



HNP Brief #2

Pharmaceuticals: Counterfeits, Substandard Drugs and Drug Diversion

March 2005

Introduction

Pharmaceutical products are attractive candidates for illegal trade, especially in developing countries. They are easily transportable, have high value per unit, and most importantly, their quality cannot be assessed readily by lay persons or even experts without the aid of a quality testing laboratory. The fact that in some countries the risk of prosecution is low and profit margins are high for counterfeiting pharmaceutical drugs, has enticed criminal organizations to become involved, some reportedly with links to the narcotics trade or other forms of organized crime.[4]

Between obvious criminal intent and legal business activities, thousands of small businessmen and traders also make a living manufacturing and distributing drugs that do not adhere to international standards. These drugs are usually marketed through street sellers, but in several countries they find their way into pharmacies and the public supply chain as well. For many people in poor countries with weak regulatory systems, the likelihood that their hard earned money is spent on fake or ineffective drugs can be as high as 50%. Counterfeit and substandard drugs can lead to major adverse outcomes in consumers ranging from treatment failure to outright deaths: it estimated that the use of fake drugs causes thousands of deaths and even larger numbers of severe cases of illness every year.[1, 2]

The scale of the problem and its consequences make action against counterfeit and sub-standard drugs a priority in our efforts to improve access to medicines for the poor.

Definitions

Counterfeits are usually defined as drugs that are deliberately made as fake copies of the original branded or generic drugs, imitating design, colors and other visible features. In many cases they contain only filling materials without any active ingredients. Or they may contain insufficient or an excess of active ingredients, or active drug substances other than the ones specified in the label. Examples of counterfeiting include antidepressant pills in an antiretroviral package, or a cheap antibiotic such as penicillin re-packaged and re-labeled as a more expensive one. Counterfeits with potentially toxic content, such as ampoules for injection

containing non-sterile water or cough syrup made with diethylene glycol mark the most dangerous end of the spectrum. The latter case led to the death of 89 people in Haiti and 30 children in India in 1995 and 1998.[2]

Substandard drugs are manufactured with the intent of making a genuine pharmaceutical product, but the manufacturer saves costs by not following GMP (Good Manufacturing Practice) or using poor quality raw materials. Another potential problem relates to inadequate storage or transport conditions, leading to deterioration of the product. The performance of such medicines is questionable. If the specifications for dissolution are not met, the drug may pass the digestive system without being absorbed. If the amount of active substance is reduced, patients will be under-dosed with potentially severe consequences. If the product causes over-doses, side effects or toxic complications may result.

Drug Diversion refers to medicines that have been donated or sold under special conditions, for example to support a public health program, but are diverted and then sold for profit in the private market. A recent example of this is the appearance on the streets of Nairobi of antiretrovirals that had come from a public treatment program.[11]

Economic consequences

Counterfeits, substandard products and drug diversion have a negative economic impact on the overall financing and delivery system of pharmaceuticals. Medicines that are stolen from warehouses and re-sold on the private market or outside the country are not available to the patients for whom they were intended. Public funds used for purchasing these drugs are wasted. Substandard and counterfeit drugs destroy consumer confidence in healthcare systems. In the absence of a credible system for quality enforcement, doctors and patients tend to prefer branded, more expensive imported products. This makes it difficult to implement a rational drug policy based on generic Essential Drugs.

Dimension of the problem

Over the last few years, data have been collected on the presence of substandard and counterfeit drugs in

various markets. These data show that the problem is substantial in parts of the world that do not have effective regulatory systems.[3]

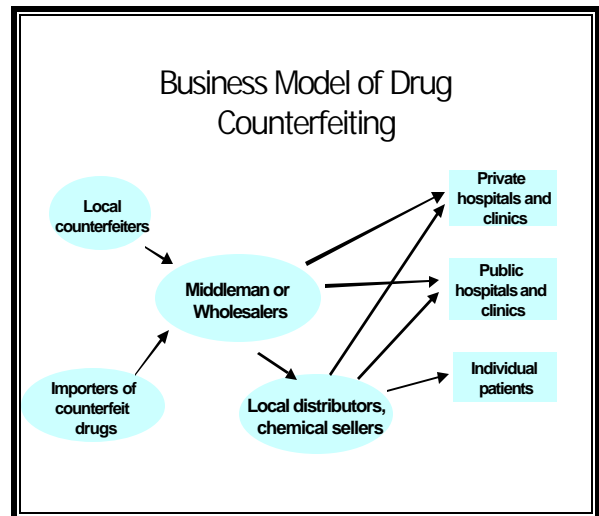
- The estimated value of the overall global trade in fake and sub-standard medicines is more than 30 billion USD.[1]
- WHO estimates that 25% of medicines sold in poor countries are counterfeit. Rates up to 40% have been quoted for specific drugs in some places in Argentina, Mexico and Colombia.[2]
- Investigators hired by multinational pharmaceutical companies have found large-scale illegal manufacturing plants that can produce millions of fake pills per day.[4]
- A recent FDA report suggests that the rate of counterfeiting in Southeast Asia is approximately 10%. In parts of China, up to 50% of certain drugs found in the marketplace were fakes.[5]
- A 2001 Lancet article reported that 40% of artesunate products (a modern, effective malaria treatment), bought in various southeast Asian markets, contained no active ingredient. Follow-up studies found that the problem had not been solved, and that in fact counterfeiters had significantly improved their packaging, to resemble the original products.[6]
- In Nigeria, the percentage of fake drugs was reduced from 70% to 35% after a three year campaign led by the National Agency for Food and Drug Administration and Control.[7]

