BMJ Global Health

Quality assurance systems of pharmaceutical distributors in low-income and middle-income countries: weaknesses and ways forward

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To cite: Nebot Giralt A, Bourasseau A, White G, *et al*. Quality assurance systems of pharmaceutical distributors in low-income and middle-income countries: weaknesses and ways forward. *BMJ Global Health* 2020;**5**:e003147. doi:10.1136/bmjgh-2020-003147

Handling editor Seye Abimbola

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Received 15 June 2020
Revised 19 August 2020
Accepted 1 September 2020

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ABSTRACT

Introduction Access to quality-assured medicines is an essential prerequisite for universal health coverage, and pharmaceutical distributors play an important role to assure the quality of medicines along the supply chain.

Methods We retrospectively assessed the compliance with WHO quality standards, that is, the Model Quality Assurance System for Procurement Agencies (MQAS) or the good distribution practices (GDP), of a convenience sample of 75 public, private-for-profit and non-for-profit distributors, audited by QUAMED in 14 low-income and middle-income countries (LMICs) between 2017 and 2019. We calculated the compliance per quality assurance activity, and we defined the percentage of compliant distributors, that is, the percentage (%) of distributors with MQAS or GDP levels of $\geq$2 for each activity.

Results The distributors in our sample were mainly private for-profit (66/75). Only one MQAS-audited distributor out of 11 was found compliant with all MQAS-activities, while none out of 64 GDP-assessed distributors were found compliant with all GDP activities. The GDP-assessed distributors were generally less compliant with WHO standards than MQAS-audited distributors. Common weaknesses and strengths were observed. The activities with lowest compliance were quality control, and physical storage conditions, while those with highest compliance were warehouse organisation and stock control.

Conclusions The quality systems of pharmaceutical distributors in LMICs remain weak. For preventing harm caused by poor-quality medicines, a comprehensive and stringent regulatory oversight should be urgently implemented; the WHO MQAS-standards and GDP-standards should be incorporated in national regulations; and reliable information on the quality systems of distributors (and manufacturers from which they buy) should be publicly available.

Key questions

What is already known?

- Two studies published by our groups in 2017 and 2018, indicated that the quality systems of pharmaceutical distributors in low-income and middle-income countries are generally weak, and insufficient to prevent and detect the supply of poor-quality medicines.

What are the new findings?

- In our convenience sample of distributors, mainly belonging to the private for-profit sector, only 1 out of 75 was fully compliant with the adequate standards as set by WHO.
- The greatest failures were observed in areas purely related to quality assurance, while slightly better results were observed for activities that are also important for commercial reasons, such as warehouse management and stock control.

What do the new findings imply?

- In order to prevent harm to medicines' final users, stringent regulatory oversight on pharmaceutical distributors should be urgently implemented at country level across all sectors, as neither financial incentives nor the level of wealth of countries seem to push, alone, towards enforcement of quality assurance systems.
- The availability of reliable information on distributors' quality system, with a cross-cut information on manufacturers sites' performance and products' quality, would also be of great help—particularly nowadays, as the COVID-19 crisis has magnified challenges in pharmaceutical supply and quality assurance.
- This would imply carrying out regular monitoring exercises, and investigating the relationships between potential oligopolies along the pharmaceutical supply chain and the commitment to quality assurance.

INTRODUCTION

Access to quality-assured medicines is essential for universal health coverage (UHC).[1] Unfortunately, the globalisation of pharmaceutical production and distribution was not accompanied by a strengthening of National Medicines Regulatory Authorities (NMRA) in low-income and middle-income countries (LMICs). Only less than 30% of WHO Member States have an NMRA able to

enforce adequate quality standards.[2–4] Hence, the quality of medicines remains at risk in LMICs.[5] The epidemiology of poor-quality medicines is well known particularly for antimalarials,[6–9] but poor-quality medicines are a transversal problem,[10] documented for antibiotics,[11–14] non-communicable diseases,[14–17] reproductive health[18] and many essential or life-saving medicines.[19–21] Quality problems are due to poor manufacturing, distribution or storage practices.[21] For instance, the high prevalence of poor-quality oxytocin is caused by a mix of poor practices at manufacturing, wholesalers and outlets level.[18 22 23] Poor-quality medicines often go unreported, particularly where robust pharmacovigilance and postmarketing surveillance systems are lacking.[21] They result in avoidable morbidity, mortality[7 21] and drug resistance,[9 13] and their economic impact can be disruptive, as recently observed in Nigeria and the Democratic Republic of Congo (DRC).[23–25]

