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ORIGINAL ARTICLE

The integrity of the antimicrobial supply chain in Bangladesh: assessing the regulatory environment and contextual challenges

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Abstract

Most low- and middle-income countries lack the regulatory capacity to contain substandard and falsified (SF) medicines. Innovations for strengthening regulatory systems are needed to protect public health. We assessed the integrity of the antimicrobial supply chain in Bangladesh. We employed qualitative methods comprising policy content analysis, and literature and database reviews. Using a framework modified from the World Health Organization's and the United States Pharmacopoeia's, the Bangladesh National Drug Policy (BNDP), was evaluated for provisions on medicines quality assurance mechanisms. We used newspaper, peer-reviewed, and post-marketing surveillance reports to assess prevalence of SF antimicrobials. The BNDP contains provisions for quality assurance. Newspaper reports identified circulation of substandard antimicrobials. We identified only six peer-review studies testing antimicrobial product quality with three studies reporting out-of-specifications products. We suggest three strategies for strengthening the regulatory system: community-based surveillance, task shifting, and technology-enabled consumer participation.

Keywords Antimicrobials · Supply chain · Regulation · Medicines quality

Key messages

- Regulatory capacity challenges in low- and middle-income countries (LMICs) constrain effective control of the supply chain against the entry and spread of substandard and falsified medicines.

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- Innovations such as community-based surveillance, task shifting, and technology-enabled consumer participation could support national regulatory systems strengthening in LMICS.

Introduction

Maintaining the integrity of the pharmaceutical supply chain to prevent the entry of poor-quality medicines continues to be a regulatory challenge for many countries. In 1995, a report of fatal diethylene glycol poisoning following the administration of contaminated paracetamol syrup to children emerged from Bangladesh [1]. This case echoed similar incidents in the late 1930s in the United States, contemporaneously in Nigeria, and subsequently in other countries, most recently in February 2020 in India [2–6]. In 2017, the World Health Organization (WHO) estimated the global prevalence of Substandard and Falsified (SF) medicines at 10.5% based on data from mostly Low- and Middle-Income Countries (LMICs). In April 2020, supply chain disruptions induced by the recent COVID-19 pandemic led to a rise in the incidence of falsified chloroquine, one of the medicines *that was regarded as having putative efficacy* against SARS-Cov2, in the World Health Organization (WHO) regions of Africa and Europe. These examples illustrate the persistence and prevalence of the challenge to pharmaceutical supply chain integrity, especially in LMICs, and the need for effective, proactive, and continuous regulatory oversight to protect public health. For LMICs with capacity constraints, there is need for innovative approaches to strengthen regulatory systems.

The WHO defines poor-quality medicines as those that are substandard and falsified (SF). A substandard medicine is one that is out of specification, or fails to meet quality checks, while a falsified medicine is one that deliberately misleads as to content, or manufacturer [7]. The impact of poor-quality medicines extend beyond the individual to health systems and economies [8]. Poor-quality antimicrobials contribute to antimicrobial resistance (AMR) with transnational impact, *for instance, excess childhood mortality from pneumonia and malaria arising from the use of SF antimicrobials*, reinforcing the need for stringent regulatory controls to ensure product integrity in the supply chain [9, 10].

In most countries, the duty of ensuring the quality of medicines in the supply chain rests with the national medicines regulatory authority (NMRA), a public body with the technical and constitutional authority to provide oversight. However, most LMICs have limited regulatory capacity to perform all the functions necessary to protect the medicine supply chain against the entry of SF medicines [11]. Current approaches to strengthening regulatory systems focus on improving capacity at the NMRA. The persistence of the problem of SF medicines in LMICs calls for further innovations in regulatory medicines quality assurance.

