Regulatory Harmonization

Updating medicines regulatory systems in sub-Saharan African countries

An effective medicines regulatory system ensures that all pharmaceutical products on the market are safe, effective and consistently meet approved quality standards (1). The World Health Organization (WHO) works with its Member States in assessing national regulatory systems to identify gaps, develop strategies for improvement and support countries in their commitment to build national regulatory capacity.

The WHO report, *Assessment of medicines regulatory systems in sub-Saharan African countries* (2), synthesizes the findings of rapid assessments performed over the last eight years of national medicines regulatory authorities (NMRAs) in 26 African countries: Angola, Benin, Botswana, Burkina Faso, Burundi, Cameroon, Chad, Democratic Republic of Congo, Cote d’Ivoire, Djibouti, Ethiopia, Gabon, Ghana, Kenya, Malawi, Mali, Mozambique, Niger, Nigeria, Rwanda, Senegal, South Africa, Sudan, United Republic of Tanzania, Uganda, Zambia. Although the emphasis of the missions was on capacity-building rather than a standardized comparison of indicators, the findings give a useful insight into the regulatory situation in Africa and potential areas for collaboration. The report sheds light on the urgent need for regulatory capacity strengthening in African countries and proposes action for sustainable progress. A summary of the report is set out on the following pages.

Medicines regulation in developing countries

Medicines are essential to health care and should be available to the inhabitants of every country. Medicines regulation aims to ensure that medicines circulating in national markets and international commerce are safe, effective and of good quality, are accompanied by complete and correct product information, and are manufactured, stored, distributed and used in accordance with good practices.

Affordable products are now available with the potential to dramatically reduce morbidity and mortality in resource-constrained countries. Although African countries import most of their pharmaceuticals, the African Union has recently started to promote local manufacture of medicines in Africa.

Globalization of commerce and the merging of pharmaceutical companies has led to an increasing breakdown of national boundaries in medicines supply. Substandard and counterfeit pharmaceutical products are now reported from all parts of the world (3). The problem is greatest in developing countries, which have insufficient funds for medicines procurement, and even fewer resources to enforce quality standards and protect the medicines supply chain.

Norms and standards for medicines quality are becoming more sophisticated and make the assessment of new chemical entities especially challenging. WHO continues to develop international norms and standards to serve as guidance for national regulatory systems. In practice however, medicine quality standards are subject primarily to the requirements in
force in the country of destination (4). Regulating the increasingly complex channels of medicines supply requires constant vigilance, adaptation and considerable organizational capacity and resources.

**Aim of the WHO report**

*Assessments of medicines regulatory systems in sub-Saharan African countries* presents assessments of regulatory systems conducted in 26 sub-Saharan African countries over the past eight years. It identifies regulatory gaps and suggests priority activities to strengthen regulatory capacity.

At the request of each country, national medicines regulatory authority (NMRA) assessments were carried out between 2002 and 2009 by teams composed of WHO experts, staff from NMRA and/or external consultants. Written terms of reference and an agenda for the visits were agreed beforehand with the regulatory authority being assessed. The duration of the visits varied depending on the complexity of the country’s regulatory functions, most visits took approximately three to five working days.

Data were collected by interviewing personnel, reviewing documents (manuals, records, reports, files), analysing data and/or observing activities. Findings were recorded on a comprehensive data collection tool developed by WHO (5) which has since been complemented by a detailed guidance document (6). A draft report was submitted to the regulatory authority after the visit together with a drafted proposal for a plan of action. The main aim of the visits, and the design of the tool itself, were geared towards identifying priorities for strengthening regulatory capacity. They were not intended to provide comparable indicators of regulatory capacity over time.

The strengths and weaknesses identified by the country reports are a reflection of their technical judgement of the authors together with the views expressed by relevant national regulatory officials.

**Country profiles**

The 26 countries included in the report represented 88% of the population of sub-Saharan Africa in 2007. Key economic and health-related data are also summarized in the report (2).

Pharmaceutical sector data contained in country reports indicated that African countries generally had:

- Limited pharmaceutical production capacity, while most depended mainly on imports.
- Some pharmaceutical manufacturing activity catering mainly for domestic and regional demand. However, there were some exporting countries.
- A diverse distribution chain, with various types of unauthorized outlets suggesting the presence of an informal market.

