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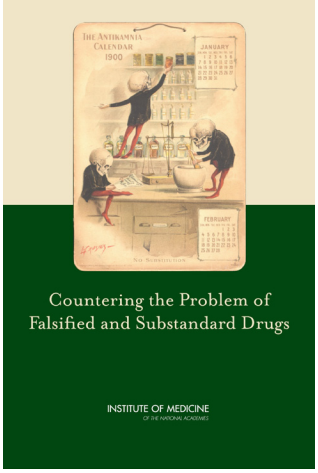
Countering the Problem of Falsified and Substandard Drugs



Falsified and substandard medicines provide little protection from disease and, worse, can expose consumers to major harms. Bad drugs pose potential threats around the world, but the nature of the risk varies by country, with higher risks in countries with minimal or non-existent regulatory oversight. Developed countries are not immune, however. In the United States, for example, negligent production at a Massachusetts compounding pharmacy sickened more than 600 people, killing 44, from September 2012 to January 2013. The vast majority of problems, however, occur in developing countries where underpowered and unsafe medicines frequently compromise treatment of deadly diseases and accelerate drug resistance, affecting millions.

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It is difficult to measure the public health burden of falsified and substandard drugs, the number of deaths they cause, or the amount of time and money wasted using them. But a network of security divisions at 25 major pharmaceutical companies found that falsified or substandard drugs were sold in at least 124 countries in 2011.

Tackling this global problem requires international cooperation, but disagreements, most notably about common definitions, have hampered coordinated efforts. The Food and Drug Administration asked the Institute of Medicine (IOM) to convene a committee charged with assessing the global public health implications of falsified, substandard, and counterfeit pharmaceuticals to help jumpstart international discourse about this problem. The committee's report, *Countering the Problem of Falsified and Substandard Drugs*, narrowly defines the term "counterfeit" to mean a drug that infringes on a registered trademark, and the committee centers its attention on substandard and falsified drugs, problems of public health consequence.

The Root Cause of Substandard Medicines

Substandard medicines are those that fail to meet the regulatory authority's specifications. Substandard medicines are made improperly: they may not dissolve or may be made from incorrect or impure ingredients.

The root cause of substandard drugs is neglect of good manufacturing practices. Running a manufacturing facility according to international best practices takes substantial resources; factories must meet standards, workers must be trained, and independent quality control staff must be hired. In developing countries, some manufacturers flout best practices, aided by lax regulators or domestic pressures to turn a blind eye to such problems in order to promote local industry.

There are a number of steps needed to transform raw chemicals into finished drugs. Manufacturers in the poorest countries purchase the building blocks of medicine, including active pharmaceutical ingredients, from foreign chemical suppliers and then formulate and package the drug, the final stages of drug manufacturing. China exports 77 percent of active ingredients made domestically, a $4.4 billion industry; India exports 75 percent of the $2 billion in active ingredients made there.

Good Quality Comes at a Price

It takes substantial working capital to assure quality medicine manufacture. Cutting corners lowers expenses but raises risks for consumers. Ingredients can cost thousands of dollars per kilogram; buying high-quality active pharmaceutical ingredients can double the cost to the manufacturer. And, because the cost of the active ingredient represents the lion's share of the medicine's price, scrimping even modestly on the active ingredient can vastly boost profit. Costs can be shaved in other ways as well: by not rigorously cleaning equipment between runs, which can result in contaminated drugs, or by failing to invest in adequate water filtration systems, which ratchets up the risk of microbial growth.

Multinational companies that make branded and generic medicines usually operate on a large enough scale and generate sufficient revenue to recoup the expense of maintaining good manufacturing practices. This is not the case for many small companies operating on razor-thin margins.

Companies in developing countries also have limited access to capital, despite the importance of domestic manufacture of medicines to many countries' health and industrial policies. In its report, the IOM committee challenges the private sector to help responsible manufacturers in developing countries meet international quality standards. The equipment and supplies that are necessary to adhere to good manufacturing practices often must be purchased in foreign markets, using hard currency. The International Finance Corporation and the Overseas Private Investment Corporation should invest in pharmaceutical manufacturing in low- and middle-income countries, the committee recommends.

Factors That Fuel Fake Medicines

In general, crime and corruption drive the business of falsified medicines. Drug regulators, who license manufacturers and register medicines, can correct problems with licensed manufacturers, but may not be able to reach manufacturers of drugs that are falsely represented.

Falsifying medicines has been called "the perfect crime" because the cost of making a fake drug is minimal and often leaves no paper trail, making it difficult to investigate and prosecute. Spotting a fake medicine requires specialized skills and equipment since legitimate and illegitimate products often are indistinguishable and mix freely in unregulated markets.

The burden of falsified medicines disproportionately falls on low- and middle-income countries. In these countries, the cost of medicine accounts for 20 to 60 percent of health spending; and 90 percent of people pay for drugs out of pocket. A month's supply of the lowest priced generic ulcer medication, for instance, costs more than three days' wages for the average govern-

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ment worker in much of Africa, Eastern Europe, and the Middle East. Moreover, the poorest patients, served by few reliable pharmacies, have little choice but to purchase medicines from vendors who sell products of dubious quality.

Forging a strong, well-regulated generics industry in developing countries could achieve a number of positive outcomes. A robust generics market can help control the cost of medicines. But, the committee concludes, creating a stronger generic drug market will rely on rigorous regulatory systems to bolster confidence in the quality of these products. Governments in low- and middle-income countries need a strategy to act forcefully against falsified and substandard medicines. The committee recommends strengthening regulatory systems; adding inspectors to police wholesalers, distributors, and manufacturers; enforcing quality standards; and licensing only those manufacturers that meet international standards.

Strengthening Drug Distribution, International Cooperation

In modern supply chains, medicines can change hands many times in myriad countries before they reach patients. Wholesalers buy and sell medicines to meet market demand. Scarcity in one region can trigger a flurry of purchases from wholesalers elsewhere with ample supply. As back-and-forth sales occur between and among drug wholesalers, the medicine is repackaged; each episode provides an open door for falsified and substandard products to enter the market.

The IOM committee calls for strengthening the drug distribution system in order to improve the quality of medicine and protect consumers. Top among its priorities is restricting the U.S. wholesale market to firms vetted by the National Association of Boards of Pharmacy. This action would tighten the American drug distribution chain and build momentum for better controls on drug wholesalers in developing countries.

Governments in low- and middle-income countries should establish an environment in which responsible private drug sellers can thrive. The private sector will invest in retail sales of medicines if there is a compelling business rationale to do so. Governments can encourage private sector investments by providing low-interest loans, helping with pharmacists' training, and by providing incentives—such as tax breaks, scholarships, or housing subsidies—to trained staff who remain in underserved areas.

Falsified and substandard medicines—whether sold in street markets or on unregulated websites—are a grave public health problem, as they often are ineffective, promote drug resistance, and even cause severe illness and death.

Eradicating falsified and substandard drugs from the market will require strong national regulation and international cooperation. A voluntary international agreement could help to advance uniform systems for surveillance, regulation, and law enforcement, empowering countries to prevent and respond to drug quality problems. Such a code would facilitate passage of national laws and, if necessary, permit extradition of crimi-

nals responsible for falsified drugs and criminally negligent manufacture. The World Health Assembly should adopt a global code of practice to build national regulatory capacities and promote international cooperation among public health and criminal justice authorities.

Conclusion

Stakeholders around the world share a common interest in combating inferior-quality drugs. At the international level, productive discussion relies on cooperation and mutual trust. The report advocates for an emerging consensus on once-contentious terms and lays out a plan to invest in quality to improve public health.

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