African Medicines Registration Harmonisation (AMRH) Initiative: Summary, Status and Future Plans

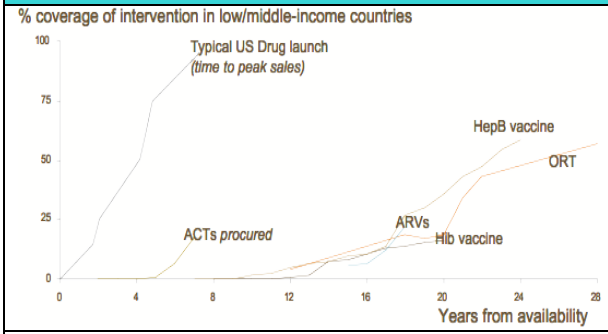
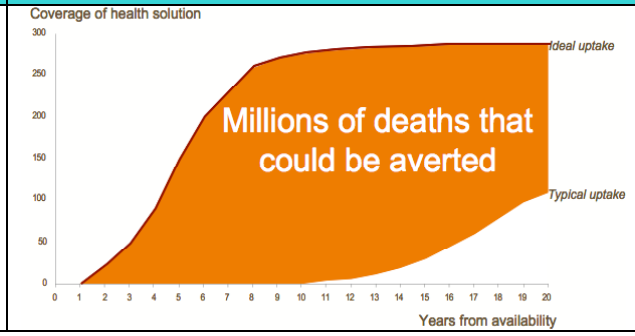
The AMRH initiative has been created to assist African countries and regions to respond to the challenges posed by medicines registration – as an important, but neglected area of medicines access. It seeks to support African Regional Economic Communities and countries in harmonising medicines registration and is seeking interested donors and other stakeholders that can help offer the requisite support.

1. The aim of the African Medicines Registration Harmonisation (AMRH) initiative

The challenge: In many African countries a lack of harmonised technical requirements and capacity for medicines registration jeopardizes timely access to essential medicines

- **Every country is obliged to regulate the pharmaceutical products sold within its borders:** This includes pre-approval scientific assessment of essential medicines (registration) so that citizens can access these medicines and be assured that they meet acceptable standards of safety, quality, and efficacy.
- **But constraints exist that make these obligations difficult to fulfill:** Many African countries lack sufficient regulatory capacity to approve medicines for sale (both in a timely fashion and in terms of ensuring acceptable quality, safety and efficacy standards). Manufacturers for their part are confronted with numerous and disparate regulations, frequent delays, and little process transparency.
- **As a result, much needed medicines lack availability in many African countries:** Fewer medicines are available in African countries than in the US, EU, etc., and prices can remain higher for longer (as manufacturers are unable to benefit from the scale economies associated with faster access to larger markets, competition is introduced more slowly and cross-country pooled procurement is delayed).

The impact: A lack of essential medicines might contribute to significant disparities in health and life-expectancy between low-income African counties and high-income countries

Low regulatory capacity and poorly harmonised registration processes may be one of the factors limiting patient access to essential medicines and other health interventions	**Poor uptake of new and existing health solutions costs millions of lives across low-income countries**
	
Source: WHO/UNICEF; World Bank; BCG analysis	

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A solution: The AMRH initiative's aim is to support African countries to overcome these constraints by building effective medicines registration through regional harmonisation and capacity building

The primary aim of harmonising technical requirements and processes for medicines registration is to improve public health, by increasing timely access to safe and effective medicines of good quality for the treatment of priority diseases. Access will be increased by reducing the time it takes for essential medicines to be registered in-country without compromising quality (including the time needed for industry to prepare their registration application/dossier) and so potentially the time taken for essential therapies to reach patients in need (depending on funding, distribution mechanisms etc.). This will require capacity building to ensure transparent, efficient and competent regulatory activities (assessment of registration dossiers and related inspections) that are able to assure the quality, safety and efficacy of registered medicines.

Overall aim:	**To improve public health by increasing rapid access to safe and effective medicines of good quality for the treatment of priority diseases**
Specific aim:	**To reduce the time taken to register essential medicines**

How could medicines registration processes in Africa be improved?

Today's current environment	A harmonised future environment
■ ~ 50 different National Medicines Regulatory Authorities (NMRAs) (working independently) to register medicines across Africa	■ Approx. 5 or 6 regional groups (each with harmonised technical requirements) coordinating registration across the entire African continent
■ Different administrative and technical requirements, processes and procedures for medicines registration across NMRAs	■ Common (harmonised) registration documentation (format and technical requirements), procedures, and decision-making processes across African regional groups
■ No clear indication of the time taken, or the maximum times allowed, for regulators to assess and register medicines	■ Streamlined processes that are faster, more predictable and better aligned to public-health needs (in terms of prioritization, conditional approvals etc.)
■ Limited transparency before or during the registration process	■ Transparent and clear procedures, and a good understanding of registration requirements and processes by all stakeholders

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What would success look like?

