Counterfeit medicines in less developed countries

Problems and solutions

Julian Morris and Philip Stevens
International Policy Network
London

Counterfeit medicines in less developed countries: problems and solutions

Written by Julian Morris, Executive Director
Philip Stevens, Director, Health Programme

International Policy Network
Third Floor, Bedford Chambers
The Piazza
London WC2E 8HA UK
t: +4420 7836 0750
f: +4420 7836 0756
e: info@policynetwork.net
w: www.policynetwork.net

Designed and typeset in Latin 725 by MacGuru Ltd
info@macguru.org.uk

First published by International Policy Press
a division of International Policy Network

© International Policy Network 2006

All rights reserved. Without limiting the rights under copyright reserved above, no part of this publication may be reproduced, stored or introduced into a retrieval system, or transmitted, in any form or by any means (electronic, mechanical, photocopying, recording or otherwise) without the prior written permission of both the copyright owner and the publisher.

About International Policy Network

International Policy Network (IPN) is a charity based in the UK, and a non-profit (501c3) organisation in the US. It is a non-governmental, educational and non-partisan organization which relies on charitable donations from individuals, foundations and businesses to carry out its work. It accepts no money from government.

IPN aims to empower individuals and promote respect for people and property in order to eliminate poverty, improve human health and protect the environment. IPN promotes public awareness of the importance of this vision for all people.

IPN seeks to achieve its vision by promoting the role of market institutions in certain key international policy debates: sustainable development, health, and globalisation and trade. IPN works with academics, think tanks, journalists and policymakers on every continent.

Counterfeit medicines in less developed countries: problems and solutions

Much of the debate surrounding counterfeit medicines to date has focused on how to prevent them seeping into the supply chains of developed-country markets. The majority of counterfeit medicines originate in Less Developed Countries (LDCs), including most of those that end up in the US and EU. Steps should be taken to change the incentives faced by counterfeiters in LDCs participating in the production and trade of counterfeit pharmaceuticals.

1. The scale of the problem

While counterfeit medicines in wealthy markets are a growing concern for physicians and law-enforcement agencies, their prevalence pales in comparison to their penetration of less developed markets. According to the World Health Organisation (WHO), 25 per cent of all medicines in LDCs are counterfeit.[1] In some countries, the prevalence is far higher:

- Counterfeit medicines constitute between 40 and 50 per cent of total supply in Nigeria and Pakistan.[2]
- In China, authorities have found that some products have a counterfeit prevalence ranging between 50 and 85 per cent.[3]
- 36.5 per cent of antibiotics and anti-malarials on WHO essential drugs list in Thailand and Nigeria are substandard (Shakoor *et al*, 1997).
- A recent survey by the WHO of seven African countries found that between 20 and 90 per cent of all anti-malarials failed quality testing. These included chloroquine-based syrup and tablets, whose failure rate range from 23 to 38 per cent; and sulphadoxine / pyrimethamine tablets, up to 90 per cent of which were found to be below standard (WHO, 2003).

In spite of a lack of hard data (Cockburn *et al*, 2005), it is clear that counterfeit medicines are not confined to a handful of therapeutic classes. This is especially true in LDCs, where the range of fakes on the markets encompasses treatments for a diverse range of conditions and ailments. The top five counterfeited medicines in the Philippines provide some illustration of this point:

1. Antihypertensive drugs (Adalat Gits 30mg Tablet)
2. Anti-asthma drugs (Ventolin Expectorant syrup)
3. Analgesic medicines (Ponstan 500)
4. Anti-diarrhoea (Diatabs Reformulated),
5. Vitamins (Propan with Iron Capsule, Ceelin 100 mg/ 5 ml Syrup, Enervon C and Iberet 500)[4]

This list is certainly not exhaustive. Other favourites for counterfeiting include drugs for treating anaemia, HIV, schizophrenia, as well as growth promotion hormone (used in the treatment of HIV). The problem also extends beyond fake pharmaceuticals to medical consumables such as non-sterile syringes and gauze and even substandard electronic medical equipment.

2. Where are counterfeit medicines being produced?

A large proportion of the world's counterfeit medicines originate in Asia. China in particular is a production centre, although precise data about the scale and scope of the problem within this country is neither widely available nor reliable. In 2001 it was reported that China had 500 illegal medicines factories[5] and while no newer data is available, it is safe to assume that number has since increased. Also in 2001, it was reported that

Chinese authorities "closed 1,300 factories while investigating 480,000 cases of counterfeit drugs worth $57 million."[6] Most Chinese counterfeit medicines that find their way into foreign supply chains first pass through the ports of Hong Kong and Shenzhen.

