost of approving medicines in African countries. Safe and effective medicines already available in other markets often took a long time, between 4 to 7 years in some cases, before reaching African patients. Reducing timelines and cost through an effective regulatory environment improves access to medicines.

The third source of motivation for AMA was the need to control the circulation of substandard falsified medical products in African markets. The weak regulatory environment caused by a variety of factors made it difficult to police and prevent the circulation of falsified substandard medical products. This is part of the reason why the Africa region is affected by a high prevalence of them. Quality failure rates of medicines circulating in some African countries can be as high as 28 percent based on WHO quality surveys and the risk of harm to patients is immense. The need to address these issues drove the desire to take a regional approach which began with the initiation of the African Medicines Regulatory Harmonization (AMRH) Initiative in 2009 to harmonise regulations on the continent and establish a foundation for the AMA.

What factors are contributing to the marketing approval of medicines in African markets taking so long?

There are a number of reasons for this situation. Variation in the way medicines are regulated between countries contributes to the significant differences in timelines from the first regulatory submission to the final approval. Timelines are also affected by the amount of resources available to a country which contributes to differences in capabilities, levels of expertise, and the efficiency with which national medicines agencies perform their regulatory functions. Also, African regulatory agencies did not routinely rely on each otherâ??s work to reduce the regulatory work burden and to clear request backlogs. The resulting duplication of efforts had the effect of delaying access and raising the cost of bringing medicines to the African market. This, in turn, increases the cost at which African patients access those treatments.

Can you describe how challenges with medicines regulation affect African patientsâ?? access levels?

In some African countries, regulatory agencies are under-resourced financially which makes them unlikely to have an adequate workforce, both in terms of numbers and expertise, and critical infrastructure like laboratories. Additionally, many countriesâ?? legislative and regulatory frameworks are not comprehensive enough to cover all of the functions that regulators must perform, which creates grey areas that require interpretation which in turn creates bottlenecks that delay approval timelines for medicines and raise the cost of approval. Ultimately, all of this constrains regulatory efficiency.

The result is a lack of predictable and consistent availability of medications to African patients. In some cases, these regulatory hurdles have discouraged pharma companies from seeking regulatory approval in the first place. Finally, the highly fragmented supply chains with multiple actors involved create a high number of potential entry points for illicit products in African countries which are difficult to control in a weak regulatory environment. The end result is that medicines are often not available, and when they are, their cost is often too high for patients with no social protection who pay out of pocket, or their quality is questionable.

How have African countries tried to solve these regulatory challenges?

The first concerted effort came in 2009 when African regulators came together to create the AMRH Initiative, a partnership platform composed of heads of African medicines agencies, geographical and economic groupings called Regional Economic Communities (RECs) like the East African Community (EAC) and the Southern African Development Community (SADC), and other partners. It was established by the African Union Executive Council with the view of one day transforming it into an African Medicines Agency (AMA).

In effect, the AMRH is the precursor and the foundation of the AMA in that since its inception it has been laying the foundation for the AMA by shaping how regulators are working within RECs like SADC and EAC. The AMRH Initiative would help countries develop a regional approach for harmonising standards for the registration of medicines through joint work sharing and collaborative reviews to address the limited technical capacity of individual countries. The AMRH has also been supporting countries with the adoption of the model law on medical products regulation and establishing Centres of Excellence as platforms for building capacity amongst medicines regulatory agencies.

What is the relevance of RECs like the EAC and SADC for the AMA?

The relevance of RECs for the AMA is the same as for the AMRH Initiative, the AMAâ??s precursor. RECs are a means for organising work-sharing between countries by geographical and economic groupings. This means that the AMA will build on the work of collaborative processes established within these same REC groupings which were established under the AMRH process. Once the AMA is established as a legal entity with a team behind it to allow it to begin operating, it is expected to assume the AMRH functions performed within the five RECs including the Economic Community of West African States (ECOWAS) and the Intergovernmental Authority on Development (IGAD).

How well are the collaborative review processes working?

The collaborative review pathways are working very well. That work so far has shown that the REC structure is a good way of simplifying how to â??eatâ?• this proverbial elephant and make it manageable. Once the AMA opens its doors, all the work of the REC groupings would be subsumed under the AMA as it continues working towards achieving regulatory harmonisation.