1	**Increased regulatory technical capacity and more efficient resource use**	NMRAs benefit from economies of scale, capacity building and the best use of skilled resources by pooling capacity to ensure timely, cost-effective registration. This would include mechanisms to avoid duplication by shared responsibility for scientific assessments and inspections and leveraging the potential of well-established regulators.
2	**Increased requests for registration from manufacturers**	Industry benefits from harmonised registration documentation (dossier format and technical requirements), increased transparency and fewer delays (and so less expense) in preparing registration applications for multiple countries. More predictable registration processes and shortened (within certain limits) timelines for registration mean that manufacturers can access larger markets faster and so creates an incentive for manufacturers to register more of their products across more countries
3	**Cost savings**	Governments, donors, and patients can achieve greater savings with more (lower-priced) generics on the market, downward pressure on prices through enhanced competition and pooled (shared) procurement
4	**Greater access to medicines**	Communities get quicker, wider access to essential medicines
5	**Donor reach and MDG success**	The reach of donors will be extended to encompass more countries in Africa and more people (as medicines affordability improves). This should result in greater progress towards the three health-related Millennium Development Goals (MDGs 4, 5 and 6)

The AMRH initiative approach seeks to support African Regional Economic Communities (RECs) and countries to harmonise medicines registration using existing political structures and building on existing plans and commitments

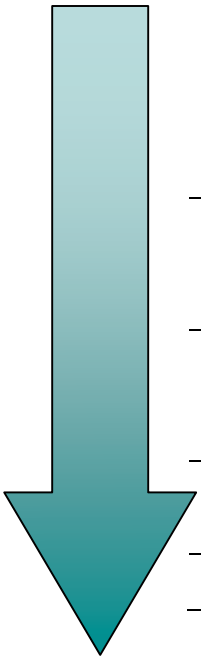
The AMRH initiative was initiated at a New Partnership for Africa's Development (NEPAD) and Pan-African Parliament (PAP) consultation meeting in February 2009, which was hosted in collaboration with their Consortium partners (see below). The meeting attracted representatives from nine of the continent's Regional Economic Communities (RECs) and over 40 national medicines regulatory authorities (NMRA). This provided a strong endorsement for the consensus plan that emerged and hence the approach that RECs and NMRAs are now taking.

This approach has been for RECs, with NEPAD and WHO support, to develop project proposals outlining their plan for medicines registration harmonisation, and for which NEPAD and WHO are now working to mobilise donor funding and other stakeholder support.

At the same time, NEPAD and WHO are developing linkages, with the aim of building an institutional structure around the AMRH initiative that will ensure broad representation and active participation of all stakeholder groups, thereby enhancing the initiative's sustainability.

The ultimate goal is to expand the initiative to encompass other health products and regulatory functions.

How will the AMRH initiative mobilise financial and technical support?



Convene key leaders to discuss the potential value of harmonising medicines registration within and across African Regional Economic Communities (RECs), review existing REC plans and processes, and discuss the possible need for continental coordination within the framework of the African Union

AMRH REC & NMRA Consultation Meeting (February 2009)

Interested RECs develop and submit summary project proposals outlining their plans for medicines registration harmonisation

First proposals submitted (May 2009) – strengthening and refining ongoing

Use summary project proposals to solicit donor support for REC projects as well as mobilize resources to facilitate continental coordination and development/facilitation/leadership

AMRH Donor & Stakeholder Discussion Meeting (November 2009)

Donors invite full project proposals where they believe that there are good prospects for success

Regional groups that receive funding begin implementing their projects (ideally in early 2010)

2. African political commitment and REC-based approach

What is the level of existing political will and commitment?

At the continental level, the African Union (AU) approved the **Pharmaceutical Manufacturing Plan for Africa** in 2007, which specifically recognises the need for African countries to strengthen their medicines regulatory systems by pooling their resources in order to achieve public health policy priorities.

Such systems are vital to assure the quality, safety and efficacy of locally manufactured products and their positive contribution to public health. Moreover, the success of local production will partly depend on intra-regional and intra-continental trade to create viable market sizes. Currently, trade in pharmaceuticals is hampered by poorly harmonised administrative and technical requirements for medicines registration, which create technical barriers to the free movement of products manufactured in Africa (and beyond) – and has negative consequences for timely patient access to quality essential medicines.