In virtually all countries included in the report, limited public funds were available for law enforcement in general and for medicines regulation in particular. Additionally, there were indications of the presence of parallel, unregulated medicines markets, posing a serious risk to individual and public health.

Nevertheless, differences did exist in the efficiency of the measures implemented among countries. This illustrates the impact of political commitment and level of resources allocated to medicines regulation.

**Regulatory framework**

**Legislation**

Written laws, Acts or Statutes enacted by Parliament give the NMRA the power to control medicines. Regulations prepared under the authority of an Act provide directions on how regulatory functions are
to be carried out. Guidelines are also needed to interpret legislation and advise on how to comply with a regulation. The way in which these legal and explanatory texts are drafted affects the efficiency of medicines regulation.

The legal framework should allow effective implementation and provide adequate powers to the NMRA. Legislation should cover all products for which medicinal claims are made as well as related manufacture and trade activities in the public and private sectors. Countries should update their medicines legislation and regulations regularly to reflect national realities and to address new pharmaceutical issues as they arise (1).

Key findings
- In most countries, legislation had evolved over many years. In only three countries had a medicines regulation Act been adopted later than 2000.
- Successive regulations and decrees had created a complex legal framework with overlaps and grey areas.
- Regulations for specific regulatory functions were missing in some countries, especially where the NMRA was undergoing transformation.

Regulatory scope
In the last few decades, expansion of regulatory scope has been considered in many countries (7). A medicine has been defined as “Any substance or pharmaceutical product for human or veterinary use that is intended to modify or explore physiological systems or pathological states for the benefit of the recipient” (8). In addition to conventional medicines for human use, this definition also includes biological medicines (including vaccines and blood products), veterinary medicines, and traditional and herbal medicines, although the latter category is challenging to define and to regulate (9).

All types of medicines should be regulated by the NMRA. At the same time, implementation of medicines regulation should not be compromised by other, non-regulatory activities exerted by the NMRA.

Key findings
- Seventeen of 26 NMRAs (65%) had the mandate to control veterinary medicines. In four countries veterinary medicines were controlled by another Ministry, such as the Ministry of Agriculture or Livestock.
- Eighteen of 26 NMRAs (69%) had some policy or provisions to deal with traditional or herbal medicines. While eleven of these registered traditional or herbal medicines, another two were about to start doing so.
- NMRAs in eleven countries (42%) regulated a wide scope of products, which included foods, poisons, pesticides, bottled water, cosmetics and/or animal food supplements.
- In seven countries, the NMRA was involved in designing and implementing national medicines strategies, implementing legislation or coordinating public sector medicines supply; in one case a clearly distinguished unit was in charge of policy issues.

Organizational forms
One central authority should be accountable for the overall effectiveness of medicines regulation. It should have government backed legal power to acquire and use resources, recruit and dismiss staff, and make independent decisions. The choice of a specific organizational form will have an impact on the autonomy, visibility and accountability of an NMRA and would affect efficiency in medicines control.
Key findings
Historically, most NMRAs in Africa started life as departments under the Ministry of Health. Organizations of this type have little autonomy. They cannot recruit their own staff, nor can they offer adequate salaries to attract and retain qualified experts. With the maturation of regulatory systems, some countries are moving away from this model and are establishing their NMRAs as autonomous bodies or as centralized parastatal agencies with their own management structures.

- Seventeen of 26 authorities (65%) were departments of the Ministry of Health, with very little or no autonomy to manage their own funds and human resources.
- Seven NMRAs (27%) were in transition or not formally constituted at the time of the visit.

Regulatory functions
NMRA responsibilities should cover all medicines regulatory functions and should be performed in a balanced fashion.

If functions are distributed between different authorities, either horizontally (e.g., ministry of health, ministry of agriculture) or vertically (federal, state/regional and local governments), a central coordinating body should be accountable for all aspects of medicines regulation in the country (1).

