



Countering the Problem of Falsified and Substandard Drugs

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Summary

The adulteration and fraudulent manufacture of medicines¹ is an old problem, vastly aggravated by modern manufacturing and trade. In the last decade, impotent antimicrobial drugs have compromised the treatment of many deadly diseases in poor countries. More recently, negligent production at a Massachusetts compounding pharmacy sickened hundreds of Americans. While the national drugs regulatory authority (hereafter, the regulatory authority) is responsible for the safety of a country's drug supply, no single country can entirely guarantee this today. Illegitimate² drugs are an international problem, and there is wide consensus that action depends on international cooperation.

Productive international discourse has been stymied, however, by disagreement about how to frame the problem. The once common use of the term *counterfeit* to describe any drug that is not what it claims to be is at the heart of the argument. In a narrow, legal sense, a counterfeit drug is one that infringes on a registered trademark. The lay meaning is much broader, including any drug made with intentional deceit. Some generic drug companies and civil society groups object to calling bad medicines counterfeit, seeing it as the deliberate conflation of public health and intellectual property concerns. This report accepts the narrow meaning of counterfeit, and, because the nuances of trademark infringement must be

¹ The terms *medicine*, *drug*, and *pharmaceutical* are used interchangeably in this report in accordance with the definitions listed in the *American Heritage Stedman's Medical Dictionary*.

² *Illegitimate*, as explained later in the report, is a parent category for falsified and substandard medicines.

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dealt with by courts, case by case, the report does not discuss the problem of counterfeit medicines.

The trade in illegitimate drugs is, however, a problem of public health consequence and the topic of this report. In order to discuss this problem more precisely, the report distinguishes two main categories of poor-quality drugs. First, there are substandard drugs, those that do not meet the specifications given in the accepted pharmacopeia or in the manufacturer's dossier. The other main category of illegitimate products is falsified drugs, those that carry a false representation of identity or source or both. Many countries also have problems with unregistered medicines, those not granted market authorization in a country. Unregistered drugs may be of good quality, though some research indicates they often are not. Unregistered medicines usually circulate outside the controlled distribution chain and are therefore suspect.

The drug failures of public health concern can be divided into two main categories: falsified and substandard. Admittedly, the distinction between the two categories is not always clear. Falsified drugs are usually also substandard; national specifications referenced in the definition of a substandard drug can vary.³ However, these terms cover the two main divisions of interest with sufficient precision. International endorsement of these two categories could advance public discourse on the topic.

Recommendation 1-1: The World Health Assembly should adopt definitions consistent with the following principles. Substandard drugs do not meet national specifications.⁴ Falsified products have a false representation of identity or source or both. Products unregistered with the regulatory authority are also illegal.

The spirit of these definitions and the exclusion of the term counterfeit are central to this recommendation. The exact wording suggested is not.

THE HEALTH EFFECTS OF FALSIFIED AND SUBSTANDARD DRUGS

Falsified and substandard drugs may contain toxic ingredients; some of the most compelling stories of pharmaceutical crime are of frank poisoning. By far the more common problem, however, is medicine that simply does

³ Some regulatory authorities may accept standards below those in international pharmacopeias. In such cases, a drug that would be generally regarded as substandard might be technically acceptable in a given country.

⁴ An emphasis on quality system failures is not essential to the idea of a substandard drug and was removed from the recommendation after the report release. The supporting text describes the committee's understanding of a substandard drug.

SUMMARY

not work. Poor-quality medicines cause treatment failure, but doctors do not generally suspect medicines as a cause of disease progression. Lifesaving medicines can be of poor quality, which may be an uncounted root cause of high mortality in low- and middle-income countries.

No class of drug is immune to being compromised. Medications for chronic and infectious diseases alike have been found falsified and substandard. A considerable body of research indicates that inexpensive antimicrobial drugs in low- and middle-income countries are frequently of poor quality. Such drugs not only put patients at risk but also encourage drug resistance, thereby threatening population health for future generations.

Substandard antimicrobials often contain low and erratic drug doses, while falsified ones can be diluted. In either case, exposing pathogens to subtherapeutic doses of medicines selectively allows the growth of resistant organisms. Poor-quality drugs have contributed to the rise of drug-resistant tuberculosis. Drug-resistant staphylococcus infections are an emerging problem, especially in India, Latin America, and sub-Saharan Africa. Antimalarial resistance threatens to undo the good that artemisinin therapies have done, threatening global malarial control programs.