The AMRH initiative falls within the ambit of this Plan and is a key component in supporting African countries to respond to AU's mandate (established in the plan) to fulfil national obligations to provide all citizens with safe, quality, and effective essential medicines.

Why a REC-based approach?

In keeping with the African Union's strategy for development collaboration across countries, the AMRH initiative is working through the continent's political structures, in the form of Regional Economic Communities (RECs). RECs exist to promote common trade, economic and market opportunities to those countries (aligned geographically) that constitute their member states. In addition to economic development, many RECs also work to promote social development and are increasingly active in the health field.

Several RECs have already supported harmonisation of medicines registration by developing common pharmaceutical policies and operational plans – backed by high-level political commitments and mandates. For example, in East Africa under the provisions of Chapter 21 (Article 118) of the East Africa Community (EAC) treaty, medicines registration harmonisation is an explicit policy priority. Likewise, in Southern Africa, Ministers of Health approved the South African Development Community (SADC) Pharmaceuticals Business Plan, with explicit goals to harmonise medicines registration.

However, implementation of these policies and plans has suffered from a lack of financial and technical resources and has not progressed significantly. Moreover, RECs continue to work largely in isolation. Coordination is needed to avoid duplication of effort and ensure consistent approaches, especially given that more than three-quarters of African countries belong to two or more RECs. This is where the AMRH Initiative can add value.

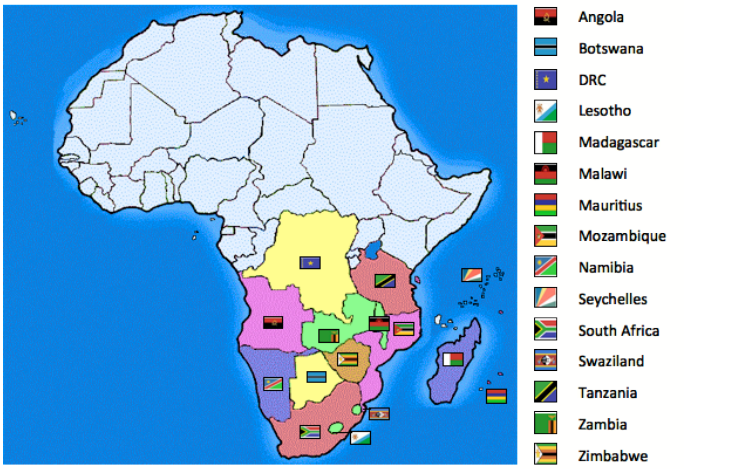
Which RECs is the AMRH initiative currently partnering with?

The African Union officially recognizes eight RECs – ranging in size from five to more than twenty-five member states – and all of which have been invited to participate in the AMRH initiative. In addition the initiative is actively engaging with other regional groups that are already active in the medicines registration field.

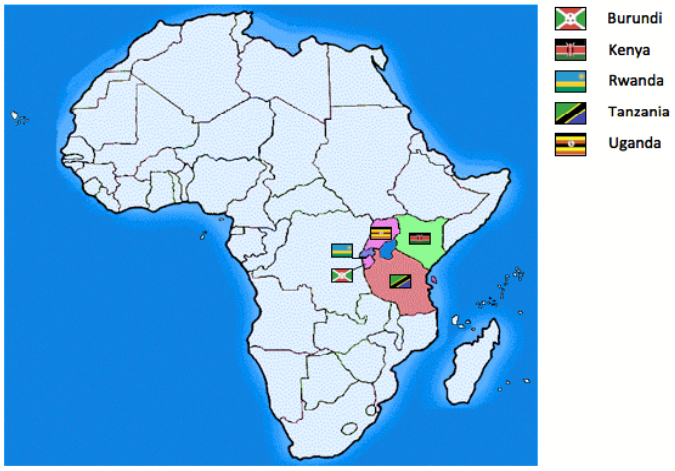
As of November 2009, the AMRH initiative is actively partnering with four regional groupings (two of which will be spearheaded by two different RECs working in collaboration) to develop project proposals in support of medicines registration harmonisation. Together these RECs constitute 41 of the Africa's 54 countries (or its 47 Sub-Saharan African countries).

The remaining countries are in north and northeast Africa and RECs that operate in these respective regions have expressed a strong interest in participating in the AMRH initiative, which aims to benefit the entire continent. Indeed, a more intensive effort in north and northeast Africa is in place for 2010.