What is your impression of how the creation of the AMA is progressing?

My impression is that itâ??s going very well. Great progress has been made recently from the adoption of the AMA Treaty in February 2019 to its coming into effect on 5 November 2021. Hosting arrangements with Rwanda are in place and a lot of work is going on behind the scenes to put in place the Director General and the governance structures. Once the Director General is nominated, which I speculate could be as soon as Q1 in 2023, progress towards the institution beginning its work should be pretty rapid. However, we cannot talk of progress with the AMA without mentioning progress made by the AMRH initiative, which predates the recent developments with the AMA and are a part of that progress.

Can the African Medicines Agency truly work? And can a full 54 countries be aligned?

I believe that the AMA can work. Consider that this is not something coming out of the blue. The recent progress we are seeing in creating the AMA as a regional institution is a culmination of more than a decade of regulatory harmonisation work done under the AMRH initiative. As we speak, the collaborative review pathways developed under the AMRH initiative have made great strides with easing some of the major regulatory bottlenecks that are facing countries within their regional communities. This in my view is a strong indication that the AMA approach works. It is feasible, and so far, it is going in the right direction. As for the size of the group, I can see how it probably looks like a futile exercise akin to herding cats.

However, there is precedent. The AMA is modelled on the European Medicines Agency (EMA), which went through a similar process of harmonising the regulatory environment of 50 European countries. The AMA is replicating the EMA model by harmonising 54 countries in Africa. The two are comparable. Progress so far tells me that this is a promising enterprise, and the world should give the AMA a chance.

Does it have enough support though? How many countries have already signed the AMA Treaty?

There is support from quite a significant number of countries. The majority â?? 43 of the regionâ??s 54 countries â?? have either signed, ratified, or signed and ratified the AMA Treaty. This means that each one of those 43 countries has taken an administrative step towards joining the AMA. In fact, enough countries have joined to allow the establishment of the AMA institution, which was achieved in November 2021. Much as we would like it to be done faster, we have to be realistic. We are dealing with political processes here. International Treaties take time to establish. Itâ??s inherent in their nature.

What about the major economies like South Africa and Nigeria â?? have they joined the AMA?

Amongst countries that have not yet taken any administrative step towards joining the AMA are some of the large economies like Nigeria and Kenya. Ghana, Egypt and Algeria have completed the full process of joining. In South Africa, the parliament decided to initiate the process of joining. **I**t is important to mention that whilst the membership of the large African economies is not needed for the AMA to begin its work, obviously, their membership would benefit the AMA in a myriad of ways.

Are there challenges to convincing countries to support the creation of the AMA by signing the Treaty?

My sense is that the biggest factor affecting the pace at which countries are signing and ratifying the treaty has more to do with the slow churning of the wheels of political processes than reticence. When I speak to government representatives, experts and heads of medicines agencies, the shared sentiment amongst them is that there are no major challenges. The business case for the AMA is strong and has already been clearly demonstrated. The AMAâ??s value proposition is widely accepted. The unanimity amongst African regulators on the need for the AMA is precisely why regulators across the continent have already been working collaboratively over the last decade under the various collaborative processes of the AMRH Initiative. The same needs that spurred countries to initiate work towards developing the AMA through its precursor, the AMRH, still exist and are as compelling as before. This shows that countries are already convinced.

However, setting up an institution like the AMA requires two processes, one technical, the other political. The technical part, which involves establishing structures for addressing the regionâ??s regulatory challenges and the pillars for the AMA have gone well. The political part is the ratification process of becoming a member. It is slow because the administrative approach for joining differs for each country. Individual countries have different political priorities and environments. Some are more efficient than others.

That said, creating the AMA is a journey. We can expect challenges to come up. My hope is, however, that the destination is so critical that leaders will remain committed to reaching it regardless of what challenges come up along the way.

Can the process be made faster and are there situations where this has happened?

Yes, I believe that when governments are motivated, for instance, by political incentives that rely on having full membership, the political process can be made to go faster. This was apparent with the countries that wanted to host the AMA like Rwanda, Algeria and Egypt all of whom were very quick to join. What this tells us is that when there is political will, even slow political processes can be expedited. Having said that, it is important to note that the pace of ratification is not necessarily having an adverse effect on AMAâ??s progress. Collaborative processes have already been established and are continuing their work regardless of the pace of ratification. The main thing is that work critical to the AMA continues to progress.