THE ECONOMIC AND SOCIAL EFFECTS OF SUBSTANDARD AND FALSIFIED MEDICINES

Falsified and substandard drugs increase costs to patients and health systems. Medicines are expensive; patients and governments waste money on ineffective ones. Lingering illnesses decrease productivity, causing workers to forgo pay and spend more on treatment. Through encouraging antimicrobial resistance, illegitimate medicines reduce the effective life of a drug. Society must bear the cost of drug development, an expense that increases as drugs become more complex.

Substandard and falsified medicines undermine confidence in the health system and in all public institutions. Fake⁵ drugs are often the business of criminal cartels. Their sale finances other crimes, buys weapons and ammunition, and conveys power to corrupt officials. Victims of falsified and substandard drugs usually do not even know they are victims and are therefore deprived of their right to redress. In many ways, the trade in illegitimate pharmaceuticals further erodes the already weak political infrastructure that allows them to circulate, part of a vicious cycle of poverty and crime.

⁵ As the report explains later, *fake* is a commonly used synonym for *falsified*.

THE MAGNITUDE OF THE PROBLEM

It is difficult to measure the population burden of falsified and substandard drugs. Governments and industry monitor problems with drug quality, but this information is not usually public. The Pharmaceutical Security Institute, a network of the security divisions of 25 major pharmaceutical companies, has data that indicate that the illegal trade and manufacture of medicines is a global problem. It affected at least 124 countries in 2011, and the burden is disproportionately felt in the developing world.

Data from the U.S. Food and Drug Administration (FDA) Office of Criminal Investigations indicate that pills and tablets are the most commonly compromised products they investigate, mostly produced by individual criminals, not negligent businesses. Interpol, an international organization that facilitates police cooperation, has conducted 11 operations against illicit medicines since 2008. Police working in Interpol raids have confiscated tons of suspect products, leading to hundreds of investigations and arrests.

Much of the scientific literature about drug quality is in case studies: reports from clinicians who uncover substandard or falsified drugs in their routine work. This kind of report provides context on how and when different kinds of drugs are compromised; it can also trigger epidemiological investigation. Nonprobability or convenience samples are by far the most commonly used method to study drug quality. Such studies indicate serious problems with antibiotics in poor countries and antimalarial drugs in sub-Saharan Africa and Southeast Asia.

The best estimate of the burden of illegitimate drugs comes from systematic random samples, collected by patient actors from a representative cross section of drug sellers. Such studies are logistically complicated and few. More research in accordance with the recent guidelines on medicine quality assessment reporting would advance understanding and monitoring of the problem.

Lack of clarity regarding the magnitude of the falsified and substandard medicines market holds back coordinated international action. The World Health Organization (WHO) is developing a system for the global surveillance and monitoring of falsified and substandard drugs. Consistent use of this system, eventually linking it to national pharmacovigilance systems, would advance international action and give a more nuanced understanding of the type of falsified, substandard, and unregistered medicines in circulation and the extent of the trade.

Recommendation 3-1: Governments should establish or strengthen systems to detect substandard, falsified, and unregistered medicines. This surveillance should be integrated with established public health

surveillance systems. Analysis and reporting should precisely describe the product's quality, packing, and registration.

CAUSES OF SUBSTANDARD DRUGS

The factors that encourage the proliferation of falsified and substandard drugs are different but overlapping. Failure to adhere to good manufacturing practices is the root cause of substandard drugs. Quality-control processes and verification add expense to manufacture, as does maintaining sterile water filtration and air handling systems. Proper quality control includes dealing only with quality-assured suppliers, but small- and medium-sized manufacturers often neglect supplier quality because of logistical obstacles and cost.

Multinational companies, both innovator and generic, operate on a scale that allows them to recoup the costs of running high-quality factories. Initial capital investments and infrastructure problems stand between quality medicines and many small- and medium-sized medicine manufacturers. Small- and medium-sized firms and companies in Africa have a difficult time securing business improvement loans. The only capital available to these companies is their profits, and reinvesting profits is not a quick or reliable path to building a modern manufacturing infrastructure. The companies need hard currency loans, which their national banks cannot supply.

The International Finance Corporation and the Overseas Private Investment Corporation can work to encourage better private sector pharmaceutical manufacturing in developing countries. With the initial investments made, governments can take on the more manageable role of encouraging partnerships with foreign manufacturers.