Key findings
- Four of the 26 NMRAs (15%) carried out functions of marketing authorization, licensing, inspection, quality control and pharmacovigilance together under one umbrella.
- Seventeen NMRAs (65%) had access to a functional national regulatory quality control laboratory, while seven of these laboratories were part of the NMRA. In one of the remaining countries, there was an NMRA laboratory which had ceased to function.
- Most countries had fragmented regulatory systems. Gaps and overlaps of responsibilities were common, especially in licensing (involving the Ministry of Public Health or Ministry of Trade) and inspection (involving pharmaceutical councils, regional authorities or public health inspectorates).
- Decentralization and cooperation between authorities was problematic; 12 reports highlighted the lack of communication at operational level.
- In many cases, regulatory functions were not operational and in some cases authorities were not legally delegated.

Structure and management
Funding
Sustainable funding for NMRAs should be derived from various sources:

- Fees, which contribute significantly to operational costs without being too high to discourage applications.
- Public funding, to ensure a certain independence from the parties that MNRAs are mandated to regulate.
- Donations to supplement limited public funds.

NMRA should have the autonomy to retain and use fees collected for services provided for their own purposes.

Key findings
- Most NMRAs derived their funding from more than one source, although the proportions varied from one country to another.
Fees were commonly charged for initial marketing authorization, renewal and retention. More rarely, fees were charged for importation of medicines, inspection, analysis of samples and registering persons and premises.

Generally, the fees were lower than the cost of services rendered, and were not retained or redistributed in full.

Nine NMRAs depend on government funding, with all fees paid directly to the treasury and not redistributed. Four NMRAs also receive donor funding. Funds allocated by the states were not always released on time.

None of the NMRAs assessed had adequate and sustainable funding to cover operations.

**Human resource management**

Personnel engaged in medicines regulation should be individuals of integrity and be appropriately trained and qualified.

Human resource development programmes should be made available to enable staff to keep up with developments in pharmaceutical science and technology.

**Key findings**

In general, human resource management was virtually non-existent. This was the case especially where an NMRA was not given importance by the Ministry of Health. As a result, lack of qualified staff affected critical regulatory functions while specific shortcomings included the following.

- Only two of the 26 NMRAs (8%) had a human resource development plan, which was however not specific to the tasks of the NMRA. Specific training needs and difficult access to sources of current information were noted in most countries.

- Job descriptions for key personnel were described as absent in five countries, and as unclear or outdated in four. Four reports mentioned the absence of an organigram.

- In some authorities, responsibilities were not assigned appropriately. One NMRA director was at the same time the director of the national laboratory, resulting in an unmanageable workload. Three others were simultaneously in charge of public sector medicines supply or tenders, creating a potential conflict of interest.

- Four reports mentioned the absence of a legal adviser on the NMRA’s payroll.

**Quality management systems**

NMRAs perform critical and sensitive functions such as handling and assessing marketing application dossiers containing confidential information, inspecting facilities and handling site master files. A quality management system (QMS) should ensure that the operations of an NMRA are carried out to defined, uniform standards, and that each step of the regulatory process is identified and documented.

**Key findings**

- Four NMRAs (15%) were in the process of implementing a QMS and had elements of the system in place, two others were drafting a system.

- None of the NMRAs had implemented a comprehensive QMS.

**Impartiality and transparency**

Medicines regulation is a public policy that regulates private sector activities in order to attain the promotion of public health. Conflicting interests therefore need to be recognized and managed appropriately.
To provide credible regulatory services, NMRAs must have specific measures in place to avoid conflict of interest in decision-making, to ensure confidentiality, to make their rules and decisions transparent, and to consult with stakeholders.

**Key findings**

- Nine of the 26 NMRAs had a dedicated web site. Five of these were in need of updating, one was not functioning correctly at the time of the visit. As at November 2009, seven additional sites were identified (10).
- Consultation with stakeholders took place in most countries, although it tended to be limited to specific issues or groups.
- Current information was not always publicly available: lists of approved products or establishments were often missing and/or outdated. Little information was made public on decision-making.
- Twenty-three of 26 NMRAs (88%) had no written declaration of interest or confidentiality agreements in place, although some had general rules of conduct such as a code for civil servants. In the three countries which did have a specific written system, this did not apply to all technical staff involved.

**Medicines registration**

A core regulatory function is the authorization of medicines based on a scientific assessment of their safety, efficacy and quality.