South East Asia more generally is a major source of counterfeit medicines. According to the WHO, Cambodia had 2800 illegal medicine sellers and 1000 unregistered drugs on the market in 2003. The same report showed that Laos had about 2100 illegal medicines sellers, while in Thailand, substandard medicines account for approximately 8.5 per cent of the total market.[7]

One 2002 study by government officials showed that 9 per cent of all drugs tested in **India** were substandard .[8] Some 15,000 generics manufacturers operate in India.[9] Although the majority are legitimate, a small minority are likely to be 'fly by night' operations that do not comply with proper standards. Most of the counterfeit medicines in **Nigeria** originate in India, a fact that lead the Nigerian authorities to threaten to ban the import of all drugs from India in 2003 (Raufu, A., 2003). However, it should be noted that 70 per cent of the Indian domestic market is supplied by around 20 companies that regularly pass inspections from visiting officials from Western countries.[10]

Counterfeit medicines also abound in **Latin America**, with instances reported in Argentina, Brazil, Colombia, Venezuela, Mexico, Peru and Guatemala: **Mexico** is a major global source of counterfeit medicines, with the trade standing at an estimated value of US$650mn per year – equal to around 10 per cent of total drug sales in the country.[11]

In **Russia**, it is estimated that counterfeits constitute between five and ten per cent of the total market.[12] In 1999 alone, 1,500 lots of Russian-made drugs failed to pass quality tests.[13]

3. The impact of counterfeit medicines

Counterfeit medicines can cause harms in various ways: the presence of toxic chemicals frequently causes injury or death; inappropriate delivery systems and/or inadequate amounts of active ingredient prevents the drugs from working effectively and, again, can lead to injury or death; more broadly under-dosing fosters resistance to the active chemical. In the cases of HIV/AIDS and malaria, this latter aspect is particularly worrying.

Harmful

Counterfeit medicines often contain agents that are injurious to health, as for example when 89 people in Haiti died after ingesting cough syrup manufactured with diethylene glycol (a chemical commonly used as anti-freeze). This particular product was made in China, transported through a Dutch company to Germany, before winding up on the Haitian market. A similar case occurred in Nigeria in 1995, resulting in the death of 109 children and again in Bangladesh (Hanif et al, 1995).

The dangers of widespread counterfeiting were illustrated in 1996 during a meningitis epidemic in Nigeria. Some 60,000 people were inoculated with counterfeit vaccines, resulting in the deaths of 2,500 people (Pecoul *et al*, 1999).

More importantly, counterfeits medicines typically provide inadequate doses of drugs, either because too little active ingredient is included in pills or because the delivery vehicle (including otherwise 'inactive' ingredients) are inappropriate (for example, chemicals that are not water-soluble). As a result, patients receive too little medicine and die or are far sicker would have been the case if they had received an adequate dose.

It is estimated that in China between 200,000 to 300,000 people die each year due to counterfeit or substandard medicine. However, this "official" statistic may over- or under-state the true number of cases.[14]

Drug resistance

Perhaps one of the most worrying implications of the global boom in counterfeit medicines is the acceleration of new, drug resistant strains of viruses, parasites and bacteria. If drugs contain too little of the active ingredient, not all the disease agents are killed and resistant strains are able to multiply and spread.

Malaria

This is already being observed in the treatment of malaria. Counterfeiters around the world have cashed in on the massive demand for the latest and most effective antimalarial drug, artemisinin. A field survey conducted in 2004 showed that 53 per cent of artemisinin-based antimalarials in a range of South East Asian countries contained incorrect levels of active ingredient (Dondorp et al, 2004), which implies that swathes of patients are receiving the incorrect dose. The direct consequences are death and serious injury resulting from improper treatment.

In addition, malaria parasites exposed to inadequate (subtherapeutic) concentrations of artesunate may result in the multiplication of parasites resistant to the drug (White, 1999). Even though Artemisinin has only been widely available since the late 1990s, scientists are already reporting cases of resistance. According to Dr Dora Akunyili, the head of Nigeria's national drug regulator, the racket in fake medicine is directly responsible for this resistance, and is a contributing factor to the doubling of malaria deaths over the last 20 years.[15]

HIV AIDS

HIV/AIDS treatment is also under threat from counterfeit medicines. The recent discovery of counterfeit antiretrovirals (stavudine-lamivudine-nevirapine and lamivudine-zidovudine) in the Congo (Ahmad, 2004) raises the prospect that the first line therapies for treatment of HIV/AIDS could soon be rendered useless. With few new research leads in the pipeline, this could have grave implications for the people of sub-Saharan Africa [need a ref for the paucity of new ARVs].