Recommendation 4-1: The International Finance Corporation and the Overseas Private Investment Corporation should create separate investment vehicles for pharmaceutical manufacturers who want to upgrade to international standards. Governments can complement this effort by encouraging partnerships between local and foreign manufacturers.

In practice, it is difficult to distinguish the quality failures that are to blame on a manufacturer's inability to meet international best practices from those that come from a decision to cut corners and produce inferior products for poorly regulated markets. When a producer capable of meeting international standards fails to do so consistently and only in product lines sold to the poor, one may conclude that noncompliance is part of a more insidious system.

Rich countries enforce high quality standards for medicines, and manufacturers recognize the need to use quality ingredients and good manufac-

turing practices to sell in these markets. United Nations agencies and larger international aid organizations will also refuse to do business with companies that cannot meet stringent regulatory authority quality standards. Manufacturers are aware, however, that low- and middle-income countries are less likely to enforce these standards. When a manufacturer produces medicines of inferior quality for less exacting markets it is known as tiered or parallel production.

When regulatory checks on production are inconsistent, good procurement practices can ensure that quality medicines get the largest market share. The firms that offer the cheapest prices do so by buying impure ingredients and cutting corners in formulation. Good procurement dictates that the cheapest tenders are not accepted if they are of dubious quality, but it is difficult not to be swayed by price. Proper precaution in medicines procurement can prevent poor-quality products from infiltrating the market. Good procurement puts a strong emphasis on controlling corruption and promoting transparency. The WHO's Model Quality Assurance System for procurement agencies lays out the steps necessary for efficient and open procurement of the best-quality medicines possible.

Recommendation 4-2: Procurement agencies should develop a plan, within the next 3 to 5 years, to comply with the World Health Organization's Model Quality Assurance System for procurement agencies and work to remove any barriers to compliance.

CAUSES OF FALSIFIED DRUGS

In practice, one difference between falsified and substandard medicines is that the drugs regulator, having the authority to license manufacturers and register medicines, can act against unscrupulous or careless manufacturers. There is no such remedy when the manufacturer is falsely represented. The regulator can only confirm that the producer is unknown and turn the case over to law enforcement. The police and detectives who inherit these cases have a difficult job gathering sufficient evidence for a prosecution there is usually little if anything to tie the falsified drug in the market to the culprit.

Criminals run lucrative businesses making and trafficking fake medicines, and these crimes are mostly opportunistic, emerging where regulatory systems are weakest. When criminals target the products of multinational, innovator pharmaceutical companies, the companies' security staff build evidence for a conviction. Police are also investigating more pharmaceutical crimes, but most police action is limited to brief raids. It is difficult for police to keep up momentum for sustained action on pharmaceutical crime, especially given the immediate pressure to investigate murders and other violent crimes.

CAUSES OF BOTH FALSIFIED AND SUBSTANDARD DRUGS

Much as poor-quality drugs are often both falsified and substandard, some potentiating factors encourage both kinds of problems. The high demand and erratic supply of drugs, weak regulatory systems, and uneven awareness contribute to the trade in both falsified and substandard drugs.

Medicines are what economists describe as an inelastic good; changes in the unit price of the medicine have proportionately little effect on the demand. Price inelasticity, combined with a high relative price, make medicines a major expense for patients around the world. The drug market is not stable; both price and supply fluctuate. Drug shortages drive up the price of medicines and push consumers to unregulated markets.

Reducing the costs and increasing the availability of medicines would help prevent drug scarcity. The WHO has recommended generic substitution as a way to keep medicine costs down, but this depends on a supply of quality generic medicines on the market. For generic manufacturers, companies that generally run on low margins, the costs of proving bioequivalence and preparing a manufacturer's dossier for regulatory review can be prohibitive to market entry. Different regulatory authorities have different, often widely divergent, requirements. To complicate the problem, many small regulatory authorities lack the technical depth to evaluate the bioequivalence data that generics manufacturers submit.

The high cost of market authorization impedes the development of a strong generics industry in poor countries. A more robust generic drug market could help prevent the drug shortages and price spikes that encourage the sale of poor-quality products. Regulatory authorities can work to better harmonize their procedures, thereby improving their own efficiency and reducing barriers to market entry for good-quality generics manufacturers. The use of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use Common Technical Document format for registration would ease the regulatory burden on generics companies. Regulators also reap a spillover benefit of more convergent regulatory systems without negotiating cumbersome mutual recognition agreements.