Do you feel that the momentum behind the AMA is real?

I am very positive that the momentum we have seen since the adoption of the AMA Treaty in 2019 followed by the AMA being formally established through the AMA Treaty on 5 November 2021, and the hosting arrangements being put in place with Rwanda is genuine. I expect that this momentum will continue in 2023 for the following reasons. Firstly, the AMA will take over the work of the AMRH Initiative which has been gathering momentum over many years. I see no reason to assume that the strong will that has brought it this far would suddenly grind to a halt. Secondly, there are incredibly talented and determined leaders driving the AMA from medicines agencies across the continent. Their strong commitment is visible through the growing number of national medicines agencies that are raising their own game through the attainment of higher levels of regulatory maturity. Just this year alone, several African regulatory agencies were certified as operating at WHO maturity Level Three, one step from the highest possible level. We can be sure that they want to see the AMA to the finishing line, and so, we can expect them to get the job done.

What in your view would it take to maintain the momentum so far generated?

Having a leader of the AMA in place will be critical to facilitate and expedite progress because the AMA will not be able to start operating until it has a Director General with a clear mandate supported by a governing body and a team. Beyond that, additional components needed to maintain the momentum include having this institutional framework supported by three critical elements. First, governments need to make a strong commitment to support the AMA politically and financially, second, the institution needs to be financed sustainably, and third, it should be able to develop and retain talent critical to driving AMAâ??s institutional success.

What is the mandate of the AMA going to be?

The AMA Treaty talks of a number of mandates, although we are still to get a clear picture on how recommendations within the Treaty itself will be implemented in practice. Inevitably, one of the AMAâ??s most important mandates will be to support countries to adopt the medicines model law, which aligns inter-country regulation of medical products and establishing Centres of Excellence as platforms for building capacity amongst African regulatory agencies.

I feel that the AMAâ??s mandate will deliver the best value in areas where it is able to strongly complement the work of medicines agencies of country, focusing on areas in which the capacity of countries is either lacking or limited. For instance, most countries have challenges with performing regulatory review of highly complex innovative products such as biologics like vaccines and biosimilars. If the AMA manages to provide a mechanism for the joint review of those types of products, including their clinical trials and joint inspections of active pharmaceutical ingredients (API) manufacturing sites at a continental level, it would enable African populations to access some of these essential medical products.

Could there be conflicts of mandates between the AMA and national-level medicines regulators?

Yes. Conflict is most likely to arise in areas that countries consider too sovereign to delegate to the AMA. For example, most countries consider their medicines agenciesâ?? ability to generate revenue by collecting fees to be sovereign and they are generally not willing to delegate that responsibility. So, the AMA must strike the balance of improving country efficiency whilst avoiding potential areas

of conflict. A good example of striking such a balance is the ZaZiBoNa collaboration (comprised of Zambia, Zimbabwe, Botswana and Namibia) which later morphed into the SADC Initiative, which is considered to be one of the most successful of the current AMRH collaborative regulatory processes. ZaZiBoNaâ??s success is largely attributed to the fact that the individual agencies of participating countries have been able to maintain their power to collect revenue through application fees. Avoiding conflict or effectively managing it will be important to AMAâ??s success.

Do African medicines regulatory agencies have a preference on what AMA should focus on?

Obviously, I do not speak for the medicines agencies, but I do speak with many of their experts and leaders. The one preference that is widely shared amongst experts and leaders including heads of regulatory agencies is that the AMA would create the greatest benefits for national, regional (REC) and continental levels if it largely performs administrative functions. The sentiment is that as much as possible, the AMA should leave technical functions to be performed by national agencies and technical working groups. This means the AMA should have a structure that leaves much of the core technical work to be performed by experts situated within national medicines agencies of countries. These experts would work with one another in collaborative review processes and technical working groups.

Do you have an opinion on how that approach could impact the AMA?

In my view, the benefit of this approach is that it could mitigate the possibility of countries losing talent to the AMA creating a potentially competitive and detrimental environment between the AMA and national regulators. Therefore, the most optimal structure is one that would allow most talent to stay within national agencies but with enough scope to contribute to the AMA as required.

What would harmonisation through the AMA help countries achieve?