To assess applications for marketing authorization, NMRAs need:

1. Legislation giving the NMRA the power to grant, renew, vary, suspend and withdraw marketing authorizations.

2. Guidelines for applicants setting out the conditions, content and format of applications, and the detailed technical requirements against which dossiers will be assessed, based on international guidelines (11–13).

3. Standard operating procedures (SOPs) to assess submissions, and standard formats to communicate and publish the outcomes.

4. Involvement of an advisory committee and expert assessors in adequate numbers with specific, current expertise.

5. Logistics for management, secure storage, retrieval and exchange of data with other regulatory departments, as well as access to current scientific and technical information.

6. Mechanisms to consider decisions from more stringent NMRAs.

**Key findings**

- Some evaluation of technical documents was performed in 19 of 26 countries (73%) to varying degrees of stringency, at least for generic medicines.

- The technical standard of evaluations was generally not in line with WHO standards. For example, in at least four countries, guidelines did not exist. At least three NMRAs did not require the manufacturer to have GMP certification. At least six NMRAs did not assess summaries of product characteristics (SPC).

- The capacity to assess applications for new innovator products was almost non-existent.

- NMRAs in seven countries conducted only an administrative review of documents, or no review at all at the time of the assessment.
Legal basis and regulations

- Eighteen of 26 NMRAs (69%) operated within a legal basis which empowered them to assess applications for marketing authorization, with regulations that briefly outlined the requirements or listed the components of dossiers to be submitted for different types of products.

- Provisions for renewal of marketing authorizations were in place, usually every five years.

- Seven countries had provisions which exempted wide ranges of products (such as public sector imports or donations) from registration or from specific requirements irrespective of quality risk. For example, in one country, all oral solid-dose anti-infectives were exempt from in vivo bioequivalence studies.

Guidelines

Some countries had guidelines which described the required content of submissions and gave brief instructions, but did not give sufficient guidance on technical issues such as bioequivalence and stability. Others described the administrative steps and others provided only checklists. A specific format for submissions was not required in any of the countries.

- Only three NMRAs (12%) provided detailed technical guidelines (but not in line with WHO Guidelines).

Procedures for assessment

Written SOPs for dossier assessment were either absent or they described only administrative steps such as checking the completeness of dossiers, payment of fees or inclusion of samples, or were checklists outlining elements of the assessment methodology.

- Adequate SOPs for dossier assessment were in place in only three countries.

Timeframes for assessment of applications ranged from three months to five years, depending on the complexity of assessments and available resources. Fast-track mechanisms existed for certain product types. Two reports mentioned the short preparation and meeting times available for committee members to make their decisions, meaning that they may not be able to read all documents and carry out any real assessment.

- Although overall assessment time frames were long, little time was available for an in-depth thorough assessment by experts due to scheduling difficulties and backlogs.

Expert assessors

Most NMRAs had formal advisory committees. However, not all committees were operational, bringing assessment to a halt in two countries. Eleven countries used external experts, two of them exclusively. Appointment of committee members and experts was not necessarily based on specific regulatory expertise, and provisions for confidentiality and declaration of interest were lacking in most countries.

- Twenty-four of 26 country reports (92%) mentioned the shortage of adequately qualified assessors as an obstacle to timely dossier evaluation.

Logistics

- Only four NMRAs (15%) had appropriate archiving space to store confidential data securely.

- Only six of 26 countries (23%) had coherent, networked computerized systems designed for medicines registration. Nine (35%) had only manual systems.

The latter shortcoming affected transparency and information-sharing with other
departments. Lists of registered products were not readily available, which made it difficult to verify the registration status of medicines circulating in the market and those being imported. The countries which did publish a list did not include the approved summary of product characteristics (SPC) needed to verify package inserts, information for health professionals and advertising claims.

**Recognition of decisions made by other NMRAs**

Certificates of pharmaceutical products (CPPs) issued under the provisions of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce (14) were commonly requested as part of applications, but usually without considering the capacity of the issuing regulatory authority to certify that the data on the certificates was correct. Conversely, one report from an exporting country mentioned that the NMRA “issues CPP without ascertaining that all prerequisites as specified by WHO are fulfilled”.

- Only two NMRAs (8%) explicitly relied on other regulatory bodies/organizations which they considered stringent, including the WHO Prequalification Programme (15).