Recommendation 4-3: Regulatory authorities in low- and middle-income countries should use the International Conference on Harmonisation Common Technical Document format for product registration to better harmonize their procedures and reduce application costs for manufacturers. To the same end, they should also conduct joint inspections and use a common inspection report.

An influx of generic medicines will only reduce the circulation in falsified and substandard drugs when there is a system to assure consumers of medicines' quality. A functioning medicines regulatory authority is a necessary condition for a robust generic medicines market. Strengthening the drugs regulatory system, building the inspectorate, enforcing quality standards, and licensing in accordance with international standards are essential to improving drug quality. Without a competent regulatory authority to inspect wholesalers, distributors, and manufacturers, opportunities to corrupt the drug supply abound.

A strategy for compliance with international standards can help reduce redundant work and fragmentation. Both industry and regulators should agree to work toward the priorities identified in the strategic plan, an openly shared document.

Recommendation 4-4: Governments in low- and middle-income countries should support their regulatory agencies to develop strategic plans for compliance with international manufacturing and quality-control standards. In the least developed countries, international organizations should support their efforts.

Large pharmaceutical manufacturing nations such as India and China suffer from fragmented regulatory systems and an unclear division of responsibilities between state and national governments. The United States has similar problems, evidenced by the recent fungal meningitis outbreak brought on by a contaminated injectable steroid drug, compounded under unhygienic conditions at the New England Compounding Center. Lack of clarity about the relative authority of the FDA and state pharmacy councils to regulate compounding pharmacies contributed to the outbreak. Neither the state of Massachusetts nor the FDA had clear control over the New England Compounding Center. Confusion about their responsibilities created a regulatory gap. Similar confusion causes regulatory gaps in other countries where national and local governments share responsibilities for drug regulation.

During times of crisis, such as the meningitis outbreak, public interest in drug quality peaks, but it can be difficult to maintain. Patients in developed countries have long taken a safe drug supply for granted. They may not realize the risks of circumventing the regulated distribution system. In poor countries, patients are often more aware of the problem, but there are knowledge gaps, especially among the poorest and least educated. Effective communication campaigns can raise awareness of the problem and give consumers empowering messages on how to protect themselves. Such campaigns have effectively promoted change in rich and poor countries alike.

Recommendation 4-5: Governments and donor agencies should fund development of effective communication and training programs for consumers and health workers on understanding the quality and safety of medicines.

Targeted health worker education on falsified and substandard medicines would improve understanding of the problem around the world. This education should emphasize the correct reporting channels health workers can use to confirm suspected cases of bad drugs. Illegitimate drugs are a potential threat in all countries, though risk varies widely from country to country. An effective communication campaign should present accurate information in a way that empowers patients to protect their health.

THE DRUG DISTRIBUTION CHAIN

The modern pharmaceutical supply chain is complex. Medicines are made from ingredients sourced from different countries. Final formulations are then exported, and packaging, repackaging, and sale can happen in many other countries. Drugs change hands many times between the manufacturer and patient; every transaction is an opportunity for falsified and substandard products to infiltrate the market. Drug quality around the world could be improved with changes to the drug distribution system.

The systems differ markedly between developed and developing countries, however. Fewer, larger firms control manufacture and the wholesale drug markets in developed countries, where most patients get medicines from licensed pharmacies or dispensaries. In low- and middle-income countries, multiple parallel distribution systems of varying efficiency run in the same country. It is also difficult and expensive to transport medicines over poor roads to remote villages, as supply chain managers in poor countries must do.

The first step on the drug distribution chain is the wholesale market. There are two kinds of drug wholesalers: primary wholesalers who have written distribution contracts with manufacturers and buy directly from them, and secondary wholesalers who buy from other intermediaries. Both kinds of wholesalers buy and sell medicines to accommodate market demand. When they see that a medicine is scarce in one region, they can buy the same medicine from other wholesalers that may be flush with it. The markets are constantly fluctuating; products change hands many times. Wholesalers may repackage products repeatedly, and in the repackaging fake products can gain authentic labels.

In the United States, thousands of secondary wholesalers trade medicines, causing drug shortages and exploiting them for profit. Limiting the

secondary wholesale market to vetted firms would improve the U.S. drug supply. The National Association of Boards of Pharmacy (NABP) wholesaler accreditation process requires criminal background checks on senior staff and proof of professional standards in record keeping and drug storage and handling. Some states require NABP accreditation of wholesalers, but unscrupulous businesses can seek out states with lower standards for their headquarters. And, because the wholesale trade is national, weaknesses in one state's system can become vulnerabilities in another.