Harmonising the regulatory processes of countries through a continental approach under the AMA would enable countries to deploy the best available regulatory expertise to provide greater certainty for patients by ensuring the timely availability of quality, safe medicines, more consistently and at a cost that is accessible to patients. How would the AMA achieve this? By enabling regulators to pool limited resources and achieve more with less through coordinated collaborative review processes. Alignment would not only help regulators reduce the administrative burden, it would also help them apply similar standards regardless of the country, making medicines agencies more efficient and effective. The AMA would also help simplify rapid exchange of information on important issues like medicines safety or the control of substandard falsified medications, making rapid responses possible.

Could the AMA help improve the African clinical trials environment and help the pharma industry improve diversity in clinical trials?

Absolutely! I have heard it said that pharma industryâ??s reticence to perform clinical trials in African countries is because of the perception that the capacity to regulate clinical trials does not exist. This is of course not entirely true. Regulatory capacity for clinical trials exists. However, it needs to be

strengthened and expanded. A number of African countries already have a strong R&D environment and many clinical research capabilities already exist within countries like South Africa, Kenya Tanzania and others. However, the challenge is that the currently available capabilities are not enough for a continent of this size and magnitude of health needs. If the AMA is successful in expanding those capabilities to more countries by facilitating regular training, working groups and other collaborative processes designed to further strengthen the clinical environment, this could help address one of industryâ??s biggest challenges during clinical studies -lack of diversity in clinical trials. This is a major issue that the pharma industry needs to address. Think about it, less than 3 percent of clinical trials done globally are done on the African continent. In my view, the pharma industry needs to begin proactively improving diversity in clinical trials because regulators like the US FDA are considering making diversity of clinical trials a requirement during submissions. Africa is an ethnically diverse continent that could facilitate enhanced diversity in clinical trials to the mutual benefit of industry and patients globally.

What specific actions could the AMA take to strengthen clinical trials in Africa?

The AMA could use collaborative platforms like the African Vaccine Regulatory Forum (AVAREF) technical committee to coordinate the development of clear guidelines for clinical trial design, defining correlates of protection and clinical endpoints, drawing on work done in other regions and providing clinical trial oversight. Collaborative mechanisms could also help to define correlates of protection and the minimum standards to be met for clinical trial approvals during outbreaks including for products that are based on new platform technologies like mRNA or adenoviral vector expression systems where regulatory capacity may still be weak at country level. The AMA could equally facilitate and strengthen the sharing of data around clinical trials for products needed to respond to specific health emergency situations like Ebola. This could be data for the roll out, continuous monitoring and the risk-benefit analysis of R&D products during disease outbreak situations. Strengthening the governance of clinical trials would provide assurances to investigators about timelines and processes which could help attract more investigators to perform trials on the African continent.

Can the AMA help address challenges in accessing quality medicines and vaccines in Africa?

The AMA can indeed help address challenges to access, particularly in areas where lack of access to medicines is due to regulatory challenges, for instance, in the evaluation of biologics and immunological products where there are capacity constraints on the continent. The same is true for products that are based on new technology platforms such as mRNA platform technologies, vectored vaccines, nanotechnology or other types of new technologies where capacity is still to be acquired. Building such capacity would enable those medications and vaccines to be made available to patients in African countries. Similarly, the AMA would improve access in cases where regulatory capacity limitations have prevented timely and cost-effective approval of medicines. It could also help by limiting the circulation of illicit medical products.

What role can the pharma industry play in the establishment of a robust medicines regulation system in Africa?

Three things come to mind. Firstly, by simply using the African regulatory system more, the pharma industry would strengthen the regulatory environment. This means seeking marketing approvals in

African markets, including for innovative therapies, vaccines and biologics in order to take advantage of the harmonised processes. This would expose African regulators to the experience of evaluating innovative products they may not have encountered before because of pharma not seeking regulatory approval in African markets. Secondly, the pharma industry can strengthen the clinical trial regulatory environment by increasing the number of clinical trials it performs on the African continent. This would also enable the industry to address its own challenge â?? the lack of diversity in clinical trials. Thirdly, pharma could invest in bringing parts of its product value chains to the African manufacturing ecosystem, which would strengthen the regulatory environment. After the Covid-19 pandemic, it is clear that regionalising supply chains is one of the best ways to mitigate against disruptions caused by international trade restrictions such as import bans that are typical of emergency situations. Pharma companies like Sanofi, Pfizer and Janssen have taken steps to shorten their supply chains by partnering with African biotech companies to perform fill and finish on the African continent demonstrating that this is a feasible strategy. There is tremendous scope for pharma to partner with African biotech companies in order to shorten supply chains to the region.

