

FAKING IT

Globalisation has helped increase the risks of counterfeit drugs endangering human life. **Andrew Jack** looks at the scale of the problem and the latest attempts to crack down on crime

When US investigators earlier this year identified vials of the cancer medicine bevacizumab (Avastin) without the active ingredient, they began a probe that led them on a complex trail via intermediaries in Barbados, the United Kingdom, Denmark, and Switzerland into Turkey and the Middle East.

The falsified product, which was sold through dozens of medical practices within the US, highlighted how even citizens of one of the world's richest countries with extremely tight regulation are vulnerable to the health threats from counterfeit drugs.

Substandard medicines, whether the result of deliberate action or neglect, have long been a health hazard in developing countries. The absence or wrong dose of the active pharmaceutical ingredient, and contamination with harmful substances, may harm unsuspecting patients and has resulted in many deaths, although it is often difficult to identify the medicine as the cause.

But most examples in the industrialised world have been limited to medicines purchased by consumers through the internet, which circumvent doctors and pharmacists. The more recent spread of counterfeits into the mainstream pharmacy supply chain has triggered fresh concern and action by policy makers. None was more striking than the adulterated heparin that was linked to more than 80 deaths in the US in 2008. The heparin had been made in China in a way that was deliberately hard for quality assurance tests to identify.¹

Securing drug distribution is difficult, with those seeking reforms not only struggling against organised criminal groups but also torn between public health concerns and divergent commercial perspectives of competing equipment and software providers, as well as rival drug companies holding varied views.

Defining the problem

The first difficulty is with definitions, since problem medicines can include drugs with intentionally fraudulent ingredients, those with unintentional substandard content because of

poor manufacturing, and high quality products that risk violating patent rules. Each requires different responses.

Another difficulty is estimating the scale of the problem. The World Health Organization in the past suggested that 10%-30% of medicines in developing countries were fakes, while stressing the problem affected less than 1% of medicines in Western countries.² However, it has backtracked on providing figures. Recent briefings on its website have become less specific, relying on a handful of surveys focused on specific drugs in particular countries, such as 3000 HIV patients in Kenya affected by falsified batches of the antiretroviral combination treatment Zidolam-N (lamivudine, zidovudine, and nevirapine).³

Roger Bate from the American Enterprise Institute for Public Policy Research, led a study published this year that found that 8% of anti-malarial drugs purchased in Ghana, Nigeria, and Togo contained insufficient active pharmaceutical ingredient.⁴ In a separate study of anti-infective drugs in cities in lower and middle income countries, his research team found an average failure rate of 10%.⁵

Drug companies, while paying close attention, have been reluctant to speak out or share figures, partly to avoid undermining public confidence in their products. More recently, the industry's Pharmaceutical Security Institute has released data showing a sharp rise in the number of fake drug cases over the past decade.⁶

The statistics highlighted a slight decline for the first time last year to just under 2000 incidents worldwide and 1300 arrests, with most taking place in Asia. Genitourinary, anti-infective, and cardiovascular drugs topped the list. Yet the institute's figures do not reveal the specific drugs, the quantity involved, or the nature of the failures of the medicines identified.

Individual court cases provide the most detailed information, but the time lag is considerable. And the cases that reach court represent only a small proportion of those that come to investigators' attention because obtaining evidence, arrests, extradition, and successful prosecution is difficult in the complex cross-border trade.

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Beijing, China: women prepare to destroy 50 tons of confiscated fake medicines

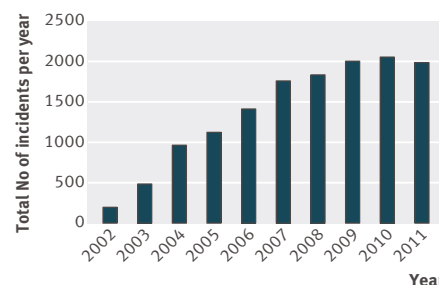
Intellectual property confusion

The difficulties of tackling counterfeit medicines are increased by confusion surrounding exactly what is meant by the term counterfeit. European customs figures for 2011 show counterfeit medicines accounted for 24% of all border seizures, with 2500 cases involving 28 million packets at an estimated retail value of nearly €28m (£23m; \$36m).⁷ But these relate to confiscation linked to the violation of intellectual property rights, not necessarily drugs that are harmful to patients.

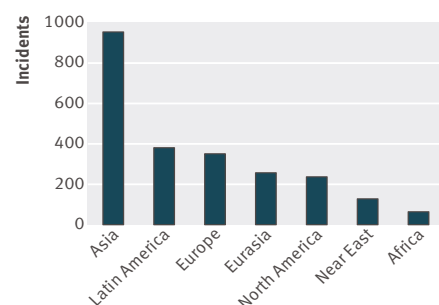
For example, Cipla, the Indian drugs company, ultimately won a settlement last year after batches of its low cost generic version of Eli Lilly's psychiatric drug olanzapine were among a series of shipments seized at Schiphol airport in the Netherlands en route to Latin America.⁸ Although Cipla would have been breaking intellectual property rights if it had planned to sell the drugs in the EU, it was shipping them to other markets where the product complied with local patent laws.