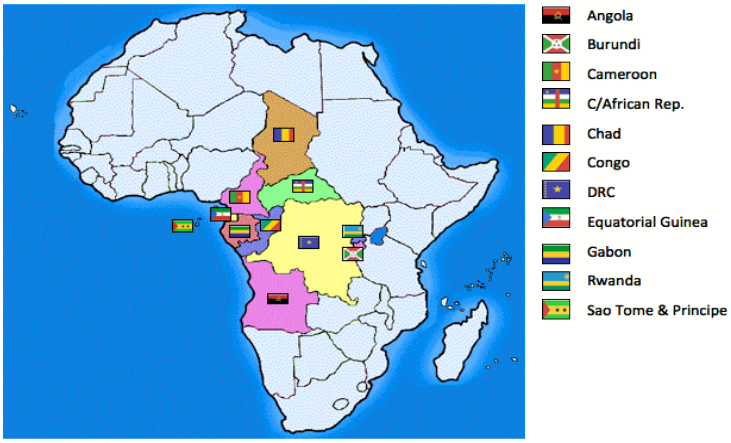
Southern Africa: SADC (South African Development Community) – 15 member states



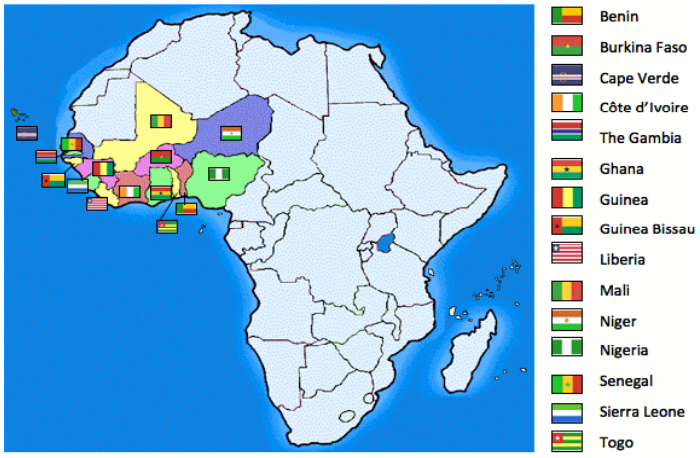
East Africa: EAC (East African Community) – 5 member states



Central Africa: ECCAS (Economic Community of Central African States) **and OECAC** (Organisation de Coordination pour la lutte contre les Endémies en Afrique Centrale) - 11 combined member states



West Africa: ECOWAS (Economic Community of West African States) **and UEMOA (**Union Economique et Monétaire Ouest Africaine) – 15 combined member states



3. AMRH initiative timing and critical success factors

This initiative is timely for several reasons:

Market Dynamics

– Medicines prices for many of Africa's high priority diseases have come down in recent years e.g. through the availability of generic versions of HIV/AIDS therapies and greater purchasing volumes (by international donors such as GFTAM, PEPFAR and UNITAID). It is therefore important for countries to ensure that they can rapidly and efficiently assess the quality, safety and efficacy of these medicines in order to fully realise their potential public health benefits.

- There are also encouraging signs when it comes to developing new medicines to treat priority (including neglected) diseases in Africa (through Product Development Partnerships and other innovative mechanisms to incentivise R&D) meaning a strong product pipeline. Again timely registration will help to more rapidly realise the potential public health benefits.
- As medicines prices have started to come down, donor interest has moved towards the health of the pharmaceuticals market more broadly and there is a growing appetite to support health systems strengthening – including medicines regulation and distribution systems.

Political Commitment

- RECs are rapidly moving towards stronger economic integration, which hastens the need to reduce technical barriers to trade, such as poorly harmonised medicines registration requirements. For example the EAC established a customs union in 2005, plans to operationalise the EAC common market in 2010 and monetary union in 2012, and ultimately to achieve full political federation.
- Many RECs are already working towards medicines registration harmonisation, have ministerial mandates and commitments in support of this and/or existing frameworks and preliminary plans in place. This is what the AMRH initiative seeks to build on.
- There is growing support for the New Partnership for Africa's Development (NEPAD), and its REC-based approach as the continent's engines for growth and development. NEPAD has been adopted as the Africa's preferred development strategy and has received support from the UN General Assembly, amongst others. The NEPAD Secretariat is an organ of the African Union, based in South Africa. It is active in a number of sectors. The AMRH initiative is a collaboration of NEPAD Health, NEPAD Science and Technology and the African Union Commission.

Consequently, many of the key conditions for achieving success are already in place or under development.