It is important not to guess, but to ensure the quality of medicines, and the quality systems of manufacturers and distributors.[26] WHO provides guidance on good practices globally.[27 28] Two guidelines are of particular interest for procurement and supply: the 2020 Good Distribution and Storage Practices for medical products (GDP)[29] and the 2014 Model Quality Assurance System for Procurement Agencies (MQAS).[30]

Procurement and distribution of medicines are managed by a variety of public, private and non-governmental actors in LMICs, including importers, procurement agencies, distributors, retailers.[31] Their customers are often insufficiently aware of risks entailed by poor management of medicines.[26 32] In 2017, our group published an evaluation of the WHO MQAS-compliance of public and non-for-profit international and national procurement agencies active in sub-Saharan Africa, showing insufficient compliance with stringent criteria, particularly for prequalification (PQ) of products and suppliers.[33] In 2018, we published an evaluation of the quality assurance (QA) system of private pharmaceutical distributors in 13 LMICs, which found a low compliance with WHO GDP standards.[34] Both studies were based on retrospective data from QUAMED, a not-for-profit network that aims to improve access to quality medicines in LMICs (https://www.quamed.org/). The partners of QUAMED are non-governmental organisation, international organisations or central purchasing agencies in the South that purchase medicines for medical programmes carried out in LMICs, either in the humanitarian, development of public health sectors. Among other things, QUAMED assesses the quality systems of pharmaceutical suppliers, for orienting its partners toward reliable suppliers when they do in-country purchases.

To follow-up on market evolution, we now conducted a third evaluation, to further explore the QA systems of private and public pharmaceutical distributors audited more recently.

METHODS

This quantitative retrospective study assessed the compliance with the WHO MQAS-quality and GDP-quality standards of a sample of public, private-for-profit and private non-for-profit pharmaceutical distributors, audited by QUAMED in 14 LMICs between January 2017 and December 2019. The key definitions used in the study are described in table 1.

Sampling

Secondary data were obtained from the access-controlled QUAMED database, which includes the reports of all evaluations conducted from 2010 until today. Suppliers are audited if they have a valid licence, if they are current or potential suppliers of QUAMED partners, as indicated by the QUAMED partners that run medical programmes in a given country, and if they voluntarily agree to undergo the audit.

Evaluations are conducted by a pool of qualified technical experts, bound to confidentiality and disclosure of conflicts of interest. Their minimum skills and qualifications are defined by a standard operating procedure.

Depending on activities covered by a distributor, QUAMED conducts an 'MQAS audit' or a 'GDP assessment'. The decision on the kind of audit/assessment that should be conducted, depends on whether the distributor also has the potential to implement its own PQ system for the product-manufacturer couple (ie, for preselecting suppliers and individual products), or if it only relies on the licences and marketing authorisation granted by the national regulator. The first group generally includes international procurement agencies, central medical stores and some other distributors-importers; for all of them, an MQAS audit should be conducted, based on the WHO MQAS guidelines. The second group generally includes distributors that are mainly acting at local level; for them, a GDP assessment based on the WHO GDP guidelines will be more appropriate. Generally, the total number of suppliers assessed or audited per country represents a relatively small proportion of all in-country distributors, particularly for the second group. An MQAS audit may take up to 2–3 days, and findings are reported in a qualitative narrative text and in a quantitative rating, while a GDP assessment generally takes half-a-day, and findings are reported in a qualitative narrative text and in an open-ended answers questionnaire. If several distributors are assessed in a same country, they altogether belong to a 'local market assessment'.