The lack of mechanisms and procedures that would enable NMRAs to benefit from the scientific assessments and inspections carried out by other well resourced and established regulators is a major cause of concern, as most of the authorities in the region have limited human resources and scientific expertise. (See Figure 1.)

**Licensing of pharmaceutical establishments**

Health budgets in African countries are low and a high percentage of health costs are paid out of pocket. There are many types of medicines outlets not managed by a pharmacist. Concerns about the parallel medicines market were voiced in most country reports, such as this typical statement: “The illicit medicines market has become a real plague in the country. All therapeutic classes can be found, including psychotropic medicines, and there is no national strategy to combat this situation.”

A mandatory system of licensing manufacturers, wholesalers/distributors and retailers is essential to ensure that medicines conform to acceptable standards of quality, safety and efficacy until they reach the end user. Licensing must be complemented by inspections and market surveillance.

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**Figure 1. Resources for medicines registration**

![Bar chart showing resources for medicines registration](image)
NMRAs should ensure that all premises and practices used to manufacture, store, distribute and supply pharmaceutical products to patients comply with current guidelines on good manufacturing practice (GMP), good distribution practice (GDP) and good pharmacy practice (GPP).

**Key findings**

- All countries except one had systems in place to license pharmaceutical establishments.

- Authorities other than the NMRA were involved in licensing in 16 countries (62%), resulting in overlaps, grey areas and gaps in the control of pharmaceutical activities.

- Decentralization of licensing, involving regional authorities, was not organized efficiently. Lack of coordination was commonly highlighted; lax control of licensing by local authorities was mentioned specifically in three country reports.

- Licences or renewals were granted without inspection in some instances.

- In practice, good practices requirements were poorly enforced. In one country only one of many established manufacturers was licensed.

**Import and export control**

With the rapid introduction of high-technology medicines into import, export and distribution networks (including e-commerce), the safety, quality and efficacy of medicines on the market are matters of considerable concern.

Setting in place a registration system should not be considered as the only mechanism to guarantee the quality of products on the market. It should be complemented by other control measures such as the authorization of each act of importation of pharmaceutical products on the basis of the product’s registration status.

Products for export should be subject to the same standards as those for domestic consumption.

**Key findings**

- Control of imported products was weak. In at least eight countries (31%) there was no efficient system to verify the marketing authorization status and exemptions for imported products.

- Cooperation with police and customs was consistently described as problematic.

- Control of exports was not stringent. One report mentioned manufacturers’ illegal practice of issuing “free sale certificates”, which leaves all control to the receiving country.

**Inspections**

Inspections conducted on pharmaceutical facilities should enable medicines regulatory authorities to monitor whether pharmaceutical activities are carried out in accordance with approved standards and guidelines. The efficiency of inspections has a direct impact on the extent to which medicines control is enforced.

A legal basis must be in place for inspections and enforcement. Planning of routine inspections should be implemented to regularly check compliance with relevant good practices in place.

A quality management system (16) should ensure that inspections are planned, conducted, documented and followed up in a consistent way, based on risk assessment.

Sufficient qualified inspectors and logistic resources must be available to cover the area to be regulated.
Key findings

- A legal basis empowering the relevant authority to perform inspections was in place in 17 countries.

- GMP was not required in at least nine countries. In at least two countries where GMP was required, none of the established manufacturers had GMP certification.

- Only five of 26 countries (20%) had published GMP guidelines meeting WHO standards (two had national texts, and another three used the WHO text). Only one country had adequate GDP guidelines.

- SOPs for inspection, if any, were mostly in checklist format and were not comprehensive.

- No NMRA had a comprehensive quality management and planning system for inspections in place.

- Shortages of qualified inspectors were a universal problem. The need for specific training of inspectors in current GMP was commonly highlighted.

- Potential conflicts of interest were noted. Inspectors could be pharmacy technical directors or supervisors in at least three countries. Pharmacists from private retail and manufacturing facilities were used as inspectors in another.

- Inadequate logistic resources, especially means of transport and communication, were a major constraint. The effectiveness of inspections suffered from these constraints. (See figure 2.)