1	African political commitment	Joint decisions by key parties on African Health Strategy – African Union Commission – African Union Conferences of Ministers – Pan African Parliament	✓
2	African ownership	RECs and countries jointly own the initiative – Full political mandates in place (or in progress) – Progress on common pharmaceutical policies, operational plans, common medicine registration standards etc.	✓
3	Existing regional structure for harmonisation	Regional Economic Communities provide a structure for harmonisation – Recognized by African Union – Functioning trade agreements & activities already in place	✓
4	Timely resourcing of initiative	Previously planned common standards failed due to a ***lack of technical, financial and human resources, at both national and regional level***	⇨

4. The project Consortium

The Consortium brings together political, technical and donor organizations, in response to RECs' technical and financial support needs, with respect to harmonisation of medicines registration. Beyond working to mobilise financial and technical resources for project implementation, the Consortium is promoting and facilitating inter-REC communication, coordination and shared learning. It is also working to develop linkages and build an institutional structure around the AMRH initiative to ensure the broad representation and active participation of all stakeholder groups, thereby enhancing its sustainability.

The Consortium is actively seeking other interested parties to collaborate and offer their support

Existing Consortium Partners	**Political/technical/organizational:** – World Health Organization (WHO HQ, AFRO and EMRO) – New Partnership for African Development (NEPAD) – Pan-African Parliament (PAP) – African Union Commission (AUC)	**Donors:** – Bill & Melinda Gates Foundation (BMGF) – UK Department for Int'l Development (DFID) **NGOs:** – William J. Clinton Foundation
Consortium Objectives	1. Mobilize political and high level support and financial and technical resources for AMRH 2. Promote and facilitate inter-REC communication, coordination, technical consistency and shared learning with respect to AMRH. Build a continental initiative. 3. Provide technical support to assist with: priority setting and plans for regulatory harmonisation; a common format for registration documentation and common technical requirements for assessing the quality, safety and efficacy of medicines; good regulatory practices; regulatory capacity building (for assessment and inspections); and regulatory decision-making and communication	
Communications	– NEPAD manages AMRH initiative communications and is responsible for liaising with REC and NMRA partner institutions on behalf of the Consortium and in line with its steering and coordination role – Other members of the Consortium also utilise their networks and institutional relationships to publicise and promote the AMRH initiative – An AMRH initiative newsletter is published as needed (the second edition was published in October 2009) and an AMRH initiative website is in process	
Funding	The Consortium has some initial funds committed but more is needed (both money and in-kind technical support/resources) to fully operationalise the AMRH initiative.	

What are the roles and activities of current Consortium partners?

Some of the key contributions of the Consortium partner are outlined below. In practice, however, the Consortium has adopted a collaborative and consensus-driven approach in all aspects of its work – meaning a high level of participation from each of the partners across the full range of Consortium activities.

NEPAD: Political advocacy, administrative and planning support to the Consortium, mobilising, coordination and sharing between various RECs, political link to African Union, Pan-African Parliament and African Union Commission, identifying and mobilizing other donors for the Consortium

WHO: Developing global norms and standards, regulatory support to NMRAs (building on former and ongoing activities in the region), technical support to RECs in preparing project proposals, mobilizing other donors, technical support to RECs in implementing the approved projects, promoting continental and global consistency of regional Harmonisation efforts and materials

Donors (Bill & Melinda Gates Foundation, DFID): Mobilizing other donors to participate in the Consortium; participating in the technical review of summary project proposals, identifying and approving project proposals for funding in 2010.

Other stakeholders: The William J. Clinton Foundation is providing in-kind support through a dedicated project resource in the form of a consultant seconded to the NEPAD Secretariat.

5. Consultative proposal development approach and status

Following initiation of the AMRH initiative at the end of February 2009, several RECs submitted summary project proposals describing their high-level plans for medicines registration harmonisation at the end of May 2009.

Following their review, the Consortium actively partnered with four REC groupings (EAC, ECCAS/OCEAC, ECOWAS/UEMOA and SADC) to support them in strengthening and moderately expanding their proposals. In the first instance, this involved written feedback from the Consortium followed by a visit from a NEPAD delegation to explain the Consortium's feedback and agree a timeline for next steps. Given the importance of NMRA consultations and ownership, NEPAD has also made some funding available for RECs and their constituent NMRAs to jointly ensure that their project proposals reflect their shared vision for harmonised medicines registration.

This is unfolding as a two-stage process consisting of smaller writing workshops (utilising NMRA experts from the region), followed by broader NMRA endorsement meetings, with representation from all member states and guidance from WHO and NEPAD. The proposals are then being taken through the REC decision-making structures to secure Ministerial approval.

In this way, member state REC/NMRA joint ownership and political commitment is being strengthened – significantly increasing the prospects for project success. The following table illustrates REC workshops/meetings that have take place or are planned.

