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Regulatory Harmonization vs. Divergence: A Critical Review of ICH, WHO, and PIC/S in Global Drug Approvals

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Abstract:

The global pharmaceutical landscape is marked by concerted efforts toward regulatory harmonization through organizations such as the International Council for Harmonisation (ICH), the World Health Organization (WHO), and the Pharmaceutical Inspection Co-operation Scheme (PIC/S). These initiatives aim to standardize technical requirements for drug development, manufacturing, and approval, facilitating faster access to safe and effective medicines worldwide. However, persistent divergences in national regulations, particularly in low- and middle-income countries (LMICs) like those in Africa, undermine these goals, leading to delays, duplicated efforts, and inequities in drug access. This review critically examines the progress and limitations of these harmonization bodies, highlighting challenges such as political barriers, resource constraints, and varying implementation capacities. With a focus on African perspectives, it explores regional initiatives like the African Medicines Regulatory Harmonization (AMRH) and the nascent African Medicines Agency (AMA), underscoring their potential to bridge global-African divides. Drawing on recent developments as of 2025, the paper argues for enhanced reliance mechanisms, transparency, and political commitment to achieve true convergence. Recommendations include tailored capacity-building for African regulators and integration of local manufacturing needs into global standards.

Keywords: Regulatory harmonization, ICH, WHO, PIC/S, Drug approvals, Africa, AMRH, Global health equity

1. INTRODUCTION

The approval of new pharmaceuticals is a cornerstone of public health, ensuring that medicines are safe, effective, and of high quality before reaching patients. Yet, the fragmented nature of global regulatory systems poses significant barriers to timely drug access. In an era of pandemics and rising non-communicable diseases, harmonizing these systems is imperative.

The ICH, established in 1990, leads efforts to align scientific and technical standards across major markets like the EU, US, and Japan. Complementing this, the WHO provides normative guidance for LMICs, while PIC/S focuses on good manufacturing practices (GMP) inspections to foster mutual recognition. Despite these advancements, divergences persist driven by national priorities, economic disparities, and differing interpretations of guidelines. In Africa, where over 80% of medicines are imported and regulatory capacities vary widely, these issues exacerbate health inequities.

The African Union's AMRH initiative, launched in 2009, seeks continental alignment but faces implementation hurdles.

This review synthesizes global harmonization efforts, critiques divergences, and emphasizes African contexts, aligning with the African Journal of Biomedical Research's emphasis on biomedical/pharmaceutical sciences with global-African lenses. It draws on peer-reviewed literature, policy documents, and recent 2025 updates to propose pathways forward

The regulation of pharmaceuticals forms the backbone of modern health systems. Medicines, whether innovative new chemical entities, complex biologics, or generic formulations, must undergo rigorous evaluation to ensure that they are safe, efficacious, and of assured quality before being made available to patients. This regulatory process, however, is highly complex, resource-intensive, and fragmented across different jurisdictions. Each country or regional bloc operates under distinct laws, policies, and technical guidelines, creating redundancies and inefficiencies that directly affect the availability of life-saving medicines, particularly in low- and middle-income countries **(LMICs).**

1.1 The Global Need for Harmonization

The pharmaceutical industry is inherently global. A drug discovered in one country may be manufactured in another, packaged in a third, and distributed across dozens of markets. In such a transnational environment, divergent regulatory requirements slow down innovation and increase costs. Studies estimate that bringing a new medicine to market can cost between USD 1.5–2.6 billion, with approximately 30–40% of this expenditure attributed to regulatory compliance and duplicated studies required by different agencies. For instance, prior to harmonization efforts, companies often had to repeat toxicological or clinical trials in multiple regions simply to satisfy differing national standards.

Harmonization initiatives emerged as a response to this inefficiency. The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), formed in 1990, brought together regulators and industry from the US, EU, and Japan to develop common guidelines on quality, safety, and efficacy. Parallel efforts from the World Health Organization

(WHO) provided global normative guidance and prequalification services to support LMICs. Meanwhile, the Pharmaceutical Inspection Co-operation Scheme (PIC/S) standardized good manufacturing practice (GMP) inspections, enabling mutual recognition among participating inspectorates. Collectively, these initiatives aimed to create a level playing field that would shorten drug development timelines, enhance public confidence, and facilitate faster access to essential medicines.

1.2 Divergences in National Priorities

Despite more than three decades of progress, true convergence remains elusive. National sovereignty, political priorities, and local health challenges continue to shape how regulations are implemented. For example, while the ICH guideline on stability testing (Q1A) is widely adopted, tropical countries often require additional stability data reflecting high temperature and humidity conditions not addressed by standard models. Similarly, regulatory agencies in countries such as India and Brazil mandate local clinical trials for bioavailability and bioequivalence (BA/BE), even when robust international data are available, to ensure ethnic and environmental relevance. These divergences, though rational from a national perspective, introduce significant delays and costs at the global level.

1.3 Consequences for Patients and Public Health

The impact of regulatory divergence is most acutely felt by patients. When companies face delays in obtaining approvals across multiple jurisdictions, life-saving therapies may reach some population's years later than others. A stark example is seen in the case of oncology medicines, where patients in sub-Saharan Africa often wait 2–5 years longer to access treatments already approved in Europe or North America. During the COVID-19 pandemic, divergent and uncoordinated regulatory pathways contributed to delays in vaccine access across Africa, with over 1.5 million preventable deaths attributed to inequitable distribution and late rollout of effective vaccines.

Furthermore, fragmented systems create vulnerabilities in supply chains and open the door to substandard and falsified medicines. The WHO estimates that 1 in 10 medical products in LMICs is substandard or counterfeit, with Africa bearing a disproportionate burden due to weak regulatory oversight and porous borders. Harmonization can help by setting clear, consistent quality standards and enabling cross-border enforcement.

1.4 The African Context: Challenges and Opportunities

Africa presents a unique case study in the harmonization debate. The continent is home to 54 countries, each with its own regulatory authority, ranging from relatively advanced agencies such as South Africa's Health Products Regulatory Authority (SAHPRA) to under-resourced offices with only a handful of trained staff. Over 80% of medicines in Africa are imported, largely from India and China, making quality oversight particularly challenging. The lack of regulatory capacity not only delays the registration of new medicines but also allows counterfeit products to proliferate.

Recognizing these challenges, the African Medicines Regulatory Harmonization (AMRH) initiative was launched in 2009 under the African Union (AU) and NEPAD. The program

promotes reliance and mutual recognition through regional economic communities (RECs) such as the East African Community (EAC), the Southern African Development Community (SADC), and the Economic Community of West African States (ECOWAS). More recently, the establishment of the African Medicines Agency (AMA) in 2021—expected to become operational by 2025 represents a historic step toward supranational regulation, similar to the European Medicines Agency (EMA). If successful, AMA could transform the pharmaceutical landscape by reducing approval times, strengthening GMP oversight, and fostering local manufacturing.

1.5 Scope of the Present Review

This paper critically reviews the global state of regulatory harmonization, focusing on the roles of ICH, WHO, and PIC/S, while contrasting these with persistent divergences in national systems. Special emphasis is placed on the African context, where harmonization efforts are underway but face significant hurdles. The review synthesizes evidence from peer-reviewed literature, policy reports, and recent updates (2023–2025), aiming to:

1. Examine the progress achieved by global harmonization bodies.
2. Identify persistent technical, political, and economic challenges that fuel divergence.
3. Analyse Africa's regional harmonization initiatives and the potential role of AMA.
4. Propose actionable recommendations to strengthen global–African regulatory convergence.

By situating Africa at the centre of the global harmonization discourse, the article aligns with the mission of the African Journal of Biomedical Research to highlight biomedical and pharmaceutical issues of relevance to the continent within a global framework.