Quality control

Quality control (QC) aims to verify that products comply with the specifications of the marketing authorization. QC testing of pre-marketing samples can be useful to some extent, although applicants may take measures to ensure that their registration samples will not fail. However, the same quality standards may not be met by each batch of product put on the market. QC testing of post-marketing samples thus acts as a deterrent against negligent or fraudulent manufacturing and trading practices.

NMRAs should have access to a quality control laboratory with adequate capacity to undertake quality surveillance.

Figure 2. Resources for inspections
QC facilities should have sufficient qualified personnel and the necessary equipment and materials, and must operate according to established standards. A quality management system, such as ISO 17025 (17), provides a framework for QC laboratories to operate according to defined procedures and standards. WHO’s good practices for national pharmaceutical control laboratories (18) and guidance on good laboratory practice (19) provides detailed advice on organizational and technical issues.

If dossiers are assessed and samples tested, good collaboration between assessors and laboratory staff needs to be in place.

**Key findings**

- A QMS was in place at five (29%) of the 17 functioning regulatory laboratories; three others had partial systems which were lacking essential elements and were not fully operational.

- Satisfactory staffing and equipment were in place in the majority of cases, but six laboratories were housed in inadequate buildings.

Ten reports mentioned QC testing for pre-marketing applications. However, the laboratories were not always given the relevant dossiers, manufacturer’s reference materials and validated methods.

**Market surveillance**

**Product quality monitoring**

Substandard pharmaceuticals may circulate on the market if good practices in manufacturing, distribution and storage are not adhered to.

In addition, counterfeiting — the production and distribution of medicines that are deliberately and fraudulently mislabelled with respect to identity and/or source — is becoming an increasing problem. It requires a coordinated response from different sectors both at country level and internationally (20). In both cases, the deficient products pose a risk for individual and public health.

A risk-based system of inspections and sampling should be in place to monitor the quality of pharmaceutical products on the market. Manufacturers should be obliged to report complaints and quality problems to the NMRA. An effective recall procedure to remove defective products from the market should be in place.

The NMRA should coordinate an anti-counterfeiting programme with all concerned parties, including industry, customs, police and any other stakeholders involved in trade or distribution of pharmaceuticals.

**Key findings**

- Fourteen of 26 NMRAs (54%) lacked a quality monitoring programme altogether; seven had the capacity to test samples in case of complaints or in the framework of specific programmes, and only five (19%) had a systematic approach.

- Twenty of 26 NMRAs (77%) lacked a written procedure to organize an effective recall; of the existing six procedures three needed clarification. Five reports noted the lack of batch traceability needed to recall products. This finding is consistent with the general absence of published GDP guidelines.

- Anti-counterfeiting measures included inspections and surveillance in five countries and awareness programmes in three. No country had a specific, comprehensive programme in place at the time of the visits.

**Pharmacovigilance**

Pre-marketing clinical trials are usually conducted on a small number of volunteers. Not all adverse reactions can be
anticipated from these studies. NMRAs should implement a system to monitor adverse events. For this to be effective, there must be a high probability for adverse events to be identified and reported, reports must be reviewed and validated by experts, results must be fed back, and appropriate regulatory action must be taken.

**Key findings**

- Eight of 26 countries collected reports on adverse events, with three of the programmes being sufficiently established to contribute a sizeable number of results. Seven of the eight countries were members of the WHO Programme for International Drug Monitoring (see http://www.who-umc.org/).

- Where it existed, pharmacovigilance was generally not well integrated with other regulatory activities. Also, clinical surveillance measures implemented by specific national or NGO treatment programmes were not organized or envisaged.

**Medicine promotion and advertising, provision of drug information**

Information propagated through promotion and advertising can significantly influence the way in which medicines are prescribed by health professionals and used by consumers. Inaccurate and misleading information therefore poses a health risk.

NMRAs should control promotion and advertising to ensure that any claims made correspond to the approved summary of product characteristics (SPC). They should also provide independent information on medicines to the public and health professionals.

**Key findings**

- Most countries had some legal provisions for the control of medicines promotion. Seven of 26 countries (27%) controlled pharmaceutical promotion to varying extents.

- In 19 countries (73%) there was no control of promotion and advertising in practice, meaning that even if the regulations were in place, they were not implemented.