African Region	REC	Writing Workshop	NMRA Endorsement Meeting	Proposal status
East	EAC	16th-19th Sept 2009	21st-25th Sept 2009	Second draft submitted
West	ECOWAS/UEMOA	28th – 30th Sept 2009	12th – 14th Oct 2009	Second draft submitted
Central	ECCAS/OCEAC	26th – 28th Oct 2009	Q1 2009	Initial draft submitted
Southern	SADC	Q1 2009	Q1 2009	Initial draft submitted

6. Key features of emerging REC project proposals

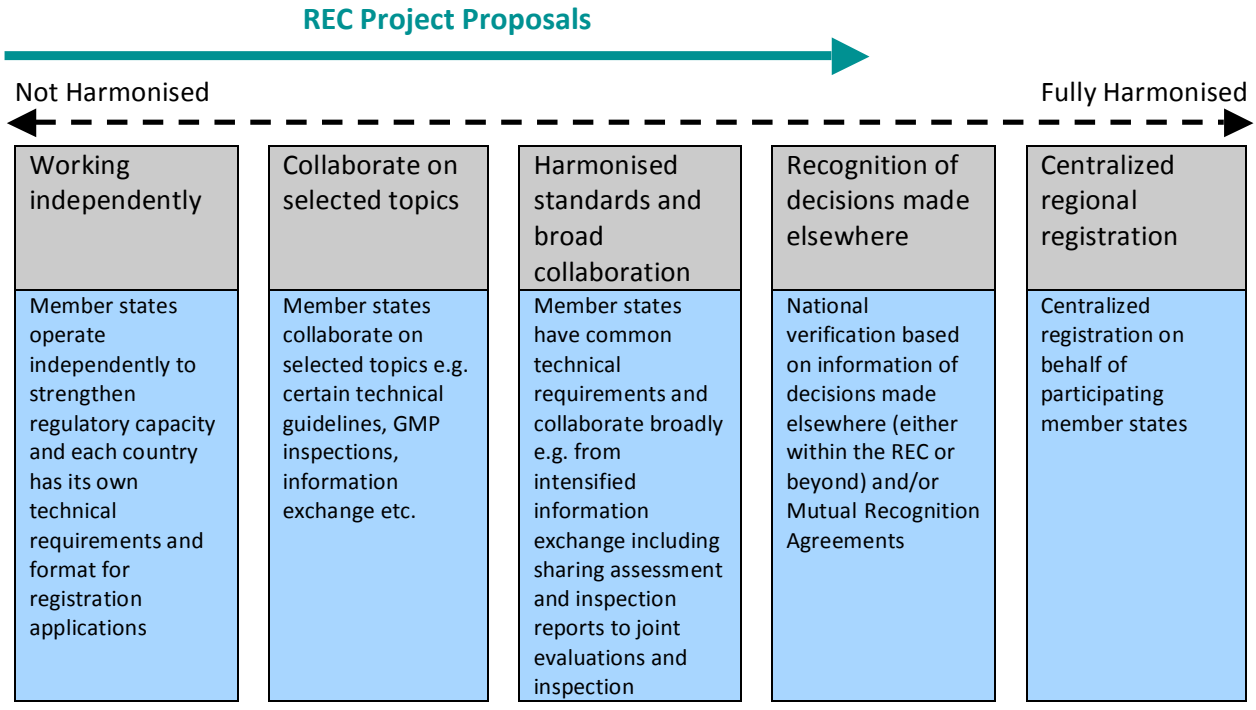
What is the duration and scope of the proposals?

The REC project proposals focus on priority essential medicines - mostly (though not exclusively) multi-source generics. These will be defined by the RECs according to region-specific disease burdens, in order to maximise the benefits to public health.

Based on Consortium guidance, the duration of project proposals is five years, although the start date will vary depending on when individual project proposals are finalised, as well as when funding becomes available.

How far will the projects move RECs towards full medicines registration harmonisation?

In most cases REC member states will progress from working independently to achieving harmonised standards (initially within their region and then across the continent at a later stage) and collaborating broadly over the five-year period. Beyond this, it is expected that RECs will benefit from scientific assessments carried out by other well established regulators and WHO Prequalification Programme by recognizing decisions made by these bodies and incorporating these into national decision-making processes, as part of their efforts to streamline processes and adopt/strengthen risk-based approaches to medicines registration (i.e. tailor work effort according to perceived risk, based on a variety of factors including whether or not the medicines has been approved elsewhere).