Differently from our previous studies that separately addressed different categories of distributors[33 34] and building on this experience, both the MQAS-audit and GDP-assessment reports were included in the sample of the present study, if they were conducted between 1 January 2017 and 31 December of 2019, and available in QUAMED database. The initial exclusion criterion 'distributors settled in countries in war or conflict situation' was not applied. We had assumed that these reports would be incomplete, but it appeared that it

Table 1 Key definitions

Good Distribution Practices (GDP)	A WHO guideline that provides orientation for distribution of pharmaceutical products. Depending on the national and regional legislation on pharmaceuticals, these guidelines may apply equally to products for human and for veterinary use. The guidelines cover products for which a prescription is required by the patient, products which may be provided to a patient without a prescription, biologicals and vaccines.[29]
Model Quality Assurance System for procurement agencies (MQAS)	A WHO guideline that provides detailed guidance to procurement agencies on quality assurance practices.
QUAMED Local Market Assessment (LMA)	An assessment, carried out by QUAMED experts on demand of QUAMED partner/s, of a convenient sample of pharmaceutical distributors and manufacturers operating in a given country, aiming to assess if WHO quality standards are met.
QUAMED MQAS audit	An audit of a pharmaceutical distributor / procurement agency that relies on the licences and marketing authorisation granted by the national regulator, and also has the potential to implement its own prequalification system for the product-manufacturer couple (ie, for preselecting suppliers and individual products). It is carried out by QUAMED experts on demand of QUAMED partner/s, and based on the WHO MQAS guidelines. It usually takes 2–3 days per distributor/procurement agency.
QUAMED GDP assessment	An assessment of a pharmaceutical distributor that relies on the licences and marketing authorisation granted by the national regulator and does not have the potential to implement its own prequalification system for the product-manufacturer couple (ie, for preselecting suppliers and individual products). It is carried out by QUAMED experts on demand of QUAMED partner/s as part of a LMA, and based on WHO GDP guidelines. It usually takes half-a-day per distributor.
MQAS QUAMED rating	A rating developed by QUAMED, based on the WHO MQAS, and aiming to rate each assessed activity in five different levels of compliance (0–4). In this study, we used the most recent version, revised by the QUAMED Technical Committee in 2019, and finalised on 28 August 2019 .
GDP QUAMED rating	A rating developed by QUAMED, based on the WHO GDP and aiming to rate each assessed activity in five different levels of compliance (0–4). In this study, we used the most recent version, revised by the QUAMED Technical Committee in 2019, and finalised on 28 August 2019.
MQAS/GDP level of compliance	A level of compliance attributed to each activity in the QUAMED ratings for MQAS and GDP, going from 0 (non-compliance or low compliance) to 4 (high compliance). Level 2 corresponds to the minimum acceptable requirement in terms of compliance.
Activity	For the scope of this study, an 'activity' indicates a specific area of pharmaceutical quality assurance (see 'QUAMED ratings').
Quality assurance (QA) criteria	For the scope of this study, a QA criterion is built by bringing together a group of activities with a similar or convergent scope (see 'QUAMED ratings').
Percentage of compliant distributors	For the scope of this study, this indicator was defined as the percentage (%) of distributors, out of all those included in the analysis, with an MQAS or GDP level of 2 or more.
Product-manufacturer couple	The process by which a pharmaceutical distributor should verify and evaluate a product dossier and the relevant manufacturer site documentation, as a condition to accept it for purchase. It is generally based on a risk assessment strategy

was not the case. Our initial sample included 12 MQAS-audited distributors and 85 GDP-assessed distributors. We excluded one MQAS audit, due to incomplete results; 13 GDP-assessed distributors, because they did not supply medicines but medical devices; and 8 GDP-assessed distributors, because of incomplete results. The final sample consists of 11 MQAS-audited distributors in 5 LMICs and 64 GDP-assessed distributors in 10 LMICs and 1 autonomous region in Iraq.

Data entry

The QA activities drawn from QUAMED ratings were grouped into 5 'QA criteria' (table 2). We evaluated the reports of MQAS audits, comprising 17 activities; and the reports of GDP assessments, comprising 14 activities. In line with previous work, the activity 'procurement' was not included. All data were entered and analysed in a password-protected Microsoft Excel 2010 database.

For each activity and distributor, we allocated a level of compliance according to QUAMED ratings, ranging from 0 to 4. Levels 0 and 1 correspond to 'non-compliance' and 'poor compliance' (unacceptable), level 2 to 'fair compliance' (acceptable) and levels 3 and 4 to 'good' and 'full compliance' (more than acceptable). Different compliance levels for a same activity are comparable

Table 2 Correlation between QUAMED MQAS and GDP ratings, activities and QA criteria