The aim of this study, as part of a broader *Boston University's Social Innovation on Drug Resistance program*, was to assess the integrity of the antimicrobial supply chain in Bangladesh to understand the regulatory environment and contextual challenges. Understanding local contexts including the prevalence of SF medicines and gaps in regulatory approaches is important to any initiative to address these

challenges [12]. While the WHO report gives a global prevalence of SF medicines, there are scant reports from many WHO geographical regions, including the WHO Southeast Asian region. Bangladesh, located in the WHO Southeast, has a large human and animal population. We purposively and conveniently selected it as a model as part of a broader project examining antimicrobial resistance and medicines quality. The objectives were to evaluate the regulatory policies, and other mechanisms, for assuring the quality of antimicrobials in Bangladesh, and identify any reports or publications on the prevalence of SF medicines.

Methods

We used qualitative methods—document, literature, and database reviews—to assess regulatory policies and any quality issues in the antimicrobial supply chain in Bangladesh. We performed a document review by searching the website of the NMRA, the Directorate General of Drug Administration (DGDA), for policies and regulations governing the pharmaceutical supply chain in March 2020 [13].

To evaluate the policy, we modified the regulatory functions frameworks of the WHO and the United States Pharmacopoeia, USP [14, 15] to construct a framework covering pre-marketing authorization to post-marketing surveillance mechanisms for oversight of the five tiers of the pharmaceutical supply chain (Table 1). This framework grouped regulatory mechanisms into four: current Good Manufacturing Practice (cGMP); Good Distribution Practice (GDP); Good Pharmacy Practice (GPP) guidelines; and Pharmacovigilance. The four mechanisms comprised 10 functions. We identified and described the relevant sections of the policy document corresponding to these grouped functions. We also noted and described any other quality assurance mechanism specific for antimicrobials identified from the authors' practice experience or knowledge.

To assess market surveillance and quality issues and to map reports and publications on SF medicines and market surveillance activities, we conducted a combined literature and database review as follows:

1. *Literature review for reports on SF medicines* To identify media reports of SF medicines in circulation, or supply chain/market surveillance, or both, we performed a literature search for gray literature (non-peer-reviewed newspaper reports) for the period 2017–2020. We conducted the literature search twice, in December 2018 and April 2020. We describe the search strategy and data extracted in the Supplemental Material.
2. *Publications on quality testing* We reviewed published literature on *Banglajol* (an online service providing access to Bangladeshi Journals), EMBASE, and Google Scholar to identify reports of quality evaluations of antimicrobials in circulation in Bangladesh. We did so on 18–19 May 2020, as detailed in the Supplemental Material.
3. *Database reviews for post-marketing surveillance reports* We searched three databases—the United States Pharmacopoeia, USP, Medicine Quality Database

Table 1 Framework for assessing the regulatory policy document of Bangladesh as adapted from WHO and USP, grouping 10 regulatory functions under four regulatory mechanisms covering all supply chain elements [14, 15]

Supply chain element(s)	Regulatory mechanism	Regulatory functions
Manufacturers and importers	Current Good Manufacturing Practice (cGMP) requirements	(i) marketing authorization or registration, including labeling requirements
		(ii) licensing
		(iii) inspection
		(iv) quality control
		(v) clinical trials and generics equivalency tests
		(vi) compliance
Distributors	Good Distribution Practices (GDP)	(vii) GDP
Demand points	Good Pharmacy Practice (GPP) guidelines for appropriate use	(viii) Prescription only sales of antibiotics (Pharmacies and medicine outlets) & Standard Treatment Guidelines (Hospitals, and other healthcare facilities)
		(ix) Licensing of persons (competency to own medicine outlets) as well of the premise
All	Pharmacovigilance and market surveillance	(x) Market surveillance activities

These regulatory functions are not intended to suggest the full complement of regulatory activities of any NMRA. For example, we did not evaluate provisions for control of advertising/promotion. However, they encompass the five main functions performed by NMRA as listed by the WHO, including marketing authorization, licensing, inspection, quality control and pharmacovigilance; as well as seven out of eight key functions as listed by the USP [14, 15]

(MQDB) [16], the Oxford's Infectious Disease Data Observatory's Medicine Quality Monitoring Globe database (MQMG) [17], and the DGDA database [18]—for any records of quality issues with antimicrobials marketed in Bangladesh. We conducted these searches in May 2020. For the first two databases, we used "Bangladesh" as a key word and noted any report of a poor-quality medicine. For the DGDA database, we retrieved reports of any post-marketing surveillance.