Recommendation 5-1: State licensing boards should only license wholesalers and distributors that meet the National Association of Boards of Pharmacy accreditation standards. The U.S. Food and Drug Administration, in collaboration with state licensing boards, should establish a public database to share information on suspended and revoked wholesale licenses.

Similar weaknesses plague the wholesale system in developing countries, and action in the American market might give regulators around the world example and encouragement to tighten controls on the chaotic wholesale market.

More stringent licensing requirements can improve the wholesale system, but drugs will still need to move from factory to the vendor, passing through many hands before reaching the patient. With every transaction on the chain, there is a risk of the drug supply being compromised. Criminals take advantage of places where the distribution chain breaks down and medicines depart from the documented chain of custody. Drugs that leave the proper distribution system are called diverted drugs; the markets that trade diverted drugs or, more generally, markets that trade with little authorized oversight are called gray markets.

Drug diversion is the means through which medicines approved for sale in one country are sold in others, where they may not be registered. Small thefts and large heists compromise the integrity of the drug distribution chain and confidence in the quality of medicines. In rich and poor countries alike, drugs often circulate outside of the main distribution channels without a drug pedigree, a record of a drug's every sale and owner.

Drug pedigrees depend on attaching some form of unique identifying numbers to products. Products that lack identification numbers, or products with identification numbers that cannot be accounted for throughout the distribution chain, must be treated as falsified and removed from the market even if they come from licensed manufacturers. Radio frequency identification, traditional and two-dimensional barcodes, and mobile verification are methods for serialization that can facilitate drug tracking.

Recommendation 5-2: Congress should authorize and fund the U.S. Food and Drug Administration (FDA) to establish a mandatory track-and-trace system. In the interim, the FDA should convene a working group of stakeholders, including the International Federation of Pharmaceutical Manufacturers and Associations and the Generic Pharmaceutical Association, to promote voluntary track-and-trace for all supply chain actors in accordance with existing guidance.

Tracking pharmaceuticals through the global distribution chain with unique serial numbers is a good defense against criminal infiltration. A method of tracking individual packages of medicines from the factory to the consumer could greatly reduce the chances of a dangerous product being sold at a reputable pharmacy. Problems will remain, however, with unlicensed drug shops. Medicines retail, the last leg of the drug distribution system, is often the most chaotic.

The drug distribution system becomes more disordered as the products leak out of regulated distribution chains. The risk increases as drugs move farther from manufacturer. Licensed pharmacies and dispensaries can control the quality of their stock, at least inasmuch as they can trust their wholesalers. There are no such efforts at quality control in the unlicensed market. Unlicensed vendors may approach medicines dispensing as any other sales job and not want a customer to leave without making a purchase. In general, these vendors exploit the chaos inherent to street markets and dry goods shops in low- and middle-income countries and online drug stores in middle- and high-income ones.

A simple lack of alternatives pushes consumers in developing countries to buy medicine from unlicensed vendors, who may sell pills loose from large plastic bags or subdivide blister packs. Despite this and other gross violations of good practice, the shops often operate with the regulators' tacit approval, because they are the only source of medicines outside of major cities.

There are also too few trained pharmacy staff in developing countries, especially in sub-Saharan Africa and South and Southeast Asia. In many countries, the few trained pharmacists work in industry. Community pharmacy practice, especially in rural areas, suffers. Having a trained community pharmacist oversee every drug store is not an option in the parts of the world most hurt by falsified and substandard medicines. Governments should take action to increase the reach of legal drug shops staffed by sellers with appropriate minimum training.

Recommendation 5-3: Governments in low- and middle-income countries should provide an environment conducive to the private sector establishing high-quality medicines retail in underserved areas. Govern-

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ment incentives could encourage this. To the same end, governments, the World Health Organization, and the International Pharmaceutical Federation should support national pharmacy councils and education departments to train tiers of pharmaceutical personnel.

The private sector will invest in medicines retail if there is a good business reason to do so. Governments can take steps that would encourage private sector investment and create an environment where responsible private drug sellers will thrive. Governments can provide low-interest loans for improving drug shops and encourage private-sector accreditation or franchising programs. They can also work with their national pharmacy councils to set out tiers of training, including vocational training, for pharmaceutical personnel. Governments can also give incentives to keep trained staff in underserved areas.