MQAS audits	GDP assessments	Activities		Quality Assurance criteria	
		1	QA system	QA criterion A General quality assurance requirements	It includes the essential elements required for a stringent quality management system, that is: a documentation system with standardised norms and procedures that define all activities of the QA system; human resources management; self-inspection; continuous improvement; management of corrective and preventive actions. The activity 'computerised systems' is also included in this
		2	Documentation system		
		3	Computerised systems		
		4	Human resources		
		5	Self inspection		
		6	Product Qualification	QA criterion B Continuous product qualification	It describes the capacity of the distributor to select products from manufacturers with an adequate level of compliance with Good Manufacturing Practices (taken as an indicator of the quality of the products as supplied by the manufacturer). This criterion is only used for MQAS assessments—not for GDP assessments.
		7	Manufacturing site assessement		
		8	Qualification decision (qualified sources monitoring)		
		9	Control at reception	QA criterion C Quality control (QC) and reception	It integrates activities covering upstream quality assurance requirements, including the reception activities (eg, verification of documentation, quality checks, sampling procedures, etc), and other QC requirements (eg, risk assessment, sampling plan, management of out-of-specifications, etc).
		10	Quality control		
		11	Warehouse organisation	QA criterion D Storage and handling specific products	It integrates activities required for adequate storage (eg, physical conditions, warehouse organisation, management of cold chain, stock control, etc) and the management of specific products (recalled, returned, quarantined, falsified, etc).
		12	Physical storage conditions		
		13	Management of the cold chain		
		14	Stock Control		
		15	Handling non conformity products		
		16	Dispatch	QA criterion E Dispatch and transport	It corresponds to the distribution activities downstream, including preparation of orders, dispatch and transport. This criterion did not exist as such in our previous studies, but the activities where already evaluated.
		17	Transport		
			Procurement	N/A	Not included

GDP, good distribution practices; MQAS, Model Quality Assurance System; N/A, not applicable; QA, quality assurance.

between QUAMED MQAS and GDP ratings. The data entry methodology was piloted by double-entering four GDP and two MQAS-reports by two different experts, and by comparing results. The outputs helped to frame the process. Data entry was then carried out by a single researcher, in two steps: first, reading in-depth the MQAS or GDP report, the GDP standardised questionnaire and its quantitative value; second, rating the MQAS-compliance or GDP-compliance of each activity (0–4). In case of doubt, a conservative approach was taken and the lower level was chosen. If the researcher considered that some information was lacking, incomplete or not relevant, the activity was rated N/A, and no level attributed.

Data analysis

Like in previous studies,[33 34] findings were analysed and reported by activity. However, unlike in previous studies, the compliance was not further analysed by QA criterion, because not all distributors in our sample conduct all activities that constitute a criterion, and this would have made comparisons across distributors not meaningful. Thus, we defined the Percentage of Compliant Distributors (PCD) for each activity, that is, the percentage (%) of distributors with MQAS or GDP levels of 2 or more. The PCD was further calculated for each country, for aggregated GDP-assessed distributors only, for all the activities rated. An overall descriptive analysis of GDP data at country level was not deemed appropriate as the final data set was too small and asymmetrical for this purpose.

Ethics

The QUAMED database was accessed under confidentiality agreement. All distributors had accepted to be assessed, provided that findings are not distributed

outside QUAMED. We guarantee their confidentiality by not making individual distributors identifiable.

RESULTS

Overall, 11 MQAS-audited and 64 GDP-assessed distributors were included in our analysis. Out of them, 4 were public, 5 private not-for-profit, and 66 were private for-profit.

Distributors were from 14 Asian and sub-Saharan countries, namely Afghanistan, Burkina Faso, DRC, Ethiopia, Jordan, Kenya, Mali, Niger, Nigeria, Rwanda, Tanzania, Uganda and Yemen; Kurdistan, an autonomous region in Iraq, was also included. All countries are classified by the World Bank as low income, except Jordan (high middle income) and Kenya, Nigeria and Tanzania (lower middle income).

Overall level of compliance with who MQAS and GDP (all activities)

Only one MQAS-audited distributor out of 11 was compliant with all 17 MQAS-activities. None out of 64 GDP-assessed distributors were compliant with all 14 GDP-activities.

MQAS-compliant distributors

The 17 MQAS-activities were grouped into 5 QA criteria (table 3). First, we evaluated the level of MQAS-compliance for each activity and distributor. Second, we calculated the PCD for each activity. Since not all distributors were equally documented for all activities, the PCD's denominator (N) varies: 12 activities have n=11, whereas 5 have n<11. For instance, six distributors did not have their own internal PQ system, because they rely on headquarters or on main suppliers, usually located abroad. Since QUAMED auditors could not assess the PQ process on-site, the PCD for activities grouped under QA criterion continuous product qualification was calculated for five distributors only.