Results

These results provide a composite view of the regulatory environment (policies and post-marketing surveillance) and media and peer-reviewed reports and publications, respectively, on the quality of antimicrobials in the pharmaceutical supply chain in Bangladesh.

Policies

We identified four documents presenting government's policies for ensuring medicine quality in Bangladesh: Drug (Control) Ordinance 1982, The Drug (Control) (Amendment) Ordinance 1984, Drug Control Ordinance 2006 and National Drug Policy 2016 [13]. The National Drug Policy 2016 (NDP) is the current document guiding quality assurance throughout the supply chain, and builds upon previous versions from 1982, the first in independent Bangladesh. It codifies both the protectionism—the deliberate policy of protecting domestic industries from foreign competition—and supply chain medicines quality assurance mechanisms for Active Pharmaceutical Ingredients (API) and Finished Pharmaceutical Products (FPP) for use in human and animal health in Bangladesh. The NDP 2016 aligns with the National Health Policy of 2011. It recognizes poor-quality medicines as those that are: fake, adulterated, expired, unregistered, counterfeit, misbranded, smuggled, and substandard.

We identified 10 mechanisms for quality assurance of medicines in Bangladesh in the NDP covering all four pre-defined areas and a new provision for environmental protection against antimicrobial run-offs from manufacturing plants (Table 2).

Media reports

Of 200 reports listed in *The Daily Star* newspaper of Bangladesh, 27 met the inclusion criteria. Of these, 12 reports focused on SF medicines. In three of these, the authors mentioned antimicrobials; we evaluated these (Table 3). Two of the reports evaluated concerned falsified antibiotics seized at private facilities after which authorities arrested or fined the perpetuators, or both [19, 20]. In one case authorities identified as many as seven different falsified antibiotics: most (57%, 4/7) were cephalosporins [20]. The third report addressed an expired anthelmintic distributed to a public facility.

Table 2 Policy provision of selected relevant regulatory mechanisms for the five tiers or elements in the antimicrobial/medicines supply chain

Tier	Mechanism(s)	Policy provision for medicine quality assurance in the National Drug Policy, 2016[a]
Primary manufacturer (API) Secondary manufacturer (FPP)	cGMP, inspection of manufacturers, compliance with standards and regulatory reliance[1]	Registration only for competent manufacturers meeting WHO GMP guidelines. Imports (only for certain medicines) need to comply with registration requirements of the USA, UK, Germany, France, Switzerland, Japan, and Australia for human medicines; and, in addition to these countries, the EU, Canada, South Korea and Singapore for veterinary medicines. The policy authorizes inspection of manufacturing premises for compliance with GMP. APIs are expected to comply with relevant pharmacopeial standards
	Quality control laboratory for medicine testing	The establishment and use of medicine quality testing laboratories at the National and Divisional levels by the DGDA (the National Control Laboratories), as well as collaborations with the Bangladesh Council of Scientific and Industrial Research. Additionally, it recognizes other public, private, or autonomous research organizations as third-party quality evaluators (3.12)
	cGMP training	Continuous GMP training for both manufacturers and inspectors
	Clinical trials and generic equivalence	Creation of public and private sector clinical trials and bio-equivalence study facilities (3.19)
	Product labeling	GMP manufacturing and proper labeling of veterinary medicines to guide use & prevent misuse (4.26)
	Environmental protection[2]	Effluent Treatment Plants by all pharmaceutical manufacturers in addition to relocation to non-residential areas to prevent environmental pollution
	Audit	Self-audits by pharmaceutical manufacturers using DGDA prepared checklists
Wholesale Distributor Local Distributor	GDP	Formulation of a Good Distribution Practices guideline by the DGDA (4.8c)

Table 2 (continued)