2. OVERVIEW OF KEY HARMONIZATION BODIES

The process of regulatory harmonization is not driven by a single institution, but rather by a constellation of global and regional actors, each with distinct mandates, memberships, and instruments. Among these, the International Council for Harmonisation (ICH), the World Health Organization (WHO), and the Pharmaceutical Inspection Co-operation Scheme (PIC/S) represent the most influential entities in shaping the technical and procedural landscape of pharmaceutical regulation. Together, they provide the normative backbone for drug development, evaluation, and manufacturing oversight. Yet, their scope, governance, and uptake vary, and their interplay with LMICs—particularly in Africa—remains uneven.

2.1 International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)

2.1.1 Historical Background

The ICH was founded in 1990 as a tripartite initiative between regulatory authorities and pharmaceutical industry associations from the European Union (EU), the United States (US), and Japan. Its creation was motivated by the recognition that duplicative requirements across these three major markets hindered innovation, increased development costs, and delayed patient access to new medicines. By bringing

regulators and industry together in a structured dialogue, ICH sought to establish common technical guidelines for the safety, efficacy, and quality of pharmaceuticals.

2.1.2 Structure and Governance

Today, ICH has grown far beyond its original "founder's club." As of 2025, it includes:

- 20 regulatory members (e.g., US FDA, EMA, PMDA Japan, Health Canada, Swissmedic, ANVISA Brazil, MFDS Korea).
- Industry members (e.g., PhRMA, EFPIA, JPMA, BIO).
- Observers and associated organizations, including WHO, ECDC, and several LMIC regulators.

The governance structure is built around the ICH Assembly (decision-making body), the Management Committee, and expert working groups that draft guidelines in specific domains. Decisions are taken by consensus, ensuring both regulators and industry align on technical standards.

2.1.3 Scope of Guidelines

ICH guidelines are grouped into four broad categories:

- Quality (Q): covering stability testing, impurities, pharmaceutical development (Q8), risk management (Q9), quality systems (Q10), and lifecycle management (Q12).
- Safety (S): addressing genotoxicity, carcinogenicity, reproductive toxicology, and immunotoxicology.
- Efficacy (E): ranging from clinical trial design (E6 Good Clinical Practice, E17 Multi-regional Clinical Trials) to pharmacogenomics.
- Multidisciplinary (M): including electronic standards (eCTD), MedDRA terminology, and bio statistical methods.

By 2025, over 50 guidelines have been adopted, forming the backbone of pharmaceutical regulation in most high-income markets.

2.1.4 Achievements

- Reduced duplication: Standardized trial designs and dossier formats have reduced redundant studies.
- Accelerated approvals: Studies show approvals are 20–30% faster in ICH regions.
- Animal welfare: Harmonization has reduced repeated animal testing, consistent with the "3Rs" principle.
- Global influence: Many non-ICH countries voluntarily adopt ICH guidelines, making them de facto global standards.

2.1.5 Limitations and Criticisms

- HIC bias: The focus remains on challenges faced by mature markets, often overlooking LMIC realities (e.g., tropical stability, counterfeit prevalence).
- Cost of compliance: Smaller manufacturers in LMICs face high costs in aligning with ICH requirements.
- Limited African participation: No African regulatory authority is a full member, although WHO provides some liaison.
- Implementation gap: Even when adopted, many LMIC regulators lack the capacity to enforce ICH standards fully.

2.1.6 Relevance to Africa

African regulators rely indirectly on ICH guidelines through WHO

prequalification or regional harmonization programs (e.g., AMRH).

However, the absence of direct African seats in ICH decision-making means local needs

such as heat-stable formulations, or regulatory strategies for combating widespread substandard medicines are underrepresented.

2.2 World Health Organization (WHO)

2.2.1 Role and Mandate

As a United Nations specialized agency, WHO plays a normative role rather than acting as a regulatory authority. It develops global guidelines and technical standards, provides capacity-building, and supports LMIC regulators through reliance and prequalification systems. Its influence is especially strong in countries without mature regulatory systems.

2.2.2 Core Functions

- Prequalification of Medicines and Vaccines (PQ): Provides assurance that products meet international quality, safety, and efficacy standards, often serving as the basis for procurement by UN agencies and LMIC governments.
- Good Manufacturing Practice (GMP) standards: Widely adopted worldwide as the baseline for production.
- Essential Medicines List (EML): Guides national formularies and procurement decisions.
- Global Benchmarking Tool (GBT): Assesses maturity of national regulatory authorities (NRAs).
- Emergency Use Listing (EUL): Fast-track mechanism used during pandemics (e.g., COVID-19 vaccines).

2.2.3 Achievements

- Reliance pathways: Countries such as Tanzania, Ghana, and Zambia use WHO PQ as a reference for national registration, cutting approval times by more than 50%.
- Global coverage: WHO guidelines are referenced in over 190 countries.
- Health impact: WHO PQ facilitated the global scale-up of HIV, TB, and malaria medicines, saving millions of lives.

2.2.4 Challenges

- Resource intensity: PQ assessments are slow due to high workload.
- Variable uptake: Some African regulators remain reluctant to rely fully on WHO assessments, citing sovereignty concerns.
- Funding constraints: PQ relies heavily on donor funding, raising sustainability concerns.

2.2.5 Relevance to Africa

WHO has been pivotal in strengthening African regulatory systems. Most African countries directly rely on WHO PQ for procurement decisions. The Global Benchmarking Tool has identified critical gaps in pharmacovigilance, GMP inspection, and dossier review, enabling targeted technical assistance. WHO also collaborates with the African Medicines Agency (AMA) to ensure African harmonization efforts align with global norms.

2.3 Pharmaceutical Inspection Co-operation Scheme (PIC/S)

2.3.1 Origins and Structure

PIC/S emerged from the Pharmaceutical Inspection Convention (1970) among European states, later transforming into a broader international cooperative in 1995. Its aim is to harmonize Good Manufacturing Practice (GMP) standards and inspections. Unlike ICH and WHO, PIC/S does not develop drug development guidelines—it focuses specifically on manufacturing oversight.

2.3.2 Membership and Governance

As of 2025, PIC/S includes 52 regulatory authorities, among them the US FDA, EMA member states, Swissmedic, Health Canada, and ANVISA (Brazil). Membership requires a rigorous accession process, including demonstrating inspectorate capacity. Importantly, South Africa's SAHPRA is the only African member, highlighting limited continental engagement.

2.3.3 Core Activities

- Inspector training: Regular training programs and expert circles enhance inspector competencies.
- Harmonized GMP guidelines: Aligned closely with WHO GMP standards.
- Mutual recognition: Promotes trust and reduces duplicate inspections.
- Digital innovation: Recent pilots on remote inspections and data-driven GMP surveillance.

2.3.4 Achievements

- Cost savings: EU-US MRA cut inspection costs by ~50%.
- Capacity strengthening: Asian and Latin American inspectorates improved GMP enforcement significantly after PIC/S membership.
- Global consistency: Standardized inspection reports enable shared reliance.

2.3.5 Limitations

- Voluntary and non-binding: Lacks enforcement authority; members may diverge.
- High entry threshold: Many LMICs lack the inspectorate capacity required for accession.
- Limited African presence: Only South Africa is a member, excluding most of the continent from mutual recognition benefits.

2.3.6 Relevance to Africa

The absence of most African NRAs in PIC/S undermines the continent's ability to enforce GMP consistently. This gap contributes to the high prevalence of substandard and falsified medicines, estimated to represent 10–30% of pharmaceutical markets in SSA. Expanding African participation in PIC/S would greatly enhance manufacturing oversight, especially as the continent pushes for local production under the AU's Pharmaceutical Manufacturing Plan for Africa.