Out of 17 MQAS activities, 4 have a particularly low PCD, that is, quality control (45%, 5/11), manufacturing site assessment (40%, 2/5), physical storage conditions (36%, 4/11) and management of cold chain (36%, 4/11). Activities grouped under QA criteria A, General Quality Assurance Requirements, and E, Transport & dispatch, have a PCD between 50% and 67%. Activities with the highest PCD were control at reception (82%, 9/11), warehouse organisation (73%, 8/11) and stock control (91%, 10/11).

GDP-compliant distributors

The 14 GDP activities were grouped into 4 QA criteria (table 4). First, we evaluated the level of GDP-compliance for each activity and distributor. Second, we calculated the PCD for each activity. The PCD denominator (N) varies: 6 activities were calculated for 64 distributors, 4 for 63 distributors, and 1 for 59 distributors. For instance, the PCD for the activity *management of* cold chain could only be calculated for those 39 distributors that handle products requiring cold chain.

Out of 14 GDP-activities, two have a particularly low PCD: physical storage conditions (16%, 10/64) and quality control (3%, 2/64). Almost all other activities under QA criteria A, general QA requirements, C, quality control and reception, and E, transport and dispatch, have a low PCD, between 22% and 32%. Only warehouse organisation (41%, 26/64) and stock control (51%, 30/59) have a higher PCD.

Table 3 Percentage of MQAS-compliant distributors (PCD) by MQAS activities

QA criterion	Activity	PCD (MQAS level ≥2), %
General quality assurance requirements	QA system	6/11 (55)
	Documentation system	7/11 (64)
	Computerised systems	6/9 (67)
	Human resources	6/11 (55)
	Self inspection	6/11 (55)
Continuous product qualification	Product qualification	3/5 (60)
	Manufacturing site assessement	2/5 (40)
	Qualification decision (qualified sources monitoring)	3/5 (60)
Quality control and reception	Control at reception	9/11 (82)
	Quality control	5/11 (45)
Storage and handling specific products	Warehouse organisation	8/11 (73)
	Physical storage conditions	4/11 (36)
	Management of the cold chain	4/11 (36)
	Stock control	10/11 (91)
	Handling non conformity products	5/11 (45)
Dispatch and transport	Dispatch	7/11 (64)
	Transport	5/10 (50)

MQAS, Model Quality Assurance System; QA, quality assurance.

DISCUSSION

MQAS and GDP-compliance

Compared with our previous work that separately addressed different categories of distributors,[33 34] in the present study, we decided to include both the MQAS-audit and the GDP-assessment reports. This required some efforts to harmonise the data entry tools, but given that MQAS-audit and GDP-assessment target different categories of suppliers, this approach offers the advantage of a more complete picture of stakeholders across the private and public sectors.

Table 4 Percentage of compliant distributors (PCD) for GDP by activity

QA criterion	Activity	PCD (GDP level ≥2) %
General QA requirements	QA system	14/64 (22)
	Documentation system	14/64 (22)
	Computerised systems	N/A
	Human resources	14/63 (22)
	Self inspection	20/63 (32)
Quality control and reception	Control at reception	17/64 (27)
	Quality control	2/64 (3)
Storage and handling specific products	Warehouse organisation	26/64 (41)
	Physical storage conditions	10/64 (16)
	Management of the cold chain	13/39 (33)
	Stock control	30/59 (51)
	Handling non conformity products	20/63 (32)
Dispatch and transport	Dispatch	20/63 (32)
	Transport	N/A

GDP, Good Distribution Practices; N/A, not applicable; QA, quality assurance.

All the pharmaceutical distributors in our sample except one, failed to demonstrate compliance with all the evaluated MQAS- or GDP-activities. These results cannot be formally compared with the previous findings from our group, as our three studies were conducted at different time points and on a different distributors' sample, and since the evaluation tools have been improved and refined over time. However, it is possible to point at some general tendencies across the three studies. In particular, Nebot had observed that all the 18 distributors or procurement agencies in her sample showed some level of non-compliance with the MQAS standards (particularly for activities related to the selection of products and suppliers)[33]; and Van Assche *et al* had found that out of 60 private pharmaceutical distributors, only 7 showed good compliance for at least two of the assessed criteria.[34] The failure, confirmed over time, to achieve full compliance with WHO standards, remains a matter of concern for the maturity of regulatory agencies and for the performance of the pharmaceutical systems.