Tier	Mechanism(s)	Policy provision for medicine quality assurance in the National Drug Policy, 2016[a]
Demand point	GPP[3]: Prescription only sale of antimicrobials	Prohibition of sale and distribution of drugs without prescription from registered physicians/veterinaries, except for OTC drugs (3.14; 4.3 g; 4.18). The OTC list contains only three antimicrobials: two antihelminth (albendazole, mebendazole) and one antibiotic (metronidazole)
	GPP: Supervision under competent persons	Drug sale and distribution to be under the direct supervision of professional pharmacists (4.3d)
		Pharmacies to be operated only under the supervision of registered physicians or pharmacists; and for all other distribution points including private drug storage facilities and hospital pharmacies to be under the supervision of pharmacists registered by the Bangladesh Pharmacy Council (4.8e)
	GPP: Formularies, Standard Treatment Guidelines & Drugs and Therapeutic Committees for rational use	Formularies, which should be publicly available, both nationally and individually at all hospitals, to guide rational use, as well as operationalization of "Hospital Pharmacies" under the direct supervision of hospital pharmacists (4.3b&d)
		Mandating public and private hospitals with ≥ 100 beds to have an antibiotic use guideline; to be followed by similar guidelines for all types of hospitals (4.3b)
		"Drugs and Therapeutic committee to be formed in all public and private hospitals to ensure rational use of drugs including antibiotics"
All tiers	Pharmacovigilance	Pharmacovigilance at demand points, drug manufacturers, drug marketing organizations, and patients (4.13)

[a]Numbers in parentheses are the exact sections of the BNDP

[1]Regulatory reliance is a mechanism whereby one national MRA accepts products licensed in countries with stringent MRAS without the requirement for additional product registration in-country

[2]Not an integral function of MRAs. However, this mechanism is informed by AMR containment strategies

[3]Good Pharmacy Practices (GPP) considered together as one distinct mechanism

Table 3 Newspaper reports of SF antimicrobials

Date	Title of report (Ref.)	Facility	Location	SF category	Source	Therapeutic category	Use
1/2/2016	Date expired medicine in community clinics [68]	Community clinics	Sadar Upazilla, Nilphamari	Expired	Public	Anthelmintic	Human
9/11/2014	Fake medicine factories busted [19]	Factory, warehouses Factory	Amir Market, Mitford, Dhaka Kushiarbagh, Keraniganj	Spurious, fake	N/A	Antibiotics and others	N/A
7/10/2014	Fake medicine factory busted [20]	Factory	Topkhana, Dhaka	Spurious, fake	Supplier to Mitford	Antibiotics	N/A

N/A not stated

Reports on medicine quality

The search on Google Scholar identified six studies on quality evaluation of antibiotics marketed in Bangladesh (Table 4). The EMBASE search retrieved three studies already in the Google Scholar search results. We found no new relevant publications via *Banglajol*. Overall, the six studies tested between 1 and 6 different antibiotics from different manufacturers; the smallest study tested 3 different generics and the largest 39. Studies with larger samples found more out-of-specification results. Faruque et al. tested 39 samples from different manufacturers of six antibiotics—cefixime, cephradine, ciprofloxacin, metronidazole, amoxicillin, and azithromycin—and found all six to be substandard or falsified, with lower than the specified potency, or allowed percentage API content for all samples of five of these antibiotics—cefixime, cephradine, ciprofloxacin, metronidazole, and amoxicillin, and for all but samples from one manufacturer of azithromycin [21]. This study also suggests that SF medicines may be more prevalent in rural areas [21]. Uddin found that 40% (4/10) of different ciprofloxacin brands tested did not meet the dissolution specifications in the USP (or 60%, when evaluated by the British Pharmacopeia, BP) [22]. In the study by Islam et al., half (50%, 3/6) of the six different brands of antibiotics failed assay or dissolution, or both [23].

Ciprofloxacin was the most commonly (67%, 4/6) evaluated antibiotic in all six studies. Three of these studies found the ciprofloxacin samples to be substandard with out-of-specification dissolution profiles.