2.4 Comparative Analysis

While ICH, WHO, and PIC/S share the goal of convergence, their mandates differ:

- ICH provides scientific and technical guidelines for drug development and evaluation.

- WHO sets global norms and supports LMIC regulators via reliance and capacity-building.
- PIC/S ensures consistent GMP inspections and fosters mutual recognition.

These bodies complement each other but operate with different levels of inclusivity and enforceability. Importantly, none fully integrates African perspectives at the governance level, leaving harmonization efforts somewhat top-down rather than co-created.

Year	Organization	Milestone	Description
1970	PIC/S	Establishment of Pharmaceutical Inspection Convention (PIC)	Foundation for GMP inspections in Europe, extended to global cooperation.
1990	ICH	ICH Founded	Launch of harmonization efforts among EU, US, Japan regulators and industry.
1995	PIC/S	PIC/S Established	Extension of PIC to include non-European members, focusing on GMP training and mutual recognition.
2001	WHO	Prequalification Programme Launched	WHO begins assessing medicines for UN procurement, aiding LMIC access.
2009	AMRH	AMRH Initiative Launched	African Inion-NEPAD starts continental harmonization via Regional Economics Communities (RECs)
2011	PIC/S	FDA Joins PIC/S	US integration boosts Global GMP work-sharing.
2015	ICH	ICH Association Reformed	Shift to inclusive model under Swiss Law, adding emerging markets.
2016	AMRH	EAC ZAZIBONA Joint Review	East African Community reduces approvals to 7 months; pilot for AMRH.
2021	AMRH	African Medicines Agency (AMA) Treaty Signed	Supranational boy established for oversight of priority review medicines.
2023	PIC/S	MOU with ICH Signed	Joint work on inspections and guidelines convergence.
2024	ICH	E11A Guideline on Paediatric Trials Finalised	Advances inclusive clinical trail standards.
2025	AMRH/AMA	AMA Operationalized; Full Continental Coverage	North Africa joins; first joint assessments under AMA, with 5 human medicines listed.

2025	WHO	Updated Reliance Guidelines (Annex 10)	Enhances deference to stringent regulators for LIMICs.

Table: 1 Key Milestones in global and African Regulatory Harmonization

3. PROGRESS IN GLOBAL HARMONIZATION

The last three decades have witnessed unprecedented progress in aligning pharmaceutical regulatory frameworks worldwide. While complete convergence remains elusive, the establishment of shared guidelines, reliance pathways, and regional networks has fundamentally altered the global drug approval landscape. Harmonization has reduced duplicative studies, accelerated patient access, strengthened regulatory capacity in low- and middle-income countries (LMICs), and laid the groundwork for future global reliance systems.

3.1 Evolution of Harmonization Efforts

3.1.1 Early Bilateral and Regional Initiatives

In the 1970s–1980s, regulatory convergence was limited primarily to bilateral agreements (e.g., the EU mutual recognition of medicines, the US-Canada cooperation) and regional frameworks (e.g., EU regulatory unification under EMA). These models provided proof of concept, showing that mutual reliance could reduce duplication without compromising safety.

3.1.2 Formation of Global Bodies

The 1990 establishment of the International Council for Harmonisation (ICH) marked the first structured attempt at truly global harmonization. Its tripartite approach set the stage for technical guideline convergence, while WHO and PIC/S expanded the scope to LMICs and GMP inspection harmonization. Over time, this triad became the backbone of global harmonization.

3.2 Achievements in Regulatory Convergence

3.2.1 Common Technical Standards

- Common Technical Document (CTD): Perhaps the most visible success, the CTD (adopted in 2003) harmonized the structure of marketing authorization dossiers. Today, it is used in over 130 countries, including in Africa, reducing the cost and time of dossier preparation by an estimated 30–40%.
- Electronic CTD (eCTD): Enabled electronic submissions, increasing efficiency and traceability, now required in most ICH markets.

3.2.2 Harmonized Clinical and Non-Clinical Guidelines

- Good Clinical Practice (ICH E6): Adopted widely, ensuring standardized ethical and scientific principles for clinical trials.
- Multi-Regional Clinical Trials (E17): Facilitated global trial integration, reducing the need for duplicative local studies.
- Toxicology and safety testing: Reduced animal use by establishing globally acceptable study designs.

3.2.3 Good Manufacturing Practice (GMP) Alignment

- WHO GMP and PIC/S GMP guidelines are now functionally aligned, enabling mutual reliance.
- EU–US Mutual Recognition Agreement (2017) led to reduced inspection duplication, saving both regulators and industry millions of dollars annually.

3.2.4 Accelerated Access to Medicines

Studies show that harmonization has cut approval timelines significantly:

- EU centralized procedure (EMA): 210-day standard review, applicable across 30+ countries.
- Reliance models in Africa: Countries using WHO prequalification or relying on stringent regulatory authorities (SRAs) cut timelines from 3–5 years to under 12 months.
- COVID-19 example: WHO's Emergency Use Listing (EUL) enabled rapid authorization of vaccines globally, with African regulators leveraging EUL within weeks of SRA approvals.

3.2.5 Capacity Building in LMICs

- WHO's Global Benchmarking Tool (GBT) has classified 13 African regulators at Maturity Level 3 or higher as of 2024, compared to only 2 a decade earlier.
- Regional initiatives such as the African Medicines Regulatory Harmonization (AMRH) program have created harmonized guidelines for registration in East African Community (EAC) and Southern African Development Community (SADC).

3.3 Regional Progress in Harmonization

3.3.1 Europe – The EMA Model

The European Medicines Agency (EMA) remains the most advanced regional example. Its centralized procedure ensures one dossier, one scientific evaluation, one authorization valid across 30+ states. This model has inspired harmonization efforts in other regions.

3.3.2 North America

While the US FDA and Health Canada maintain independent systems, reliance and information-sharing mechanisms have grown, particularly under the Canada–US Regulatory Cooperation Council.

3.3.3 Asia-Pacific

- ASEAN has developed a Common Technical Dossier (ACTD) modelled on ICH CTD, covering 10 member states.
- Japan, Korea, and China have become ICH members, further embedding harmonization.

3.3.4 Africa

- African Medicines Regulatory Harmonization (AMRH): Established in 2009, it has created regional technical guidelines and joint review mechanisms.
- African Medicines Agency (AMA): Launched in 2021, it aims to provide a continent-wide coordination mechanism for regulatory convergence.
- Early results show joint assessments reducing registration times by 40–60% in EAC and SADC countries.

3.4 Quantifiable Benefits of Harmonization

- Time savings: CTD adoption cut dossier preparation time by 4–6 months.
- Cost reduction: Avoidance of duplicative clinical trials saves an estimated USD 1–2 billion annually for the industry.
- Expanded access: Faster availability of generics and biosimilars in LMICs.
- Global safety net: Shared pharmacovigilance databases (e.g., WHO's VigiBase, EMA's EudraVigilance) strengthen post-market safety surveillance.

3.5 Case Studies

3.5.1 HIV/AIDS Medicines in Africa

WHO Prequalification enabled rapid global procurement of antiretroviral (ARVs), standardizing quality and accelerating access. By 2020, over 25 million people in Africa were on ARVs, a feat impossible without regulatory harmonization.

3.5.2 COVID-19 Vaccines

The alignment of WHO EUL, ICH guidelines, and reliance mechanisms allowed multiple African countries to approve vaccines within weeks, compared to years under traditional models.