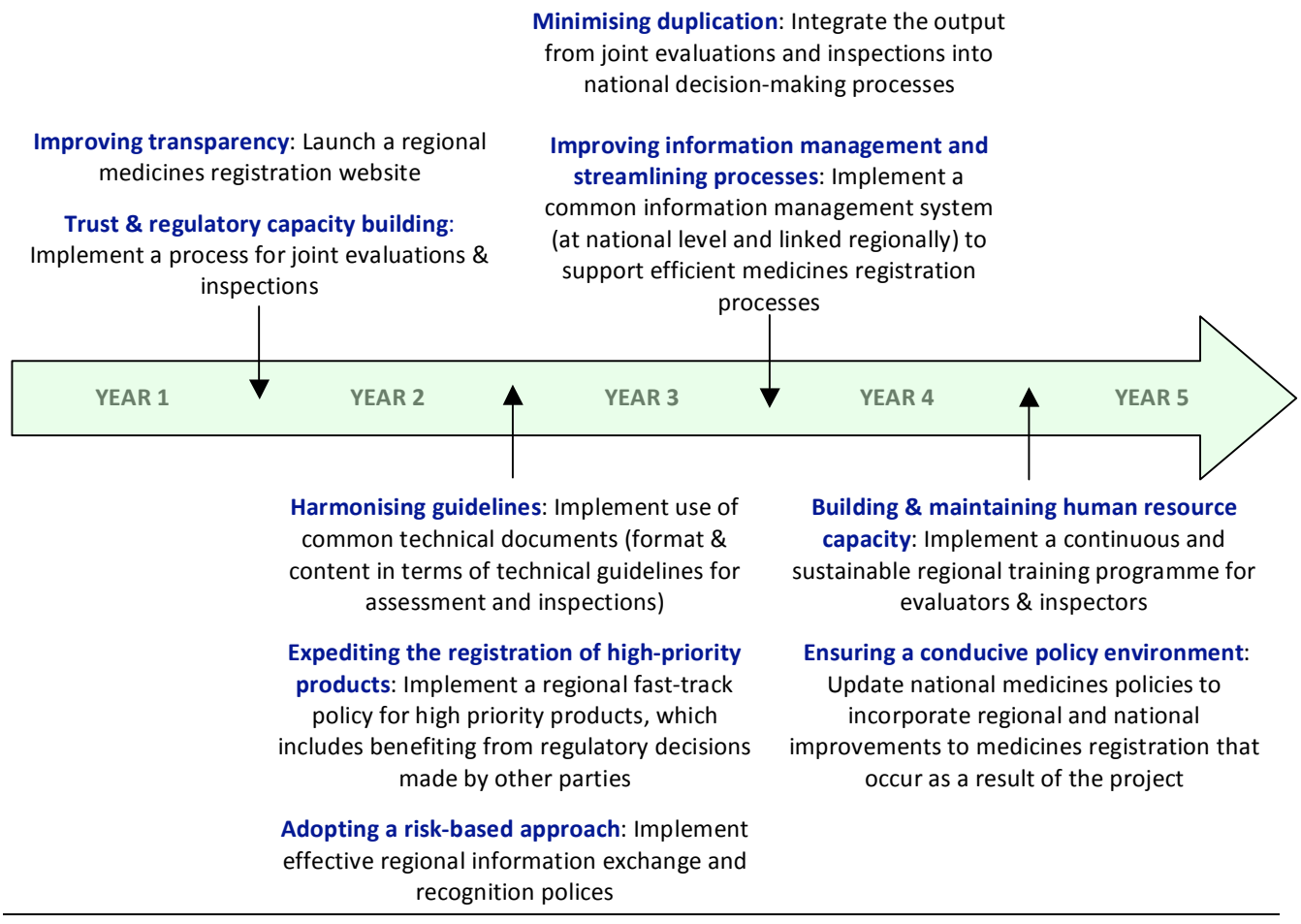
What are the broad objectives?

The Consortium is promoting a common framework, focusing on near-term steps, to promote medicines registration harmonisation. These include national implementation of a **Common Technical Document** (a harmonised format to present technical data), **harmonised technical requirements** for and/or **common procedures for the registration of essential medicines** (mostly generic pharmaceuticals as a first step), and intensive regional collaboration in support of **strengthening national and regional regulatory capacity**. RECs are tailoring their specific objectives within the broad objectives of the initiative, to ensure these meet local needs, circumstances and preferences.

What are the key milestones and timeframes?

Although the project proposals differ in their specific content, the following diagram illustrates some typical key milestones over the 5-year period. However, development work towards attaining the milestones will often begin more than a year in advance of the set milestone.

Typical key milestones and timeframes of a regional medicines registration harmonisation project



What are the projects' staffing plans, governance structures and decision-making processes?