A comprehensive matrix of cases and publications, updated every quarter, can be found on the United States Pharmacopeia (USP) website: <http://www.uspdqi.org/pubs/other/GHC-DrugQualityMatrix.pdf>

Key drivers of counterfeiting

- Monetary gain: The main reason for counterfeiting is the huge sums of money that can be made. Low manufacturing costs and high profits for fake medicines attract criminals, who see this as an easy way to make money. Profits are higher for copies of branded drugs from international manufacturers, but counterfeiters also copy generic drugs if there is enough volume to make a profit.
- Lack of legislation and enforcement: In countries where legislation or enforcement is weak, counterfeiters face low risks of being punished.
- Weak penal sanctions make counterfeiting an attractive alternative to the narcotics trade, which is punished much more severely.

- Transactions involving many intermediaries increase opportunities to insert counterfeit products into the system.
- Free trade and deregulation gives counterfeiters greater scope to introduce fake products into official channels. In some countries, policy-makers appear to believe that drug regulation is an unnecessary barrier to timely access to medicines and therefore should be reduced to a minimum.
- Lack of cooperation among stakeholders: If authorities, customs officials, police, industry and trade do not cooperate and exchange information, it is easier for counterfeiters to escape detection.
- Lack of political will: Officials in some countries regard counterfeiters as legitimate employers of local labor and their exports as providing economic benefits.
- Consumer ignorance: Consumers who are not aware of the existence of counterfeit drugs will not put pressure on retailers or report back if they experience a treatment failure.[8]



Counterfeit drugs are not limited to developing countries; the problem exists in the US and Western Europe as well.[5] However, the risk of discovery and prosecution is higher in developed markets than in developing countries with limited monitoring and law enforcement capacity.

Sophisticated counterfeiters have infiltrated the distribution chain in some countries to the extent that they mix original and fake products in the same consignment, box, container and/or batch.[4] Complex criminal organizations of international scope operate and may resort to violence to protect their franchises. A case in point: the head of the Nigerian Food and Drug Administration and Control Agency survived two

assassination attempts during her campaign against counterfeit drugs.[7]

Detection of counterfeit and substandard drugs

- Some counterfeit drugs differ from the original products in visible features such as color, print, imprint on the tablets, barcode, etc. However, in most cases, substandard and counterfeit drugs can only be identified through lab test results for the presence of key ingredients and through comparison of preparation characteristics with pharmacopeia standards. A simplified portable lab has been developed to test the authenticity for 40 compounds on the WHO Essential Drug List, which are high volume drugs that are significant for public health.[9, 10] These labs can be operated by a trained technician in the field. Most importantly, the results generated using the GPHF-Minilab matched well with results generated in a full-fledged laboratory.[9]
- Authorities in several countries collaborate with reputable pharmaceutical manufacturers. These conduct their own “market sweeps” and share information with law enforcement agencies on a regular basis in order to help eliminate counterfeit products and shut down illegal operations.

Manufacturers are increasingly moving towards developing new safety features, visible (i.e. holograms or watermarks) or invisible (i.e. fluorescent marks, invisible bar codes, chemical markers, or RFID [Radio Frequency Identification] chips).[5] However, visible features have not deterred counterfeiters. They have found ways to copy the features so well that pharmacists or consumers cannot detect any difference. Covert (invisible) features are an alternative, but special equipment is required to detect them, which makes them less effective in the field.

Policy options to fight counterfeiting

Legislative and Regulatory Framework:

In many countries, legislation relating to the pharmaceutical sector is inadequate and enforcement is weak, making drug counterfeiting an attractive area for organized crime. Legislation should lay out the role of the administration clearly, as well as the obligations and responsibilities of all parties involved in pharmaceutical manufacturing and trade. It must also provide the basis for prosecuting illegal traders and counterfeiters, setting stiff penalties that correspond to the harm to patients and to public health.

While both can harm health, different policy responses are appropriate for counterfeits and substandard drugs. The national drug regulatory authority needs adequate

resources so that it can assist viable local legal drug makers with honest intentions in upgrading their manufacturing processes to international standards.