3.5.3 Biosimilars in Emerging Markets

ICH's guidelines on comparability and WHO's standards have allowed LMICs to develop and approve biosimilars, expanding access to cancer and autoimmune therapies.

3.6 Remaining Gaps Despite Progress

Despite measurable achievements, harmonization remains incomplete:

- Uneven adoption: Many LMICs have adopted CTD but lack digital infrastructure for eCTD.
- Capacity disparity: Some regulators cannot fully implement GMP or GCP oversight.
- Sovereignty issues: Some countries resist reliance pathways, preferring independent evaluations.
- African lag: AMA is still in early stages; only a subset of states have ratified its treaty.

3.7 Synthesis

Global harmonization has transformed pharmaceutical regulation from a patchwork of national systems into a networked, collaborative ecosystem. The CTD, GMP convergence, reliance pathways, and regional initiatives stand out as landmark achievements. Yet the persistence of uneven adoption, limited African integration, and sovereignty concerns highlight that the journey toward full convergence is ongoing.

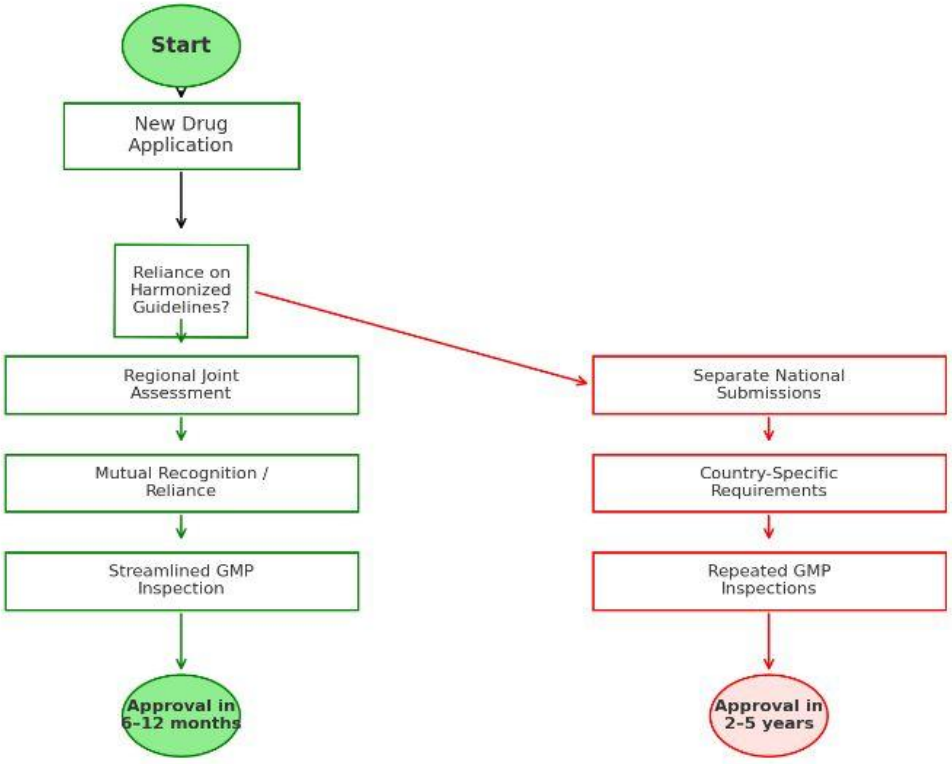


Figure: 1 Flow Chart of Drug Approval Process: Harmonization vs Divergent Pathways

4. DIVERGENCES AND PERSISTENT CHALLENGES

Despite notable progress in regulatory harmonization through ICH, WHO, and PIC/S, divergences in policy, implementation, and political priorities remain entrenched. These gaps create inefficiencies, delay access to essential medicines, and disproportionately burden low- and middle-income countries (LMICs), especially in Africa. Persistent divergences manifest across technical, procedural, political, and economic dimensions, reflecting both structural and context-specific barriers to convergence.

4.1 Technical and Procedural Divergences

4.1.1 Clinical Trial Requirements

- Local study mandates: Some countries (e.g., India, Brazil) continue to require local bioavailability or bridging studies, even when multi-regional clinical trial (MRCT) data are available. This conflicts with ICH E17, which promotes global trial integration.
- Endpoint variability: Regulatory authorities differ on acceptable clinical endpoints. For example, oncology endpoints such as progression-free survival are accepted in the US but not always in EU or African markets, creating fragmented development programs.
- Ethics review systems: While ICH E6 (GCP) is broadly adopted, African countries often lack harmonized ethics

committee structures, leading to duplicate reviews and extended timelines.

4.1.2 Labelling and Pharmacovigilance

- Divergent labelling standards: The US FDA maintains detailed pregnancy risk categories, whereas the EU and WHO require narrative risk-benefit summaries. Companies must therefore generate multiple versions of product information, raising costs.
- Pharmacovigilance reporting: While ICH E2 guidelines exist, African regulators vary widely in adverse event reporting infrastructure. Only 20% of African NMRAs are linked to WHO's VigiBase in real time.

4.1.3 Manufacturing Standards and GMP

- PIC/S vs. national GMP: While PIC/S provides standardized GMP guidance, some LMICs impose local variations. For instance, Nigeria's NAFDAC applies additional import testing requirements even for WHO-prequalified medicines, leading to delays.
- Biologics and ATMPs: Guidelines for advanced therapies (cell/gene therapies) remain inconsistent. PIC/S GMP annexes are not uniformly adopted, leaving regulatory grey zones.

4.1.4 Digital Infrastructure Gaps

- Many LMICs continue to use paper-based dossier submissions, slowing adoption of eCTD. In Sub-Saharan Africa, only a handful of regulators (e.g., SAHPRA in South Africa) are eCTD-capable, limiting true harmonization.

4.2 Political, Economic, and Capacity Barriers

4.2.1 Political Divergences

- National sovereignty concerns: Governments often resist reliance on foreign regulatory decisions, citing sovereignty. This was evident in COVID-19 vaccine approvals, where some African nations delayed adoption despite WHO EUL, waiting for local evaluation.
- Geopolitical tensions: Trade conflicts (e.g., US–China disputes) can disrupt harmonization, as regulators may impose extra requirements for strategic products.
- Brexit example: The UK's withdrawal from the EU introduced new divergences, with separate licensing pathways and pharmacovigilance databases, delaying drug availability by 6–12 months.

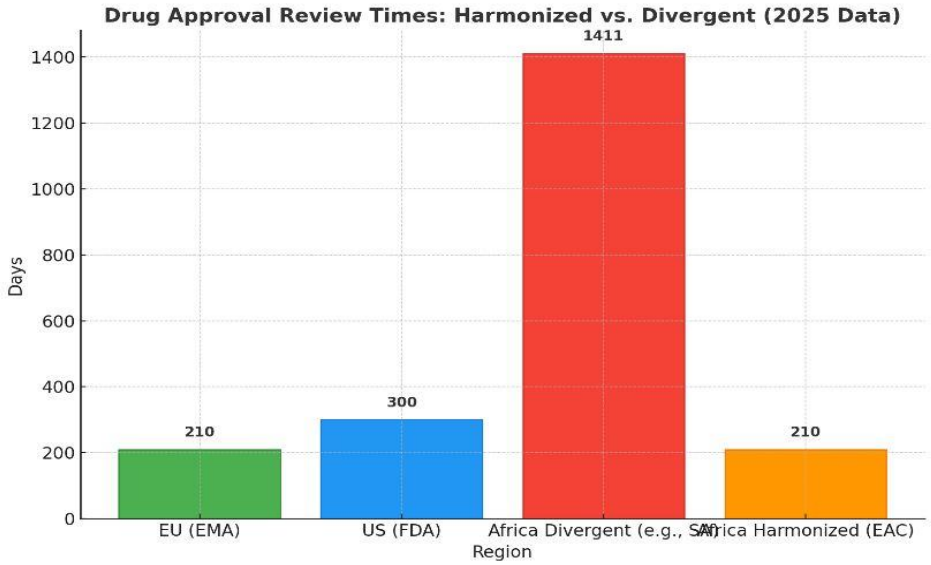
4.2.2 Economic Constraints

- Resource-intensive systems: Implementing ICH and PIC/S standards requires significant investment in trained staff, inspection systems, and digital tools. Many African regulators lack sustainable funding models, relying on donor support.
- Fee structures: Even under harmonized systems, national regulators often charge independent fees, discouraging companies from pursuing multiple African markets simultaneously.