Bird flu

Finally, counterfeit medicines could be undermining our ability to contain and treat a potential avian flu pandemic. As demand has grown for the anti-viral drug Tamiflu, one of the best current treatments for the disease, counterfeiters have ramped up production of illegitimate versions. Already, the Internet is awash with spurious Tamiflu, while consignments have been discovered as far apart as New York and Beijing. The risk is that copies containing sub-therapeutic levels of active ingredient could facilitate the development of drug resistant forms of the avian flu virus, leaving very few tools to contain a potential pandemic.

Undermining R&D

Counterfeiting can also undermine the incentives of R&D based companies to invest in future innovation. Even near-perfect copies of on-patent medicines cause harm by competing with legitimate supplies of medicines from originating companies, which reduces revenues and undermines incentives to invest in future R&D.

4. Underlying causes of LDC counterfeiting

- ***Absent or defective IP protection.*** One way to prevent the sale of unauthorised copies of medicines is to enable companies to register and enforce trademarks. These enable vendors to signal the quality of their product to potential purchasers. Trademark owners have strong incentives to ensure that the quality of their product is maintained because their reputation and hence future profitability depend upon it.In many LDCs, it is difficult to enforce trademarks – even for local companies. Where trademarks cannot be enforced, cheaply produced poor quality copies will typically crowd out good quality drugs.
- ***Lack of adequate civil liability. C***ivil law protects the consumer against mis-sold or defective goods. By enabling consumers (or their relatives) to obtain redress from the manufacturer or supplier of a harmful product, such liability both compensates those who are harmed and discourages manufacturers and suppliers from selling counterfeits. In many LDCs, however, civil law is either poorly defined or difficult to enforce.
- ***Inability to resolve disputes over property rights and contracts in independent courts.*** Underlying the lack of civil liability and weak IP protection are costly and inefficient legal systems As a result, it can often take years for cases to be heard. Many courts in LDCs are hampered by a lack of basic things such as

reliable electricity and inefficient processes, causing delays.

In many LDCs, law enforcement is also corrupt. In such places, criminal counterfeiting gangs may be able to pay corrupt law enforcement agents to turn a blind eye to their activities. If a case does make it to court, the gangs may be able to pay off the judge and thereby induce a favourable judgement.

- ***Weak or absent rule of law:*** In LDCs with a weak rule of law, political and legal decisions tend to be arbitrary and designed to benefit the elite. As a result, regulation designed to combat counterfeiting is often ineffective. Corruption within regulatory agencies and police forces exacerbates this problem, so that the enforcement of regulations is seen as an opportunity to collect bribes.

- ***Price controls. T***he imposition of price controls by governments prevents companies from selling goods at different prices to different consumers. Also, where prices are controlled at different levels in different markets, traders exploit these price differentials through arbitrage. Such trade (called parallel trade) may create gaps in the supply chain which can be exploited by counterfeiters. For example, it is often necessary to repackage drugs in order to sell them in a different market, which requires that the packages will require relabelling in the correct language. This creates opportunities for unscrupulous intermediaries to infiltrate the supply chain with fakes. Price controls in wealthy country markets therefore increases the chance that copies of patented medicines produced in LDCs will leak back into wealthy country markets.

  In addition, companies have less incentive to register products in markets where their drugs are subject to price controls, leading to shortages in supplies. They also reduce the margins made by pharmacies, making the distribution of drugs to remote and rural regions financially unviable. For example, the price caps forced on certain drugs in South Africa have been implicated in the closure of 103 pharmacies.[16] If markets are left unsupplied in this way, it presents a clear incentive for counterfeiters to fill in the unmet demand.

- ***Taxes and tariffs. L***DC governments also stimulate demand for cheaper fakes by artificially driving up the price of legitimate drugs through taxes and tariffs, which can inflate the retail price of drugs by up to 50 per cent (see table below). Many of the high tariff countries also have a significant indigenous counterfeit medicine industry and / or problem. It is unlikely that this is entirely coincidental.