Islam et al. investigated the link between AMR and SF medicine as one arm of a three-part study investigating resistance of selected bacteria to commonly used antibiotics and compliance [23]. Even though half the samples failed one of the two tests for quality, the authors commented that products were generally of sufficient quality and that AMR should not be attributed to SF antimicrobials, but to the low rates (18%, $n = 300$) of patients' compliance [23].

Post-marketing surveillance

As of the time of this study, neither the MQDB nor MQMG held records of any poor-quality antimicrobial from Bangladesh, apart from a WHO Alert on falsified oral cholera vaccine circulating in Bangladesh on MQMG. We found no reports from the DGDA's website for the study period. In 2011, Bangladesh reported a failure rate of 0.04% of medicines assessed for quality as part of its pharmacovigilance activities [24].

Discussion

We reviewed regulatory medicines quality assurance policies, media, and post-marketing surveillance reports as well as antimicrobial quality studies in Bangladesh to improve understanding of the local context and to suggest approaches to strengthening the regulatory system. This assessment of the integrity of the antimicrobial

Table 4 Reports of quality of antimicrobials in circulation in Bangladesh, 2017–2020

Study	Source of samples	Brand information (Name and manufacturer)	Name of antibiotic	Dosage form	Number of samples (generic brands)	Samples meeting specifications (%)		Qualitative comments by authors
						Assay	Dissolution	
Islam et al. [23]	Various locations across Bangladesh	Anonymized	Azithromycin	Tablet	6	100	100 (4/4)	Product quality satisfactory; AMR should not be attributed to SF antimicrobials
			Ciprofloxacin	Tablet	6	83	83	
			Amoxicillin	Tablet	4	100	100	
			Cefixime	Tablet	7	86	83 (5/6)	
			Cefuroxime	Tablet	5	100	83	
			Moxifloxacin	Tablet	4	25	100	
Rahman-Mizanur et al. [69]	Retail pharmacies, Dhaka	No	Ciprofloxacin	Tablet	5	100	100	Products of quality
Faruque et al. [21]	Rural areas of different *Upazillas* of Dhaka, Jamalpur, Faridpur, Magura, Pirojpur, Barisal, Chandpur, Rangpur, Habiganj and Chittagong	Anonymized	Cefixime		7	Nil	N/A	Substandard drugs in circulation produced by some small and middle industries
			Cephradine		6	Nil		
			Ciprofloxacin		6	Nil		
			Metronidazole		7	Nil		
			Amoxicillin		6	Nil		
			Azithromycin		7	43%		
Hasin et al. [70]	Drug store, Dhaka	Anonymized	Cefuroxime axetil	Tablet	3	100	100	Pharmaceutically and physiologically equivalent
Noor et al. [71]	Drug stores, Dhaka	Anonymized	Metronidazole	Tablet	9	100	100	Almost all brands were of quality
Uddin et al. [22]	Retail pharmacies, Dhaka	Yes	Ciprofloxacin	Tablet	10	100	40 (BP); 60 (USP)	The need to focus on quality, rather than marketing

BP British Pharmacopoeia, *USP* United States Pharmacopoeia, *N/A* not assessed, *SF* Substandard and Falsified, *AMR* Antimicrobial Resistance

supply chain in Bangladesh highlights the existence of regulations but a substantial gap in knowledge about the extent of SF antimicrobials. It also highlights innovations and existing structures that could be leveraged to improve regulatory oversight in Bangladesh.

Policy provisions, enforcement, and regulatory capacity challenges

This analysis shows that all iterations of the Bangladesh NDP recognize the need to ensure medicines quality throughout the supply chain and emphasize the need for manufacturers to fully comply with the WHO GMP guidelines. This is consistent with other countries that have incorporated WHO GMP guidelines in their quality assurance mechanisms [25]. In addition to specifying quality considerations for manufacturers, the NDP also includes GDP guidelines for storage conditions in pharmacies.