Having acknowledged the generally low compliance with adequate standards, some further distinctions can be done within our sample. The GDP-assessed distributors were less compliant with WHO standards than MQAS-audited distributors. This is in line with the findings of Van Assche *et al*.[34] If we compare the findings of Van Assche to the work of Nebot *et al*,[33] we see that GDP-assessed distributors tended to be less compliant with adequate standards than MQAS-audited distributors. The same patterns emerged in the present study, with striking differences in the PCD between MQAS-audited and GDP-assessed distributors, across the 14 activities that are common to both groups. The lowest PCD are between 36% and 40% in the MQAS-group, and between 3% and 16% in the GDP group. For instance, for the activities related to QA criteria A, general QA requirements, the PCD oscillated between 55% and 67% for the MQAS-group, and between 22% and 33% for the GDP-group.

Different reasons can explain these findings. The first relates to the intrinsic characteristics of distributors. Most distributors (either in MQAS or GDP group) in our sample belong to the private for-profit sector, and are likely to be guided by commercial drivers. This would be the case everywhere in the private sector, but in contexts with weak regulatory supervision, the commercial interests will become the main or only driver to invest or not in quality systems. In addition, the MQAS-audited distributors usually had a greater turnover, they supplied bigger customers, and some acted as importers/branches of mother/partner-companies abroad. Hence, they can be required by their own customers and/or partners to be compliant with some quality standards, and may have some more resources to do so.

There were also some common weaknesses and strengths. Two activities had the lowest PCD in both groups: quality control (45% MQAS-group, 3% GDP-group), and physical storage conditions (36% MQAS-group, 16% GDP-group). Two other activities had the highest PCD: warehouse organisation (73% MQAS-group, 41% GDP-group) and stock control (91% MQAS-group, 51% GDP-group).

Low-compliance for quality control may be due to the complexity and high costs of this activity. In addition, QC is primarily seen as a responsibility of NMRAs,[35] hence most distributors are not familiar with QC concepts and tools. It is understandable that they lack the capacity to systematically and randomly test products, as this is not required by WHO GDP.[29] However, they should be trained in risk analysis/management. In particular, distributors with important supply volumes should have a procedure for risk-based approach, that would define their capacity to organise sampling and testing for suspect products.

The low compliance for physical storage conditions indicates the failure to achieve quality in a core task of distributors, that is, adequately controlling and monitoring temperature and humidity. This is surprising, as in the past there has been emphasis to strengthen storage and distribution capacities.[33] However, such investments mainly targeted the public sector. In insufficiently regulated contexts, the private sector remains subject to the effect of market forces, which so far do not seem to prioritise investments in quality systems.[36] Furthermore, even if the control and monitoring of storage conditions is not complex, it may be costly (it requires calibrated sensors, cartography for sensitive products, and sometimes air-conditioning or ventilation systems, etc) and time consuming, especially in case of manual monitoring.

Financial incentives could explain the higher compliance observed in both groups for stock control and warehouse management. These can be seen as a mix of QA and commercial/financial component. A good warehouse management is a pre-requisite for efficient stock control. Poor stock control may cause financial losses and loss of commercial opportunities to timely address clients' needs; thus distributors would prioritise investments here. In addition, inspection of warehouse organisation and stock control are likely to be prioritised by NMRAs, particularly if they lack the capacity or time for more comprehensive inspections.

For MQAS activities alone, we observed low compliance for the activity manufacturing site assessment (40%), which is a component of QA criterion *PQ* of sources. In line with previous work,[33] this has probably multiple causes. First, distributors are required to supply medicines that hold a marketing authorisation by their NMRA, and they rely on NMRA's lists; this is legally adequate, but unfortunately it cannot take into account the NMRA weaknesses. Second, many distributors lack the technical skills needed to assess a site master file and related documentation. Third, manufacturers may not be transparent when sharing technical dossiers with customers, especially if these do not purchase big volumes. Finally, the cost of a GMP audit, is a major barrier for most distributors.[33]

Quality systems in distribution and country economic indicators

Expenditure on pharmaceuticals represents 19% of global health expenditure, but only 4% of government expenditure on healthcare. This implies a strong presence from the private sector, as in our sample, but also high out-of-pocket expenditure.[37] The wider financing arrangements for healthcare delivery vary greatly across the countries in our sample, to include health insurance schemes, fees for service and free healthcare or combinations of them. These arrangements and the overall performance of the health system may have a variable impact on procurement, distribution and access to medicines, but this was not the focus of the present analysis, and it would deserve further ad hoc research.