Duties and taxes on retail medicines

Country	*Combined total duties and taxes*
India	55%
Sierra Leone	40%
Nigeria	34%
Pakistan	33%
Bolivia	32%
Bangladesh	29%
China	28%
Jamaica	27%
Morocco	25%
Georgia	25%
Mexico	24%

Table adapted from European Commission, 2003

5. What can be done in Less Developed Countries?

In order to contain the global counterfeiting scourge, it is necessary to address those dynamics which encourage the manufacture and supply of counterfeit medicines. Since the majority of these drugs originate in LDCs, it should be a matter of priority to address those lacunae of governance which allow LDC counterfeiters to ply their trade with relative impunity.

Most importantly, it is essential that contracts, property rights and the rule of law be upheld in the countries in which the majority of these drugs are produced. When properly upheld, these formal market institutions enable entrepreneurs to participate freely in the market, leading to economic growth and technological development. When these institutions are not upheld, as is the case in most lower-income countries, people are forced into the

informal economy as a way of side-stepping the cost and difficulty of conducting business formally. And when the majority of the population subsist within the informal economy, they are unable to avail themselves of the protection that would otherwise exist from contracts or the implied reputation of trademark-protected products.

Some concrete steps to overcome these problems in LDCs include the following:

- Adjudication of disputes over contracts should be simpler and cheaper, so that contracts may be more readily enforced.
- Bureaucratic restrictions on doing business should be removed.
- The manufacturers of brand goods should be able more effectively to protect their trademarks.
- Most fundamentally, courts of law should be granted greater independence, so that their rulings are more impartial and less influenced by powerful vested interests.
- The legislature should not have the power to interfere with judicial decisions.
- The power of law enforcement agents should be curtailed and their actions subject to judicial review.
- The actions of other government agents (e.g. regulators) should be subject to judicial review.
- Regulation restricting the supply of medicines should be improved or scrapped. [17]
- Governments should reduce taxes and tariffs on all medicines. [18]

What can be done? Internationally

TRIPs

At the international level, the agreement on trade related aspects of intellectual property rights (TRIPs), which is part of the WTO Agreements of 1994 and is mandatory for all World Trade Organisation members, requires that the trademark laws of member jurisdictions are compatible with each other, a quality which is known as 'harmonisation'. LDCs that are members of the WTO should therefore have TRIPs-compliant trademark recognition.

However, the only way for aggrieved countries to enforce breaches of the TRIPs agreement is through trade sanctions. This is often not a particularly desirable option, for several reasons. First, trade sanctions hurt both parties – people in the offending country will lose much-needed export revenue and associated employment opportunities, while people the aggrieved country will lose the economic benefits of importing goods from a country that has a comparative advantage in production. To the extent that employment falls in the offending country, more people may end up with a smaller disposable income and thereby more likely to purchase cheaper counterfeit medicines.

Secondly, the enforcement of TRIPs can, in certain cases, undermine popular support for intellectual property protection, making future enforcement more difficult politically. For example, in 2001 the research-based pharmaceutical companies sought to challenge in the courts a South African law that seemingly contravened TRIPS. In response to a very vocal campaign by AIDS activists, the pharmaceutical companies withdrew their case. While the dispute was not brought in the WTO, the negative PR given to it created a persistent fear of the possible fall-out from bringing such a WTO dispute.

Bilateral trade agreements

An alternative way of persuading LDCs to institute intellectual property regimes is through tempting them with bilateral and regional free trade agreements (FTAs). Most FTAs involving the United States contain provisions that require signatory countries to bolster their intellectual property regimes. By promising access to large and lucrative markets, these agreements can be a way of persuading LDCs to respect the fundamentals of intellectual property protection, which is a vital step for curtailing counterfeiting.

Although these agreements are not as beneficial as unconditional free trade, they are a step in the right direction, freeing up trade and thereby improving economic well-being. However, they do raise complications in the form of 'rules of origin' issues, which are costly to monitor and administer. Furthermore, an overly-complex 'rules of origin' system may lead to the development of illicit trade routes which could be exploited by traders in illegitimate goods such as counterfeit medicines.

Conclusion

The counterfeiting of drugs is a global problem which will not be eliminated until the supply-side issues are addressed. The majority of counterfeit drugs are manufactured in LDCs, so reform in these countries is absolutely vital if progress is to be made. The most pressing area for reform in the majority of LDCs is the application of the rule of law, the definition and enforceability of property rights and the enforceability of contracts. Without such reforms, counterfeiters will continue to kill hundreds of thousands of people every year.

Bibliography

Ahmad, K., (2004), "Antidepressants are sold as antiretrovirals in DR Congo", *The Lancet,* 363: 713.