4.2.3 Capacity Gaps

- Human resources: Many African NMRAs employ fewer than 50 technical staff, compared to thousands at FDA/EMA. This results in review backlogs, with median timelines of 2–5 years for generic approvals.
- Inspection delays: FDA's 2024 backlog showed that 15% of global GMP inspections were postponed, largely in LMICs, affecting supply chains.
- Training needs: While PIC/S offers inspector training, African participation remains limited. Only South Africa's SAHPRA is a full PIC/S member as of 2025.

4.3 Impact on Drug Approvals



Graph: 1 Drug Approval Review Times: Harmonization and Divergent

4.3.1 Prolonged Approval Timelines

- In harmonized systems like EMA, centralized approvals take ~210 days.
- In contrast, approvals in LMICs can stretch to 2–5 years, particularly for generics and biosimilars.
- This delay denies timely patient access and discourages global manufacturers from registering in smaller markets.

4.3.2 Delayed Access to Innovation

- Oncology and orphan drugs: Divergent definitions of endpoints and post-marketing commitments delay LMIC approvals by several years.
- Biologics and biosimilars: Without clear harmonization, Africa lags in biosimilar adoption, limiting affordable access to therapies for cancer and autoimmune conditions.

4.3.3 Substandard and Falsified Medicines

- Regulatory fragmentation creates loopholes exploited by counterfeiters. WHO estimates that 1 in 10 medical products in Africa is substandard or falsified, costing $200 billion annually in healthcare losses. Weak GMP enforcement due to divergent or under-resourced

inspection systems is a major driver.

4.4 Africa-Specific Divergences

4.4.1 Fragmentation across 54 Countries

Each country maintains its own regulatory authority, leading to duplication. A single product may require up to 54 separate applications, compared to one centralized submission in the EU.

4.4.2 Uneven Adoption of Regional Harmonization

- EAC and SADC have demonstrated success with joint assessments, but ECOWAS and IGAD face political and technical barriers.
- AMRH remains voluntary, with non-binding outcomes, limiting continent-wide impact.

4.4.3 Limited Inclusion in Global Standards

- ICH and PIC/S largely reflect high-income country priorities. African needs such as heat-stable formulations, fixed-dose combinations (FDCs), and affordable biosimilars are underrepresented in guideline development.

4.5 Illustrative Case Studies

4.5.1 COVID-19 Vaccines in Africa

Despite WHO EUL and SRA reliance models, many African nations required separate national reviews, delaying vaccine rollout. This contributed to vaccine inequity: by mid-2022, <20% of Africa's population was fully vaccinated, compared to >60% in high-income regions.

4.5.2 Antimalarial Combination Therapies

WHO guidelines supported rapid approval of artemisinin-based combinations, but divergent African national processes delayed rollout. In some countries, approvals lagged by 3–4 years, undermining malaria control programs.

4.5.3 Brexit's Ripple Effects

Brexit created duplications in pharmacovigilance reporting, labelling, and QPPV (Qualified Person for Pharmacovigilance) requirements. This caused delays in UK product launches and indirectly affected supply chains to Africa dependent on UK-licensed products.

4.6 Synthesis of Divergences

While harmonization initiatives have made headway, persistent divergences across clinical, technical, political, and economic dimensions continue to fragment the regulatory environment. These divergences disproportionately affect LMICs, particularly African nations, by prolonging timelines, raising costs, and limiting access to safe and effective medicines. For harmonization to achieve its equity goals, systemic barriers sovereignty concerns, resource constraints, and misaligned priorities must be directly addressed.

5. AFRICAN PERSPECTIVES: HARMONIZATION AMIDST UNIQUE CHALLENGES

Africa presents a unique regulatory landscape characterized by diverse political systems, varying technical capacities, and high dependence on imported medicines. With 54 countries, each having its own regulatory authority, fragmented processes have historically delayed patient access and undermined quality assurance. Despite

global harmonization efforts through ICH, WHO, and PIC/S, African nations face persistent hurdles in aligning with these frameworks.

5.1 Overview of African Regulatory Landscape

5.1.1 Fragmentation and Diversity

- African regulatory authorities differ significantly in structure, staffing, and technical capability.
- Examples:
- Nigeria's NAFDAC: Well-resourced, performs stringent inspections, engages with WHO PQ.
- Central African countries: Limited inspection capacity, paper-based submissions, delayed approvals.
- Over 80% of medicines in Africa are imported, making harmonization critical for supply chain efficiency and safety.

5.1.2 Reliance on Global Standards

- Many African NRAs rely on WHO prequalification or assessments by stringent regulatory authorities (SRAs) for decision-making.
- Challenges: Local context (e.g., climate stability, heat-resistant formulations) is often not fully considered in global guidelines.
- Benefit: Reduces duplication, accelerates approval, and ensures minimum quality standards.

Case Study	Regional/ Initiative	Key Outcome	Pre-Harmonization Time	Post-Harmonization Time	Impact on Access
HIV Generics (WHO Prequalification)	Global LMICs	Fast-tracked antiretovirals	2-3 Years	6-12months	15 million + patients treated in African by 2025
ZAZIBONA Joint Assessment	EAC (AMRH)	ISO-certified QMS in 4 NMRAs	2-7 Years	(210 days)7months	40% cost savins; 85% SSA coverage via RECs
EU-US MRA (PIC/S/ ICH)	High Income Markets	Reduced duplicate GMP audits	500 + days	210 days	50% inspection cost reduction; 15 active MRAs
South Africa SAHPRA (PIC/S / Member)	Africa	Enhanced biologics approvals	1411 days	890 days	Improved local manufacturing compliance
AMA First Listings	Continental Africa	5 Human medicines harmonized	2-5 Years	12 months	Boosts equity; addresses 90% substandard drug issue.

Table 2: Case Studies on Regulatory Harmonization Impacts

5.2 Regional Harmonization Initiatives

5.2.1 African Medicines Regulatory Harmonization (AMRH) Program

- Launched in 2009 under the AU-NEPAD framework.

Goals:

- Streamline registration procedures across Regional Economic Communities (RECs).
- Enhance reliance pathways between countries.
- Strengthen capacity in dossier evaluation, GMP inspection, and pharmacovigilance.
- Coverage: Reaches ~85% of Sub-Saharan Africa via RECs like:
- EAC: East African Community
- SADC: Southern African Development Community
- ECOWAS: Economic Community of West African States

5.2.2 African Medicines Agency (AMA)

- Established 2021; operationalizing fully in 2025.

Mandate: Supranational oversight similar to EMA in Europe.

Functions: Coordinate joint assessments for priority medicines (PRNDs: poverty-related and neglected diseases).