Furthermore, it would be useful to understand what is the precise relationship between a country economic indicators and its performance on QA systems in medicines distribution. The income classification level of the country is insufficient to perform this kind of analysis, but based on data available from external sources,[38 39] it might be hypothesised that higher compliance scores could be linked to a strong government presence in healthcare, demonstrated through significant investments. Such hypotheses will need to be prospectively validated through additional research in the contexts surveyed here. Moreover, this would require measures appropriate for a multilevel healthcare market assessment, aimed at understanding the relationship between supply chain management and market forces, especially in contexts where there are only a few distributors, referred to as 'oligopolies'. Such exercise would also need to monitor and triangulate data on the in-country prevalence of substandard and falsified medicines.

Study limitations

This study has some limitations. First, we could not perform a comparison of results within and across country. The reason for this is as we worked with a convenience rather than a randomised sample, as candidates for the audit/assessment are indicated by the QUAMED partners that run medical programmes in a given country, based on their knowledge of the contexts and on their specific needs; and because the sample size is not consistent across countries. Second, an element of subjectivity is intrinsic to every assessment/audit work, for example, when the auditor applies the rating or in the narrative part of report, even if measures are taken to mitigate it (eg, by adopting standardised questionnaires and/or templates). In this study, data were extracted retrospectively from narrative reports, implying an additional small margin of subjectivity. For some activities and distributors, the information available in the source data was incomplete. Finally, we did not look at the correlation between PCD and economic indicators, to avoid ecological fallacies which in the present study would involve giving unequal weight to macro indicators (the country income classification) when compared with meso (eg, total health expenditure) and micro (eg, market size) indicators.

CONCLUSIONS

The quality systems of pharmaceutical distributors in LMICs tend to be poorly compliant with WHO quality standards. No significant improvements were observed compared with previous assessments. The observed weaknesses can have a direct impact on supplied medicines, which can be of poor quality from the start, or deteriorate because of poor practices along the supply chain. To protect patients in LMICs, it is essential to urgently implement a comprehensive and stringent regulatory oversight. In addition, the WHO MQAS and GDP-standards and tools should be incorporated in national pharmaceutical regulations. The availability of reliable information on distributors' quality system, with a cross-cut information on manufacturers sites performance and products quality, would also be of great help—even more nowadays, as the COVID-19 crisis has magnified challenges in pharmaceutical supply and QA. Hence, developing tools which monitor the pharmaceutical supply chain while taking into consideration the economic variables would be an asset for researchers and policy-makers who wish to understand and anticipate pharmaceutical market trends, working towards UHC.

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Acknowledgements The authors thank all the representatives of procurement agencies and pharmaceutical distributors who accepted to be audited by QUAMED;

and all QUAMED auditors who conducted the audits. We also thank Tom Smekens for his comments and inputs on the revised version of the manuscript.

Contributors Wrote the protocol: ANG, AB and RR, with inputs from GW, CP, PT and KVA. Data extraction: AB. Data analysis: AB and ANG, with inputs of RR. Wrote the paper: ANG, AB and RR. Reviewed the paper: RR, AB, GW, CP, PT and KVA.

Funding This study was funded by the Belgian Directorate-General for Development Cooperation (DGD) through the Framework Agreement 4, 2017–2021 with the Institute of Tropical Medicines, Antwerp, Belgium.

Competing interests RR is the Chairperson of the Institutional Review Board of the Institute of Tropical Medicine Antwerp, Belgium, which reviewed and approved the study protocol. However, she did not participate in this review, which was coordinated by the vice chair.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval This study is conducted under a research collaboration between QUAMED and the Institute of Tropical Medicine in Antwerp (ITM). The protocol was approved on 22 October 2019 by the ITM Institutional Review Board (IRB Ref. 1339/19).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on request. Motivated request to access identifiable data by country should be addressed to the corresponding author.

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