Manufacturing Standards:

- All manufacturers must be controlled according to currently accepted GMP specifications, making sure that all inputs and outputs are accounted for and there is no illegal activity using their equipment to produce fake or sub-standard drugs for the grey or black market.
- Manufacturers who produce mainly for export must also adhere to current GMP standards (regulatory oversight should cover all manufacturers, whether they produce for the local market or for export).

Procurement and Logistics:

- Procurement agencies should be required to purchase only from well-established and controlled sources.
- Samples of medicines should be tested by the national drug safety lab or a contracted lab service at the point of entry to the distribution chain.
- Governments should encourage the development of marker technologies to track pharmaceuticals through the supply chain and identify fake products. (However, tracking does not reduce the need for national inspection, sampling and quality control.)
- The logistics chain should be short and transparent. For example, deliveries from the manufacturer can be made directly to regional distribution centers instead of to a central warehouse. Modern inventory management software should be used to keep track of the movement of goods.
- The logistics chain can be outsourced to vendors with international experience, who take contractual responsibility for the integrity of the products from the source to the retail level. The relevant national agency would then need to sample and test only at the retail level.

Licensing of Distributors:

Importers, wholesalers and retailers should operate under a licensing procedure that defines clear requirements. The license should be revoked if a license holder is found to market illegal or fake drugs, or purchases drugs from a non-licensed source.

Monitoring and Law Enforcement:

The drug regulatory authority in each country should establish a post-marketing surveillance program which may include early detection for counterfeit and substandard drugs in the field; periodic inspections of points in the production and distribution chain; and a

rapid alert system for information sharing, action taking and product recalls.

Legal or contractual sanctions should apply if counterfeit or substandard drugs are found.

Law enforcement capacity needs to be upgraded by training specialists to tackle the illegal trade and to bring those who are involved to justice.

Technology:

Current technology can help to make counterfeiting more difficult, but there is no complete protection. New RFID-based systems will allow precise tracking of products, but they require an investment in the distribution chain. Their applicability in developing countries has not been tested yet.

Education:

Professionals, the general public and the media should be educated to create awareness of the dangers associated with substandard and counterfeit drugs. Countries that have invested in public education on drug quality issues have achieved measurable successes in the fight against counterfeit drugs.[3]

Collaboration:

Governments of small and resource-limited countries could establish regional centers of expertise to provide the necessary capacity and know-how for drug quality testing and training of enforcement personnel.

Financing:

Procurement based on “landed cost” (including the distribution costs for the product to the retail shelf) rather than acquisition cost of the products only can align incentives in the distribution chain and push the responsibility for drug quality at retail level to the vendors.

A payment system based on health outcomes or DRG (Diagnosis Related Groups) creates an incentive for payers to monitor the integrity of medicines supplied by healthcare providers.

Support, additional information

- United States Pharmacopeia, Drug Quality and Information Program <http://www.uspdqi.org/>
- US FDA report on counterfeit drugs <http://www.fda.gov/counterfeit/>
- WHO resources on drug quality and integrity <http://www.who.int/mediacentre/factsheets/fs275/en/>
- Pharmaceutical Security Institute: <http://www.psi-inc.org/index.cfm>
- Minilab - German Pharma Health Fund: <http://www.gphf.org>
- World Bank support: Andreas Seiter, Tel. +1-202-473-3629, aseiter@worldbank.org

Sources

1. IFPMA, *Counterfeit Drugs, a Global Health Risk*, in *Geneva Pharma Forum*, IFPMA, Editor. 2004.
2. WHO, *Substandard and counterfeit medicines*. 2003.
3. USP, *Drug Quality Matrix*. 2004.
4. *Personal Communication*. 2004.
5. FDA, *Combating Counterfeit Drugs: A Report of the Food and Drug Administration*. 2004.
6. Paul Newton, et al., *Fake artesunate in southeast Asia*. *The Lancet*, 2001. **357**: p. 1948-1950.
7. Naik, G., *Nigerian Regulator Dodges Violence to Fight Fake Drugs*, in *The Wall Street Journal*. 2004.
8. GlaxoSmithKline, *The Counterfeiting of Healthcare Products*, in *Global Public Policy Issues*. 2004.
9. GPHF, *The GPHF-Minilab - Protection against Counterfeited and Substandard Pharmaceuticals*. 2004.
10. Jaehnke, R., *Counterfeit Medicines and the GPHF-Minilab for Rapid Drug Quality Verification*. *Pharm. Ind.*, 2004. **66**(10): p. 1187-1193.
11. Siringi, S., “AIDS drugs being sold illegally on market stalls in Kenya” *Lancet* 2004, 363:377

Written by: Andreas Seiter (WB) Global Pharmaceutical Industry Fellow
Reviewed by: Yolanda Tayler (WB), Jessica Hughes (GSK), Nancy Blum (United States Pharmacopeia - USP)