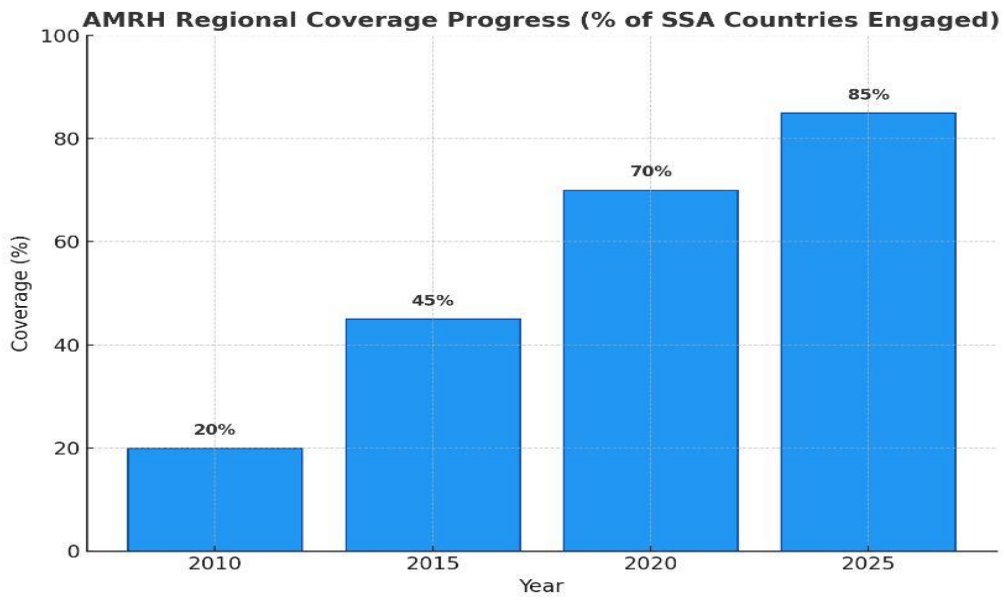
- Provide technical support to NMRAs.
- Promote regulatory convergence across RECs.

Early Outcomes:

- Reduces duplication of national approvals.
- Facilitates local manufacturing and cross-border medicine trade.

5.2.3 Regional Examples of Success

- EAC's ZAZIBONA Joint Assessment:
- Reduced generic approval timelines from 2–7 years to 7 months by 2016.
- Four NMRAs achieved ISO-certified quality management systems.
- SADC reliance on WHO guidelines:
- Streamlined registration of generics and essential medicines.
- North Africa (2025): Harmonization achieved near full continental coverage, integrating Morocco, Algeria, Tunisia, and Egypt.



Graph: 2 AMR Coverage Progress

5.3 Challenges and Obstacles in African Harmonization

5.3.1 Political and Governance Barriers

- AMRH's non-binding nature leads to uneven adoption.
- EAC successes not always replicated in IGAD due to political differences or lack of legal frameworks.
- Stakeholder exclusion (industry, patients, and healthcare professionals) limits buy-in.

5.3.2 Technical and Infrastructure Gaps

- Limited human resources: Many NMRAs operate with <50 technical staff, causing review backlogs.
- Paper-based systems: 60% of Sub-Saharan African regulators still lack digital dossier submission platforms.
- GMP inspection challenges: Only South Africa (SAHPRA) is PIC/S-accredited. Others struggle with training, resources, and inspection coverage.

5.3.3 Economic Constraints

- Separate national registration fees offset the benefits of joint assessments.
- Dependence on donor funding and project-based support (e.g., $10M AU seed for AMA) limits sustainability.
- Costs of compliance with ICH/WHO standards remain high for local manufacturers, discouraging regional production.

5.3.4 Substandard and Falsified Medicines

- Weak GMP enforcement and fragmented oversight contribute to high prevalence of substandard/falsified medicines, estimated at 10–30% of the market in Sub-Saharan Africa.

5.4 Lessons Learned and Best Practices

5.4.1 Transparency and Timelines

- Publicized review timelines, as practiced in ZAZIBONA, enhance stakeholder confidence.
- Reliance on peer regulators with stronger systems (e.g., Uganda in EAC) can accelerate evaluations.

5.4.2 Integration of African Needs into Global Standards

- Advocating for heat-stable formulations, tropical stability testing, and locally relevant pharmacovigilance standards in ICH and WHO guidelines can reduce divergence.

5.4.3 Digital Platforms and Information Sharing

- Harmonized digital submission and dossier management systems across RECs can significantly reduce duplication and delays.
- Example: ECOWAS working groups leverage regional expertise, but incompatible information management systems slow data sharing.

5.4.4 Capacity Building

- Joint training programs for inspectors, reviewers, and pharmacovigilance staff improve harmonization uptake.
- Encouraging PIC/S membership and engagement in global forums can elevate African regulatory influence.

5.5 Case Studies

5.5.1 EAC ZAZIBONA Joint Assessment

- Implemented standardized joint dossier review and GMP inspections.
- Approval times reduced from years to months.
- Encouraged regional manufacturers to submit products for multiple markets simultaneously.

5.5.2 African Medicines Agency (AMA) Pilot Initiatives

- Centralized evaluation of PRNDs facilitates faster access to neglected-disease treatments.
- Supports capacity building for smaller NMRAs in West and Central Africa.

5.5.3 Lessons from SADC and North Africa

- SADC reliance on WHO PQ ensures minimum quality standards.
- North African harmonization demonstrates that political commitment and regional legal frameworks are key to full continental adoption.

5.6 Synthesis and Key Insights

- Africa's regulatory landscape reflects both opportunities and challenges: regional harmonization reduces duplication, accelerates access, and strengthens capacity.
- Persistent obstacles include political divergence, limited resources, and weak integration into global standards.

Success depends on:

- Strengthening supranational coordination (AMA)
- Enhancing digital and human capacity
- Aligning African regulatory priorities with global harmonization while addressing local health needs

- Ensuring financial sustainability and political commitment

6. GLOBAL–AFRICAN INTERPLAY: BRIDGING THE GAP

Africa's regulatory environment exists at the intersection of global harmonization frameworks and local realities. While ICH, WHO, and PIC/S provide technical standards and guidance, African nations must adapt these frameworks to context-specific challenges such as limited infrastructure, diverse climates, and political heterogeneity. The interplay between global standards and African implementation is thus both opportunity-rich and challenge-laden, influencing access, quality, and equity in healthcare.

6.1 Reliance Mechanisms: Africa Leveraging Global Expertise

6.1.1 WHO Prequalification and Emergency Use Listings

- WHO's Prequalification (PQ) program enables African regulators to rely on internationally vetted data for faster approvals.
- The Emergency Use Listing (EUL) during COVID-19 allowed rapid authorization of vaccines across Africa.
- Benefits:
- Reduces the need for duplicate local clinical trials.
- Provides assurance of quality, safety, and efficacy.
- Limitations:
- Reliance requires technical capacity to interpret and implement PQ/EUL assessments.
- Not all African NMRAs participate fully, creating uneven uptake.

6.1.2 ICH Guidelines as a Reference

- African regulators increasingly use ICH technical standards (Q, S, E, M) for dossier evaluation, GMP inspections, and clinical trial design.
- Example: EAC countries apply ICH Q1A stability requirements, but sometimes modify them for tropical climates, highlighting the need for local adaptation.
- Benefits:
- Provides a global benchmark.
- Encourages consistency with high-income markets, facilitating international trade.

6.1.3 PIC/S and GMP Convergence

- PIC/S harmonization allows African inspectors to participate in international GMP training and mutual recognition initiatives.
- Example: SAHPRA in South Africa acts as a PIC/S model, offering guidance and training to neighbouring NMRAs.
- Limitations:
- Limited African membership slows broader continental benefit.
- Many LMIC regulators cannot fully implement digital inspection tools or advanced risk-based approaches.