- At least 13 NMRAs did not provide any independent medicines information to the public.

**Oversight of clinical trials**

Clinical trials are an essential component of pharmaceutical research and development. They serve to establish the safety and efficacy of new medicines, and to develop new treatment uses of well known medicines. Clinical trials also include *in vivo* bioequivalence studies carried out with generic medicines to establish their therapeutic interchangeability with originator products. In all these types of studies the ethical rights and the safety of trial subjects must be protected, and the methodology must be designed in such a way as to arrive at useful, scientifically valid results.

NMRAs should control clinical trials jointly with external bodies such as national or institutional ethics committees. Trials should conform with ethical principles for medical research involving human subjects and the Declaration of Helsinki (21). Guidelines by the Council of International Organization of Medical Sciences (CIOMS) provide valuable additional information on research ethics.

WHO guidelines for GCP (22) and GLP (19) should be followed. GMP of investigational products should be verified. Other more specific guidelines on clinical research may apply.

Trials should be monitored for compliance with all applicable guidelines. Investigators should be required to report on the outcomes promptly, including any serious adverse events encountered.
Key findings

- In 18 of 26 countries (69%) clinical trials were controlled to some extent, mostly with regard to ethical review.

- Where ethics committees were involved, NMRAs retained little or no control due to lack of capacity, unclear assignment of responsibilities or non-representation in the relevant committees.

- Adherence to GLP and GCP was not a requirement in 22 countries (85%); detailed GCP guidelines were found in only two countries (8%).

- Eight reports mentioned the absence of import controls and GMP requirements for investigational products.

- Only four country reports mentioned that inspections of clinical trials were being conducted.

Conclusions

The countries included in this report had legal provisions for the most essential needs of medicines control. However, their regulatory systems presented some weaknesses. Generally, the legal framework had evolved over time, resulting in a fragmentation of responsibilities with gaps and grey areas and a multitude of provisions which were difficult to implement.

Many NMRAs were allowed little power and autonomy, and were unable to oversee the full range of regulatory functions, with few having systems for accountability or managerial commitment. Lack of sustainable funding restricted operations to a great extent. Virtually all NMRAs suffered from staff shortages. For the most part, assessors and inspectors were unable to satisfactorily attain the level of scientific and technical expertise needed to fully implement regulatory tasks. Many regulatory requirements and processes were not in line with recommended WHO standards.

As a result of these drawbacks, medicines regulation was not being carried out to the fullest extent. The findings confirm the results of a 2004 questionnaire survey conducted by WHO in 38 African Member States, which found that 90% of countries were in a situation which did not allow them to adequately carry out regulatory functions (23).

Despite the universally scarce resources and the health workforce crisis experienced throughout sub-Saharan Africa, marked differences were noted in the relative efficiency of medicines control among countries, showing that political commitment at national level can make a difference.

On the positive side, many countries were greatly committed to improving their medicines regulatory capacity: reviews of systems were invited and regulatory restructuring is being adapted. However, in many cases, the transformation process has created new administrative hurdles for effective decision-making, management and release of funding.

The follow-up assessments conducted in four countries showed progress in specific areas. However, for a sound, well-resourced national medicines regulatory system to operate within the difficult conditions imposed by African markets, commitment must be long term.

The way forward should be towards effective implementation of medicines control in practice. Political will and substantial human and financial resources will be needed for this purpose. Countries will need to take concerted action if they are to expand access to medicines of assured quality and safety for their populations. It was felt that the following approaches would be the most useful in building regulatory capacity in Africa.
WHO should:

- Encourage African countries to provide NMRAs with adequate organizational structure, sufficient autonomy and sustainable resources to enable them to carry out operations.

- Encourage and assist African countries to regularly assess their own regulatory systems in a standardized way. The WHO assessment tool and the accompanying guidance have been developed for this purpose.

Countries should:

- Consider mechanisms to share the outcomes of regulatory assessments among NMRAs.

- Work towards effective implementation of all essential regulatory functions under the umbrella of an NMRA network.

- Continuously harmonize, adapt and update the legal framework for medicines regulation based on internationally recognized norms, standards and best practices.

- Provide specific, relevant training for assessors, inspectors and other technical staff, in line with current technical requirements and good practices.

References


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