In enforcing the medicines policies and laws, Bangladesh leverages other players including security and justice personnel. There is a standing Rapid Action Battalion (RAB) composed of DGDA personnel and security operatives assisted by a legislative vehicle, the Mobile Court, to ensure implementation of regulations and to impose summary penalties, and conduct post-marketing surveillance; Nigeria's arrangements are similar [26, 27].

However, regulatory capacity challenges persist. Overall, regulatory staff strength remains limited—3,700 staff oversee a supply chain with some estimated 200,000 distribution points and a product register of some 50,000 generics [28]. In 2020, the DGDA maintained offices in only 47 of the 64 districts of Bangladesh, indicative of structural challenges [18, 29]. These challenges are similar for other LMICs, including the world's largest generics manufacturer, India [30, 31].

Market surveillance and medicine quality issues

Bangladesh, in addition to meeting 98% of its pharmaceutical needs, exports medicines to more than a hundred countries [32, 33]. A newspaper report in the Business Standard of Bangladesh in February 2020 estimated that Bangladesh's pharmaceutical exports would cross the $1 billion mark in the next 2 years [34]. In May 2020, the country produced its own generic remdesivir (which had just been licensed by the United States Food and Drug Administration a month earlier as a treatment for COVID-19 cases in patients) in a demonstration of its pharmaceutical manufacturing capacity [35].

Our analysis suggests some challenges with the antimicrobial supply chain in Bangladesh for the study period 2017–2020. Ever since the first report of poor-quality medicine in the 1980s of contaminated paracetamol, newspapers reported repeated actions by RAB involving SF medicines—mostly falsified products or expired drugs [36–44].

Laboratory studies we identified from our literature review investigating the quality of antibiotics in circulation in Bangladesh and exploring the impact, or implications, complement reports we found in the mass media. The findings are troubling

considering that the evaluated antibiotics are among the top 10 most common licensed in Bangladesh [45].

Despite variability in choice of official reference—BP/USP—and methodological challenges with sample sizes, reporting styles, and authors' perceptions or views of the implications of study findings, these studies point to the presence of SF antibiotics in the supply chain.

Although mass media and medicine quality studies suggest the persistence of SF medicines for human use, the extent of the challenge is not fully understood. In a report from 2011, Bangladesh reported a low SF prevalence of $<1\%$. However, in 2019, the Consumer Protection Agency (CPA) survey estimated a high prevalence of expired medicines in pharmacies and medicine outlets in Bangladesh at 90% ($n=600$) [46].

Developments, knowledge and implementation gaps, and suggestions for regulatory strengthening

These quality issues, which persist in the presence of technically appropriate policies, are syndromic of low regulatory capacity and call for improvements in regulatory systems. We see evidence that improvements are in process, for instance in technical analytical capacity, but more is needed. In March 2020, the National Control Laboratory of the DGDA received WHO accreditation, two years after it attained the ISO/IEC 17025:2017 accreditation for laboratory testing and calibration [47]. The USP Pre-Qualification of Medicines (PQM) program provided assistance to the NMRA to build capacity for the quality assurance of medicines manufactured and distributed in Bangladesh [48]. In 2019, the DGDA received six Mini-Labs™, portable medicines quality testing devices capable of semi-quantitative analysis, for rapid screening of medicines quality during post-marketing surveillance activities [49]. There remain other capacity challenges to medicines quality assurance of antimicrobials for human and veterinary use, apart from infrastructure, including human resources [29, 50].

There is also the need for a comprehensive evidence base on the prevalence and spatial distribution of SF antimicrobials to target and guide effective regulatory actions using this limited regulatory force. The government, or development partners, could commission a nation-wide quality audit of selected, most consumed or marketed antimicrobials available for sale to the public. This would help authorities to identify possible hot-spots for the manufacture, entry, distribution, or sale of SF antimicrobials for a risk-based approach to medicines quality assurance.

Bangladesh could address existing policy implementation gaps and further strengthen the integrity of the antibiotic supply chain with three approaches.