6.2 African Contributions to Global Harmonization

- African input in guideline development has historically been limited, but is increasing:
- Inclusion of African representatives in ICH pilot initiatives (e.g., multi-regional clinical trial consultations).
- AMRH provides feedback on tropical stability, FDCs, and

local pharmacovigilance challenges.
- Potential benefits:
- Guidelines better reflect LMIC realities.
- Global harmonization becomes more equitable and context-sensitive.

6.3 Challenges in Global–African Regulatory Interplay

6.3.1 Resource Constraints

- Limited financial and human resources hinder adoption of global standards.
- Example: AU's $10M seed funding for AMA is insufficient to support continent-wide implementation of harmonized regulatory processes.

6.3.2 Political and Legal Barriers

- Divergent political priorities reduce uptake of reliance mechanisms.
- Legal frameworks for joint approvals and mutual recognition are incomplete in some regions (e.g., IGAD and ECOWAS).

6.3.3 Technical Gaps

- Inconsistent adoption of eCTD submission systems slows dossier exchange and harmonization.
- Limited participation in post-marketing surveillance networks reduces global signal detection and pharmacovigilance quality.

6.3.4 Impact on Health Equity

- Delayed approvals for generics, bio-similars and essential medicines disproportionately affect African populations.
- Example: COVID-19 vaccines: reliance pathways accelerated approvals in some countries but others delayed due to national review requirements, leading to preventable morbidity and mortality.

6.4 Opportunities for Strengthening Global–African Interaction

6.4.1 Expanding Reliance and Work-Sharing

- Encourage mandatory use of WHO PQ or SRA decisions in African regulatory assessments.
- Promote regional joint review mechanisms, such as AMRH-AMA frameworks, as models for other RECs.

6.4.2 Capacity Building and Training

- PIC/S and ICH can provide targeted training for African inspectors and reviewers.
- Digital platforms for dossier submission, GMP inspections, and pharmacovigilance reporting can be standardized across regions.

6.4.3 Enhancing Political Commitment

- Regional treaties supporting AMA and harmonization protocols must be ratified and implemented fully.
- Governments should integrate regulatory alignment into national health strategies and AU Agenda 2063 priorities.

6.4.4 Incorporating Local Needs into Global Guidelines

- African stakeholders must advocate for:
- Heat-stable formulations suitable for tropical climates.

- Locally relevant pharmacovigilance data.
- Affordable biosimilar pathways for cancer, autoimmune, and infectious disease therapies.

6.5 Case Studies in Global–African Interplay

6.5.1 COVID-19 Vaccine Approvals

- WHO EUL enabled reliance-based approvals in several African countries (e.g., Ghana, Rwanda).
- Countries without reliance pathways faced delays of 4–12 weeks, highlighting gaps in harmonization implementation.

6.5.2 Antiretroviral Drugs

- African regulators leveraged WHO PQ assessments to rapidly approve generic ARVs, contributing to a 25 million+ HIV treatment cohort.
- Demonstrates successful global–African collaboration in public health.

6.5.3 AMRH–AMA Pilot Projects

- Joint assessments of malaria combination therapies reduced registration times from years to months.
- Facilitated cross-border trade and encouraged local manufacturers to submit dossiers for multiple markets simultaneously.

6.6 Strategic Recommendations

- Strengthen reliance pathways: Mandate that African NMRAs defer to WHO PQ and ICH-compliant assessments where feasible.
- Enhance capacity building: Expand PIC/S and ICH training programs for inspectors, dossier reviewers, and pharmacovigilance staff.
- Political and financial commitment: Governments and AU member states must allocate sustainable resources for AMA and regional harmonization projects.
- Digital harmonization: Implement interoperable eCTD and pharmacovigilance systems across RECs to streamline submissions and inspections.
- Integrate African priorities into global guidelines: Ensure climate, formulation, and cost considerations are reflected in ICH and WHO technical guidance.

6.7 Summation

The interplay between global harmonization and African regulatory systems demonstrates mutual benefits and ongoing challenges. African countries gain from global technical standards, training, and reliance mechanisms, while global bodies benefit from African feedback on tropical medicine requirements, FDCs, and LMIC-specific pharmacovigilance. However, resource gaps, political divergence, and incomplete infrastructure limit the potential. Bridging these gaps requires enhanced reliance, capacity building, political will, and strategic integration of African priorities into global regulatory frameworks.

7. FUTURE DIRECTIONS AND RECOMMENDATIONS

7.1 Enhance Reliance

- Leverage global expertise: African NMRAs should systematically rely on WHO Prequalification (PQ), ICH-compliant SRA decisions, and emergency listings.

- Joint assessments: Expand regional joint review mechanisms (e.g., ZAZIBONA, SADC) across all RECs to reduce duplication.
- Post-marketing reliance: Adopt ICH Q12 guidelines for lifecycle management to accelerate approval of post-approval changes.

7.2 Build Capacity

- Training programs: Scale PIC/S and ICH inspector/reviewer programs to at least 50% of African NMRAs by 2030.
- Centres of Excellence: Establish regional hubs for regulatory science, GMP inspection, pharmacovigilance, and dossier evaluation.
- Talent retention: Offer incentives, recognition, and international collaboration opportunities to retain skilled personnel.

7.3 Foster Inclusivity

- Stakeholder engagement: Include industry, patients, and healthcare professionals in regulatory decision-making.
- African voices in global forums: Ensure active participation in ICH, PIC/S, and WHO guideline development.
- Local needs integration: Advocate for tropical stability, FDCs, and LMIC-relevant pharmacovigilance requirements.

7.4 Invest in Technology

- Digital dossier platforms: Implement eCTD submissions across RECs to enable seamless multi-country approvals.
- Integrated pharmacovigilance systems: Create continent-wide networks connected to WHO VigiBase for real-time adverse event monitoring.
- Data-driven regulation: Use analytics for inspection planning, supply forecasting, and prioritization of high-risk medicines.

7.5 Monitor Equity

- Track key metrics: Average approval timelines, guideline implementation rates, digital adoption, and prevalence of substandard medicines.
- SDG alignment: Ensure regulatory progress contributes to Universal Health Coverage, equitable access to essential medicines, and AU Agenda 2063 goals.
- Continuous improvement: Use monitoring outcomes to refine policies, harmonization strategies, and capacity-building programs.

8. CONCLUSION

Global harmonization via ICH, WHO, and PIC/S has significantly advanced the standards, quality, and safety of pharmaceuticals worldwide. However, persistent divergences driven by political, technical, and capacity gaps continue to delay approvals and restrict access, particularly in Africa.

African initiatives like AMRH and AMA demonstrate that regional collaboration, reliance on global expertise, and tailored capacity-building can bridge the gap. By focusing on enhanced reliance, capacity strengthening, inclusivity, digital transformation, and equity monitoring, Africa can not only accelerate access to safe and effective medicines but also contribute meaningfully to global regulatory convergence.

A convergent future requires political commitment, sustained financing, and African representation in global decision-making, ensuring that harmonization efforts promote equity, efficiency, and sustainability in healthcare access. In essence, global and African regulatory systems must work synergistically, integrating technical excellence with local realities, to achieve a truly unified and effective regulatory landscape.