Invariably, the projects focus on establishing a project management team or a secretariat with dedicated staffing at regional level. These will be fully absorbed and embedded within RECs' existing institutional frameworks – benefiting from a direct reporting line to member states' Ministers of Health and Heads of State, linkages to regional legislative assemblies, etc. In addition, structures already exist or will be established to enable participation of technical experts and heads of NMRAs in regional expert committees/technical working groups and project steering committees. Member state oversight and participation in decision-making processes will be complemented by the nomination or appointment of an AMRH dedicated staff member within NMRAs to provide an effective linkage between consensus-based decision-making at the regional level and effective implementation at the national level.

How will activities be sustained once funding support has ended?

Plans to sustain and expand project activities beyond the 5-year project period are being built into REC proposals. These include maintaining and growing project management structures, with financial responsibility for these assigned to the RECs and their member states, and establishing other sources of funding e.g. industry fees. For example, the EAC has plans (based on a March 2008 directive from the EAC Council of Ministers) to establish an "East African Community Medicines and Food Safety Commission (EAMFSC)" responsible for regional coordination of regulatory activities with respect to medicines and food. Project staffing under the EAC proposal will help contribute to the establishment of the Commission, as an autonomous institution within the EAC structure. Similarly, ECOWAS has made plans to upgrade the ECOWAS Medicines Registration Harmonisation Board (that will be established as part of the project) consisting of Heads NMRA and expert committees, to a regional coordinating mechanism, designated "ECOWAS Medicines Regulatory Agency (EMRA)" to be funded through member state contributions and industry fees. The EMRA will provide technical assistance to member state NMRAs as well as register critical products for public health interventions for use within the ECOWAS region.

Other sustainability provisions include:

- **Ongoing advocacy and communication** to build and maintain stakeholder (including political level) support at both national and regional level
- **Implementation of a regional update process** to ensure that the common technical guidelines that are implemented as part of the project are sustained on an ongoing basis
- **Updating national medicines policies** to incorporate regional and national improvements to medicines registration that occur as a result of projects (e.g. to reflect information sharing and recognition policies, fast-track policies etc.)
- **Development of continuous training programmes** for evaluators and inspectors, taking into account available NMRA current and projected resources, which will be implemented (using NMRA resources) on an ongoing basis to ensure that the capacity built as part of the project is sustained

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7. Estimated funding and support needs

Currently four REC groupings (EAC, ECCAS/OCEAC, ECOWAS/UEMOA and SADC) are finalizing their proposals, which will indicate the resources they will need to implement their medicines registration harmonisation plans over the next five years. A preliminary examination of these REC proposals indicates that funding will cover: personnel, REC coordination, consultants/experts (including for evaluation and inspection), training, equipment and advocacy. Each region is expected to require between $10 million and $15 million over that five-year period, including additional coordination and technical assistance. This will also depend on the size and scope of each proposal and the number of countries covered in each region. It is likely that 5 or 6 REC groupings will eventually cover the entire African continent, once the AMRH process in north/north-east Africa progresses further.

Initially the RECs will need both financial and in-kind support to launch this initiative. In-kind support may include technical assistance, training of regulatory personnel, consultation/secondment of regulatory experts and proactive information sharing. However, due to the unprecedented scale of the undertaking and the proposal development work in progress, it is not possible at this stage to exactly specify all costs. Some corrections may be necessary when more precise information about all the project proposals becomes available and projects start to roll out.

Initial support activities for RECs – provided by NEPAD and WHO -- have been partially funded so far by the Bill & Melinda Gates Foundation and UK's Department for International Development (DFID), but a number of donors have shown interest in and are engaging with the process. Only after potential donors have reviewed the final REC project proposals is it expected that funding and in-kind resources will be committed.

8. A note on national sovereignty

The AMRH process is owned and driven by African countries and RECs. In creating their project proposals, countries and RECs will tailor objectives and activities to meet their own specific needs, circumstances and preferences in line with the major objectives of the initiative. The Initiative focuses on near-term steps to promote medicines registration harmonisation, meaning that registration decisions will remain firmly that of sovereign nations.

In the longer term, and as the initiative progresses, there will be scope to build on these systems to further avoid the need to engage every country at every stage of the medicines registration process. However, such a process must continue to respect national sovereignty and will require agreements between countries and shared governance, to allow countries to opt out if they wish to do so.

This is why it is so advantageous that this initiative is hosted within the African Union and the Regional Economic Communities, which have the formal structures to address these issues. As such, the AMRH initiative is well placed to bridge the policy to implementation gap that has been hampering advances in medicines registration and other related fields.

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