Cockburn, R., Newton, P., Agyarko, E., Akunyili, D., White, N., (2005), "The Global Threat of Counterfeit Drugs: Why Industry and Governments Must Communicate the Dangers", *PLoS Medicine,* 2(4): e100

Dondorp, A., Newton, P., Mayxay, M., Van Damme, W., Smithuis, F., Yeung, S., Petit, A., Lynam, A., Johnson, A., Hien, T., McGready, R., Farrar, J., Looareesuwan, S., Day, N., Green, M. & White, N., (2004), "Fake antimalarials in Southeast Asia are a major impediment to malaria control: multinational cross-sectional survey on the prevalence of fake antimalarials", *Tropical Medicine & International Health,* 9(12): 1241.

Hanif, M., Mobarak, M., Ronan, A., Rahman, D., Donovan, J. *et al*, (1995), "Fatal renal failure caused by diethylene glycol in paracetamol exlixir: The Bangladesh epidemic", *British Medical Journal,* 311: 88–91.

Pcoul, B., Chirac, P., Trouiller, P., Pine, J., (1999), "Access to Essential Drugs in Poor Countries – A Lost Battle?" *JAMA,* 281(4)

Raufu, A., (2003), "India agrees to help Nigeria tackle the import of fake drugs", *British Medical Journal,* 326: 1234.

Shakoor, O., Taylor, R., Behrens, R., (1997), "Assessment of the incidence of substandard drugs in developing countries," *Tropical Medicine & International Health* 2(9): 839–845.

White, N., (1999), "Delaying antimalarial drug resistance with combination chemotherapy," *Parassitologia* 41, 301–308.

WHO, (2003), "The quality of antimalarials: a study in seven African countries," Geneva: WHO, available at http://whqlibdoc.who.int/hq/2003/WHO_EDM_PAR_2003.4.pdf

Notes

1 http://www.who.int/mediacentre/factsheets/fs275/en/

2 Liza Gibson, "Drug regulators study global treaty to tackle counterfeit drugs," British Medical Journal Volume 328, Number 486 February 28, 2004.

3 European Federation of Pharmaceutical Industries and Associations, "Counterfeit medicines", available at http://www.efpia.org/2_indust/counterfeitdrugs.pdf

4 http://www.manilatimes.net/national/2005/aug/16/yehey/life/20050816lif1.html

5 http://bmj.bmjjournals.com/cgi/content/full/327/7424/1126-a

6 Fackler M (2002 July 29) China's fake drugs kill thousands. San Francisco Examiner

7 http://www.who.int/entity/bulletin/volumes/81/12/WHONews.pdf

8 http://bmj.bmjjournals.com/cgi/content/full/327/7412/414-b

9 http://pharmalicensing.com/articles/disp/1120475327_42c918bf09048

10 Selling cheap generic drugs, India's copycats irk industry, available at http://chakra.org/articles/2000/12/03/indian/drugs

11 Latin America Battles Counterfeit Drug Threat, Daily International Pharmacy Alert: Washington Business Information, 2(292), 2006.

12 http://www.efpia.org/2_indust/counterfeitdrugs.pdf

13 Fake drugs worry authorities, firms, *The Russia Journal*, 2000, 3(4) 47

14 *South China Business Journal*, June/July/August, 2002

15 http://www.prospect.org/web/page.ww?section=root&name=ViewWeb&articleId=10650

16 http://www.freemarketfoundation.com/ShowArticle.asp?ArticleType=Publication&ArticleID=1093

17 Very often, the supply of drugs is reduced by the Byzantine and tortuous regulations that emanate from local drug approval agencies. These regulations make it very difficult for manufacturers wishing to export to overseas markets to register new products, thereby creating a gap in supply. This gap provides another opportunity for counterfeiters. One example is South Africa's Medical Control Council, which requires that all new medicines attain its own regulatory approval before they can be marketed in the country – even if they have already been approved by reputable foreign regulatory bodies such as the FDA. However, the extreme inefficiency of the FDA means that drugs that have already been registered for use in the US, EU and Japan wait an average of 39 months for approval in the South African system. If such delays occur on already existing medicines, it presents a clear incentive to counterfeiters to meet the artificially pent up demand in the market.

18 These artificial price inflators can price may patients out of treatment, and give them an incentive to look to cheaper counterfeit medicines to meet their needs. Abolishing these levies would return medicines to their natural prices, thereby undermining the potential profits – and incentives – of counterfeiters.