- First, Bangladesh could use existing community-based structures as tools for strengthening medicines quality assurance. There are NGOs advocating for stricter actions on SF medicines, signifying public awareness and concern. The Organization of Social and Environment Changes (OSEC) instituted a suit against the government in 2015 at the High Court in which it questioned gov-

ernment's apparent inaction to control the production of counterfeit medicines [51]. The government can leverage these organizations to help with inspections of demand points—places where consumers obtain medicines, such as pharmacies and hospitals—especially in hard-to-reach rural areas where SF medicines tend to proliferate. To standardize this approach, these NGOs could use a checklist created by the DGDA. Such a checklist could rely on visual analysis by package inspection for product licensing status and expiry date. The effectiveness of similar visual analysis checklists have been demonstrated in the Democratic Republic of Congo [52, 53]. The DGDA could use data from the quality checklists collated by these NGOs to further help create community awareness on SF medicines. There is evidence of reproductive health and TB management interventions that have led to improved health outcomes through the use of community-based approaches [54, 55]. The evidence supporting both the community-based approach for improving health outcomes in Bangladesh and the use of visual checklist for containing SF medicines in Congo suggest that these two approaches could be combined for an innovative regulatory system strengthening in LMICs. Thus, it could be useful to explore the use of NGOs and other social organizations that have shown interest in medicines quality in Bangladesh, such as the OSEC, equipped with the innovative visual checklists for objective data collection by the DGDA, as one innovative strategy for improving pharmacovigilance and regulatory inspections to check the spread of SF antimicrobial medicines.

- Second, efforts to expand capacity might include task shifting; that is, asking academic institutions to perform regular surveys on behalf of the DGDA. To strengthen output measures among several different research institutions, Bangladesh, and similar LMICs, could adopt the WHO Guidelines on the conduct of Medicine Quality Assurance Survey for uniformity in methodology and reporting [56]. LMICs with capacity challenges could mandate such independent analysts to share findings with the NMRA to promote synergies for improving the integrity of the supply chain. Although the Bangladesh NDP mentions the use of third-party medicines quality assessors, we found no information about the extent to which the Bangladesh government uses such third parties to complement efforts by the DGDA. Task shifting has been used widely to address workforce capacity challenges in the health sector in many countries, including in high-income settings [57]. It might also be useful to extend pharmacovigilance into the veterinary sector; veterinarians and para veterinarians could flag any suspected poor-quality veterinary medicines for follow-up action by the DGDA. Another approach to building capacity might be for the country to establish a separate veterinary medicines agency; Ethiopia made progress in this way [58].
- Third, scaling up existing technology platforms could lead to synergistic increases in overall regulatory capacity. In 2019, as an extension of the national pharmacovigilance system, the DGDA launched a mobile Drug Verification application for direct (voluntary) reporting by the public of adverse drug reactions, including of suspected counterfeit medicines [59, 60]. The government of Bangladesh, by mandating all antibiotic manufacturers to include Mobile Authentication Service (MAS) codes on antibiotic packs, would complement its

initiative to enforce the sale of antibiotics only in packages, among others, as a means of promoting appropriate use. This track and trace approach is in use in different forms in countries such as the United Arab Emirates, Turkey, India and in the region covered by the European Union [61–66]. Bangladesh, under an innovative intervention to increase access to government programs and information through the Aspire to Innovate (a2i) project, is leveraging information technology and >80% mobile phone ownership in its population to provide services to its citizens. Track and trace technologies already exist in its substantial fisheries and aquatic livestock sector [67]. Thus, leveraging a combination of end-user participation and technology could be another approach to improving supply chain integrity.

Conclusions

This study found evidence of regulation and regulatory actions against poor-quality, or substandard and falsified antimicrobials, and news reports and peer-reviewed studies on poor-quality antimicrobials; it did not find any current rigorous assessment of the extent of poor-quality antimicrobials. We suggest strengthening the regulatory system using three strategies: community-based surveillance, task shifting, and technology-enabled consumer participation. These approaches could expand capacity to provide a more robust surveillance of the antimicrobial supply chain.

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Declarations

Competing interests The authors declare that they have no competing interests.

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