9. REFERENCE

1. World Health Organization. (n.d.). Regulation and prequalification. https://www.who.int/teams/regulation-prequalification/regulation-and-safety/regulatory-convergence-networks/harmonization

2. Ndomondo-Sigonda, M., Miot, J., Naidoo, S., Ambali, A., Dodoo, A., & Mkandawire, H. (2018). The African Medicines Regulatory Harmonization Initiative: Progress to date. Medical Research Archives, 6(2). https://doi.org/10.18103/mra.v6i2.1668

3. Njuguna, C., Stergachis, A., & Stergachis, A. (2025). Transitioning to regulatory harmonisation for medicines: A comparison between Africa and Europe. Drug Discovery Today. https://doi.org/10.1016/j.drudis.2025.104416

4. Ndomondo-Sigonda, M., Azatyan, S., Doerr, P., Agaba, C., & Harper, K. N. (2023). Best practices in the African Medicines Regulatory Harmonization initiative: Perspectives of regulators and medicines manufacturers. PLOS Global Public Health, 3(4), e0001651. https://doi.org/10.1371/journal.pgph.0001651

5. Ndomondo-Sigonda, M., Miot, J., Naidoo, S., Ambali, A., Dodoo, A., & Mkandawire, H. (2018). The African Medicines Regulatory Harmonization Initiative: Progress to date. Medical Research Archives, 6(2), 1-15. http://journals.ke-i.org/index.php/mra/article/download/1668/1748

6. Drugs for Neglected Diseases initiative. (2013). The road to regulatory harmonization for Africa: Accelerating access to essential medicines and vaccines. https://dndi.org/wp-content/uploads/2016/03/DNDi_African_Regulatory_Report.pdf

7. Hassen, H. K., Mekasha, Y. T., Tegegne, A. A., & Ozalp, Y. (2024). A narrative review on problems in product quality, regulatory system constraints, and the concept of quality by design as a solution for quality assurance of African medicines. Frontiers in Medicine, 11, 1472495. https://doi.org/10.3389/fmed.2024.1472495

8. U.S. Food and Drug Administration. (n.d.). International regulatory harmonization. https://www.fda.gov/drugs/cder-international-program/international-regulatory-harmonization

9. Sachdeva, V. (2024). A review of international initiatives on pharmaceutical regulatory reliance and recognition. Generics and Biosimilars Initiative Journal, 13(3), 151-159. https://doi.org/10.5639/gabij.2024.1303.034

10. Market Access Africa. (2025, May 19). MAA regulatory spotlight - 12. https://www.marketaccess.africa/blogs/maa-regulatory-spotlight-12

11. MasterControl Inc. (2024, September 26). Aligning internal procedures with ICH guidelines: Challenges and solutions for pharma

manufacturers. https://www.mastercontrol.com/gxp-lifeline/ich-guidelines-challenges-and-solutions-pharma-manufacturing

12. Ramanadham, M. (2023). Global regulatory harmonization challenges and opportunities. https://cersi.umd.edu/sites/cersi.umd.edu/files/S4-1%2520Ramanadham%2520Mahesh.pdf

13. MakroCare. (2025, April 29). Global harmonization of regulatory standards: Progress and prospects. https://www.makrocare.com/blog/global-harmonization-of-regulatory-standards-progress-and-prospects/

14. Méndez, M. d. l. L. L., & Trejo, A. H. (2020, July 23). Barriers and challenges for global regulatory harmonization. https://informaconnect.com/barriers-global-regulatory-harmonization/

15. Ahonkhai, V. (2013). Areas of need for harmonized standards and barriers to progress in addressing the gaps. In International regulatory harmonization amid globalization of drug development: Workshop summary. National Academies Press. https://www.ncbi.nlm.nih.gov/books/NBK174217/

16. U.S. Food and Drug Administration. (n.d.). Regulatory harmonization and convergence. https://www.fda.gov/vaccines-blood-biologics/international-activities/regulatory-harmonization-and-convergence

17. Langer, C., & Abraham, C. (2023, September 15). Regulatory, compliance and quality challenges, learnings, and future opportunities. https://ispe.org/pharmaceutical-engineering/ispeak/regulatory-compliance-and-quality-challenges-learnings-and-future

18. Freyr Solutions. (2025, March 24). Navigating the complexities of global regulatory harmonization in pharma. https://www.freyrsolutions.com/blog/navigating-the-complexities-of-global-regulatory-harmonization-in-pharma

19. Morénas, J. (2010). Challenges of implementation of ICH Q 9: A regulatory perspective. https://admin.ich.org/sites/default/files/inline-files/Implementation_of_Q9_Regulatory_Perspective_J.Morenas.pdf

20. Narke, E. (2024, January 23). Insights into 2024 ICH guidelines that affect CMC and drug development. https://www.linkedin.com/pulse/insights-upcoming-ich-guidelines-affect-cmc-drug-development-km1ae

21. World Health Organization. (n.d.). Regional joint activities and work sharing. https://www.who.int/teams/regulation-prequalification/regulation-and-safety/facilitated-product-introduction/regional-joint-activities-and-work-sharing

22. African Union Development Agency. (n.d.). AMRH home. https://amrh.nepad.org/

23. Ndomondo-Sigonda, M. (2022). The African Medicines Regulatory Harmonization Initiative & African Medicines Agency. https://extranet.who.int/prequal/sites/default/files/document_files/Day-1_Session-4.4_MargaretSigonda_AMRH_AMA.pdf

24. African Union Development Agency. (n.d.). Who we are. https://amrh.nepad.org/amrh-microsite/who-we-are

25. World Health Organization. (n.d.). Regulatory Harmonization Initiative. https://www.who.int/teams/regulation-prequalification/regulation-and-safety/regulatory-convergence-networks/harmonization

26. International Federation of Pharmaceutical Manufacturers & Associations. (2023). Accelerating regulatory approvals through the World Health Organization collaborative registration procedures. https://www.ifpma.org/wp-content/uploads/2023/01/i2023_11.-African-Medicines-Regulatory-Harmonization-AMRH-Collaborative-Registration-Procedures.pdf

27. Swissmedic. (n.d.). The African Medicines Regulatory Harmonization (AMRH) Programme. https://www.swissmedic.ch/swissmedic/en/home/about-us/development-cooperation/african-medicines-regulatory-harmonization.html

28. Health Policy Watch. (2024, January 4). Regulatory collaboration can strengthen medicines access – African scientific conference. https://healthpolicy-watch.news/regulatory-collaboration-can-strengthen-medicines-access-african-scientific-conference/

29. Adam, S. (2024). The African Medicines Agency: Building a new gold standard in regulatory excellence. Global Forum. https://globalforum.diaglobal.org/issue/july-2024/the-african-medicines-agency-building-a-new-gold-standard-in-regulatory-excellence/

30. Regulatory Affairs Professionals Society. (2025). Industry officials: Varied global postapproval change requirement pose challenges for drugmakers. https://www.raps.org/news-and-articles/news-articles/2025/3/industry-officials-varied-global-postapproval-chan

31. Pharma Regulatory. (2025, September 20). PIC/S Guidance Explained: Comprehensive Guide to Global GMP Standards, Inspections, and Regulatory Harmonization. https://www.pharmaregulatory.in/pic-s-guidance-explained-comprehensive-guide-to-global-gmp-standards-inspections-and-regulatory-harmonization/

32. B, P. G., & R, K. (2024). Pharmaceutical Inspection Co-operation Scheme: An overview. Cureus, 16(9), e69043. https://doi.org/10.7759/cureus.69043

33. Pharmaceutical Inspection Co-operation Scheme. (2018). Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme: Joint work plan. https://picscheme.org/docview/2472

34. Pharmaceutical Inspection Co-operation Scheme. (2019). Guidance on classification of GMP deficiencies. https://www.gmp-compliance.org/files/guidemgr/PI_040_1_Guidance_on_Classification_of_Deficiencies.pdf

35. International Coalition of Medicines Regulatory Authorities. (n.d.). A regulatory pharmaceutical quality knowledge management system. https://www.icmra.info/drupal/en/strategicinitatives/pqkms/joint_reflection_paper