What lessons can the AMA learn from the EMA?

Potential lessons include, one, how to structure the governance of the AMA and its revenue to make it sustainable, and two, potential pitfalls when defining the division of labour between AMA and country agencies to ensure strong complementarities and to minimise potential conflict â?? both real and perceived â?? that could arise when engaging with various key stakeholders including the pharma industry. The AMA is modelled on the EMA and the EMA is expected to provide technical support towards the development of the AMA. This creates tremendous scope for the AMA to learn from the EMA and to adapt those lessons to the African context**.** My **Lancet** article which I co-authored with Michael Makanga, who leads the European & Developing Countries Clinical Trials Partnership in the Hague and Michel Sidibe, the African Union Special Envoy for the African Medicines Agency, explains in greater detail some of the ways that the AMA could be the key to unlocking clinical trials in Africa including what the AMA could learn from the EMA.

Are there major differences between the AMA and the EMA?

There is one major notable difference between the AMA and the EMA which makes them not comparable outside areas where there is room to learn from one another. The EMA makes recommendations to a Central legislative body, the European Commission (EC). The EC has a Parliament that is able to pass the EMAâ??s recommendations into law that European countries who are members of the EMA are then compelled to follow. The AMA will be able to make recommendations to the African Commission but they will not be binding on African Union member states. Without a corresponding legislative body or a mechanism that transforms AMAâ??s recommendations into a binding law or regulation that countries are compelled adopt, it may be difficult for the AMA to replicate all of the successes of the EMA, at least not without a special mechanism for making its decisions binding to Treaty members, in cases where this is needed.

What is the relevance of Medicines for Africa to the AMA process?

Medicines for Africa was invited to be a stakeholder in the AMRH partnership platform because it is a critical stakeholder in what the AMA seeks to achieve. Our mission is to improve the availability of medicines at prices affordable to patients. At the beginning, we sought to achieve that by becoming

a consolidating mechanism that pools the needs of buyers to create economies of scale and improve the price at which African patients access treatment. We continue to evolve. In light of the hurdles, we encounter including regulatory affairs, our work has expanded to include a strong advocacy component which involves engaging with regulators, governments, health providers, international organisations and the industry. We advocate for simpler less-costly regulatory approaches that allow patients to access quality, safe and efficacious life-saving medications faster and more reliably.

In your view, how is Africaâ??s healthcare environment likely to evolve over the next 10 years?

I expect that budget allocation over the next ten years to increasingly reflect a greater understanding of the importance of health security as a foundation for the economic security of African nations. Covid has shown this. Governments that are serious about getting on a sustainable path of economic growth and development will allocate more resources towards health.

With the WHO predicting an increasing frequency of disease outbreaks on the African continent over the next ten years, we are likely to see regional organisations like the WHO Africa and Africa CDC continuing to drive efforts to strengthen regional mechanisms for surveillance, preparedness, early detection and outbreak response. Ultimately, regional mechanisms can only be as strong as the primary care systems within countries on the continent. Covid-19 disrupted childhood vaccinations and reversed gains in vaccine-preventable diseases with tens of millions of children missing routine vaccines. Existing medical needs are currently not being met. The population is growing with expectations that governments should expand service provision for previously neglected problems like non-communicable diseases (NCDs) driven by growing awareness of their large burden on the African population, increasing screening and diagnosis. The result of these factors â?? more frequent disease outbreaks fuelled by changing climate, resurgent vaccine-preventable diseases and demand for treatment for NCDs alongside unmet medical needs will significantly increase the demand for treatment.

An improved regulatory environment under AMA supported by a growing number of national medicines agencies operating at a higher WHO regulatory maturity level is likely to progressively make the African market more attractive for clinical trials and production of medicines to serve the growing medical needs on the continent. Alongside an aggregate common market under the African Continental Free Trade Area (AfCFTA), these changes will likely make the business case for producing on the continent more compelling for companies seeking to grow their market share in the region.

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