Disorganized medicines retail is not confined to developing countries. Through the internet, unlicensed drug vendors sell around the world, mostly in middle- and high-income countries. Unlicensed internet pharmacies are similar to street drug bazaars, both in the quality of the products they stock, which is poor, and in the lack of official oversight of their operations.

In the United States the NABP runs the Verified Internet Pharmacy Practice Sites (VIPPS) accreditation program to recognize safe online drug stores. Accredited online pharmacies comply with state licensing requirements for both the state that the pharmacy is in and all the states in which it sells. Chief among these requirements are the authentication of prescriptions, observance of quality-assurance standards, and submission to regular state inspection. Accredited pharmacies display the VIPPS seal, and, because this seal could be copied, the project website lists both certified pharmacies and known fraudulent ones.

DETECTION TECHNOLOGY

The main categories of techniques for pharmaceutical analysis can be broken down as visual inspection of product and packaging; tests for physical properties such as reflectance and refractive index; chemical tests including colorimetry, disintegration, and dissolution; chromatography; spectroscopic techniques; and mass spectrometry. Within each of these categories, some technologies are appropriate for field use, while others require sophisticated lab equipment and a high level of technical expertise.

Understanding when, where, and why to use the various techniques can be difficult. The information a technique provides, as well as its reliability, cost, speed, and portability, make it more or less appropriate in any given situation. While any one test may suffice to label a drug substandard or falsified, no single analytical technique provides enough information

to confirm that a drug is genuine. One challenge in both field and laboratory testing is determining how to combine tests for maximum efficiency. It is usually best to work through tests beginning with the easiest or least expensive ones. Only if samples pass these tests should the inspector move on to more difficult or expensive ones.

Making detection technology more accessible in low- and middle-income countries would be invaluable to controlling the trade in falsified and substandard drugs. Technologies can protect consumers and are useful to surveillance staff working to generate accurate estimates of the magnitude of the problem of poor-quality drugs. An understanding of the technological landscape, the range and gaps in available technologies, and the likely improvements in the near future is essential for using technologies in developing countries.

Recommendation 6-1: The National Institute of Standards and Technology should fund the development of a central repository for existing and newly innovative detection, sampling, and analytical technologies, ranging from field and rapid screening technology to sophisticated laboratory-based assessments, to identify substandard and falsified medicines.

CODE OF PRACTICE

Individual countries have the responsibility for protecting the national drug supply. This includes regulating good-quality manufacturers, preventing poor-quality drugs from entering the market, detecting them when they do, and punishing those who manufacture and trade them. Drug regulation, surveillance, and law enforcement are the necessary components of any national response to the problem.

A voluntary soft law such as an international code of practice could encourage international action against falsified and substandard drugs. The code of practice would contain guidelines on surveillance and international reporting of drug quality problems. The code would facilitate passage of national laws on how to punish and, when necessary, extradite those responsible for falsified drugs and criminally negligent manufacture. It would also promote harmonized regulatory standards for drug manufacture and licensing.

Recommendation 7-1: The World Health Assembly, in partnership with the United Nations Office on Drugs and Crime and the World Customs Organization, and in consultation with major stakeholders, should institute an inclusive, transparent process for developing a code of practice on the global problem of falsified and substandard medicines.

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The code should include guidelines on surveillance, regulation, and law enforcement, empowering states and the international community to prevent and respond to drug quality problems.

The manufacture and trade in falsified medicines is a growing, global problem. It is difficult to estimate the amount of falsified and substandard drugs in the market or to know the toll these products take on society, the number of deaths or excess illness they cause, or the amount of time and money wasted using them in treatment. There is evidence from some convenience surveys that antimicrobial drugs are often compromised in Southeast Asia and sub-Saharan Africa. In a larger sense, all drugs sold outside of legitimate chains are suspect. This includes medicines sold in unregulated markets and most drugs sold on the internet.

This report suggests a combination of actions that could reduce the global trade in falsified and substandard medicines. Some recommendations aim to improve medicine quality in the low- and middle-income countries that unquestionably bear a disproportionate burden of the problem. Other recommendations could improve weaknesses in the U.S. system, which would help the American consumer and build momentum for global action. Eliminating falsified and substandard drugs from the market requires international cooperation. A voluntary soft law could help advance harmonized systems for surveillance, regulation, and law enforcement.