If the large pharmaceutical companies have sometimes been too aggressive in using counterfeit claims on patent violations, they have also periodically conflated the fake drugs debate with "parallel trade"—when intermediaries buy medicines in one country and resell them elsewhere below the agreed country price.⁹ The practice, which is legal within the EU, has been a particular concern in Greece, depriving patients of life saving medicines.

But there is scant evidence that parallel trade has allowed fakes to circulate in the European legitimate supply chain. One detailed analysis of



Global incidents of counterfeiting



Where counterfeit incidents occurred in 2011

Source: Pharmaceutical Security Institute

250 000 prescriptions issued through pharmacies in Belgium and Greece during 2008 did not identify a single fake drug.¹⁰

Such tensions explain why international bodies have struggled to take action against fake drugs, struggling even to build a consensus around a definition. WHO, for instance, now labels the problem as “spurious/falsely-labelled/falsified/counterfeit (substandard and SFFC) medicines.”¹¹

WHO calculates that only about 20% of its 193 member states have well developed medicine regulation. That risks promoting smuggling and illegal manufacture and distribution of medicines.

Yet a number of free trade agreements introduced in countries such as Kenya nominally designed to tackle counterfeit drugs define the term in a way that includes patent violations.¹² The result has been opposition from health organisations fearful that the agreements will block access to affordable generic medicines.

Whatever the fights over terminology, it is clear that fake drugs are penetrating even tightly regulated markets, primarily through internet sales of medicines including prescription treatments for erectile dysfunction, depression, and weight loss. In October, agencies in more than 100 countries participated in the fifth Operation Pangea, the largest effort yet to clamp down on the problem.¹³

Practical solutions

One approach is to provide assurance to purchasers by certifying legitimate registered online pharmacies, as the Royal Pharmaceutical Society’s *ipharacist.me* site does.¹⁴ Another is education designed to alert consumers to the dangers of

buying drugs online (around half of drugs bought online are estimated to be fake³). A third is the prosecution of sellers and manufacturers.

Although officials have arrested some individuals, they have found it difficult to bring prosecutions against the organisers and manufacturers, who are often based in China or Russia. That has led to fresh calls for an international treaty with more consistent and tougher criminal measures imposed.

Another approach has been to target the intermediaries in illicit online sales. The evolving strategy has been to undermine internet sales by closing down both internet domain names and financial intermediaries, starving the sellers of marketing platforms online and ways to get paid. This year, Pangaea shut 18 000 websites. There have also been negotiations with Google, Amazon, and eBay to prevent searches and sales through such sites.

A final focus has been to invest in technology to allow pharmacies, doctors, or consumers to verify whether a medicine is genuine and safe—for example, by allocating a unique number to every packet of medicine so that it can be checked on a central database. Some “high tech” approaches such as radiofrequency identification allow easy tracking of drugs but are costly to implement and are often located on crates of drugs rather than individual packets.

Simple barcodes and registration numbers for each packet are gathering popularity, with the number read by conventional retail scanners used by pharmacists. That still requires a central register containing all the different drug manufacturers’ codes, with guarantees over confidentiality of the information it contains. Efpia, the European

pharmaceutical industry trade body, has proposed such a “European stakeholder model.”¹⁵

It has won agreement with parallel traders to ensure that any repackaging of medicines for different markets does not conceal the barcode and hopes to launch the system by 2014. It is still in discussions with generic drug makers, who argue the system would prove costly, although Efpia says it would cost about 1 cent on each of the 10–12 billion medicine packets sold across the EU each year.

In developing countries, variants on the approach are also gathering momentum, with operators such as Sproxil and mPedigree, which began in Ghana and has spread across parts of Africa and Asia. mPedigree has negotiated deals with phone and drug companies so that patients can text the code of a drug packet for nothing and receive a return text verifying the number. Bright Simons from mPedigree says: “We have now expanded dramatically in South Asia, with our model focused on allowing manufacturers to implement it at the lowest cost possible.”

Technology offers the potential to give patients more power in verifying the quality of their medicines. But even if such systems become universal and cheap, that still requires education programmes to make them aware of the dangers of counterfeit medicines and the ability to gain access to medicines that are both high quality and affordable.

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Competing interests: None declared.

Provenance and peer review: Commissioned; not externally peer reviewed.

References are in the version on *bmj.com*.

Cite this as: *BMJ* 2012;345:e7836