

Protecting the safety and security of drugs

COUNTERFEIT MEDICINES THREATEN THE SAFETY AND SECURITY OF SOME OF OUR MOST COMMON PHARMACEUTICAL PRODUCTS AND BRANDS. **DAVID HOWARD**, FORMER CHAIR AND CURRENT BOARD MEMBER OF THE INTERNATIONAL AUTHENTICATION ASSOCIATION, REPORTS ON GLOBAL EFFORTS TO COMBAT THIS GROWING PROBLEM.

Millions of people regularly buy medicines over the internet, but how many of these transactions are genuine and how many consumers end up with counterfeit or substandard products? Research carried out recently suggests that as many as 60% of online products could be counterfeit or substandard.

Protecting the safety and authenticity of pharmaceuticals and drugs has never been more important. The dangers posed to global supply chains by counterfeiting, parallel imports, diversion and even theft are growing the world over, affecting not just the internet but over-the-counter purchases too.

It's a 'silent epidemic' that threatens the health and safety of consumers and is forcing drug manufacturers, retailers and regulatory agencies to step up their efforts to protect brands and products. From the BRIDGE project in Europe, a three-year trial to examine the feasibility of item marking systems, to the new Counterfeit Enforcement Act in the US, it's an issue firmly in the spotlight the world over.

GROWING GLOBAL PROBLEM

The recent outbreak of swine flu, and concern about the legitimacy of some anti-viral drugs advertised on

the internet, has thrust the issue of drug safety firmly into the spotlight once again. It's an issue that affects all countries and has an impact on a huge range of products—from vaccines for meningitis and anti-cancer drugs to everyday products including paracetamol, antibiotics and Viagra.

Counterfeiting is a major issue although a lack of solid, reliable data makes it difficult, perhaps impossible, to quantify precisely.

THE CONSEQUENCES FOR THE HEALTH OF CONSUMERS... CAN BE EXTREME, LEADING IN THE MOST EXTREME CASES TO ILLNESS AND FATALITIES.

The problem is more exaggerated in developing countries where the World Health Organisation (WHO) estimates counterfeit medicines could account for up to 30% of sales. The estimate is around 1% in the USA and other developed countries. In 2007, approximately 3.5 million packs containing counterfeit pharmaceuticals were confiscated at the European Union's borders.

How far this is the tip of the iceberg is unclear but the lack of true data is an obstacle to tackling it. What's not contested is that the problem is escalating and

creating significant problems for manufacturers and consumers. Globalisation, complicated and lengthy supply chains and 'grey' markets like the internet have created a boon for counterfeiters.

The internet, in particular, has been described as a 'Trojan horse'—significantly increasing trade in counterfeit products as consumers take advantage of the discounts and greater discretion afforded by online

purchases. Online pharmacies should be regulated just as retail pharmacies are but are far harder to police.

That's not to say OTC purchases are immune. There have been several cases in the UK where the Medicine and Healthcare Products Regulatory Agency (MHRA) has investigated cases of fake treatments being supplied through the NHS medicines supply chain.

Activities vary considerably from fly-by-night operations to sophisticated factories capable of making medications and packaging that are visually difficult to distinguish

from legitimate products. Worryingly, counterfeiters have moved from making fake medications with no active ingredients (placebos) to producing counterfeits with pharmaceutical activity—often because counterfeiters are looking for repeat business.

Counterfeiting is not the only challenge presented to the pharmaceutical industry by the globalisation of world trade. Globalisation has resulted in a shift towards making active pharmaceutical ingredients (APIs) and finished products outside the developed world—creating issues with standards and quality control.

Closely linked to this is the question of parallel imports. This doesn't happen in America but is legitimate in the EU. While parallel imports can help to reduce the cost of medicines for consumers, it has significantly complicated the supply chain process. Medicines frequently have to be repackaged by parallel importers, which can interfere with the integrity of the product, potentially affect its safety and quality and bringing about an increased risk of counterfeiting and piracy.

RISKY CONSEQUENCES

These developments pose serious risks to society. One of the most copied products is Viagra. Pfizer, makers of Viagra, last year seized more than 11 million counterfeit tablets, capsules and vials masquerading as trademarked goods. Within the last month, German authorities uncovered a counterfeit-drug ring selling fake Viagra via internet pharmacy websites. A prolonged investigation by 60 customs officers produced 46,000 counterfeit tablets and led to the freezing of bank accounts in several countries across Europe.

Selling counterfeit and substandard drugs is big business and highly lucrative. In the developed world,

expensive lifestyle drugs are copied most often. The opposite is true in developing countries where counterfeiters target drugs to treat life-threatening conditions. Money made from counterfeit drugs hits manufacturers' incomes—damaging funding and investment into new drug development—as well as hitting patients in the pocket and cutting tax revenues.

But more severe are the consequences for health and safety. Tamiflu, which has now taken over from Viagra as the spammers' product of choice, is a good example. The British Pharmaceutical Society has warned that anyone buying fake Tamiflu could end up with a product containing sugar or rat poison.

The consequences for the health of consumers using counterfeit or substandard medicines can be extreme, leading in the most extreme cases to illness and fatalities. The WHO estimates that substandard medicines contribute to as many as 200,000 preventable deaths from malaria every year around the world. Sadly, there are countless examples of fatalities caused by the consumption of similar products; including children suffering kidney failure after taking paracetamol syrup in several areas of the developed world.

MOVING IN THE RIGHT DIRECTION

Unless more is done to protect original products, and the supply chain through which they are transported and sold, the problem will grow. Clearly defined and effective strategies need to be put in place to protect brands, authenticate products and ensure their integrity to consumers.

Thankfully it's an issue that's high on the priority list of manufacturers, retailers, customs officials and regulatory bodies, which are working together to put in place effective safety and anti-counterfeiting strategies. Today, this encompasses a range of tools from the latest

authentication devices, traceability technology and on-the-spot checks to new legislation and stiffer penalties. But more still needs to be done and vigilance is required.

Big strides have been made in techniques to improve product safety and security. Manufacturers now incorporate a range of track and trace features—such as barcodes—on their products to give each drug a unique code and allow it to be traced back through the supply chain to the original manufacturer. A multitude of web-based systems are in operation that allow wholesalers, physicians, pharmacists or patients to enter a code provided by the manufacturer to authenticate the product anywhere in the world.

This is backed up by other overt and covert devices to enhance protection measures—particularly in the area of packaging and labels. A range of identifiers such as holograms, colour shifting inks, codes, images and dyes are utilised to create a multi-layered barrier.

In the field, testing devices such as spectrometers and chemical assay kits are increasingly used to check and identify counterfeits or substandard products. A drug's 'fingerprint' can be compared against standards for specific active ingredients, screening out bad products quickly and effectively. China is deploying a fleet of mobile forensic laboratories to examine medicines around the country.

Among the latest innovations are various seals that provide proof of opening and act as a major deterrent to tampering. A seal and protective wallet has been developed for the prescription drug Levitra that shows visibly when the product is opened for the first time.

But technology alone is not enough. Legislatively, the proposed new EU Pharmaceutical Directive is to be welcomed along with other initiatives. These developments will tighten up legislation and supply

chains to protect the integrity of medicines around the world.

One of the key features of the EU Directive is to make security seals and combined security features (authentication and traceability) mandatory on every pharmaceutical pack sold in Europe. This is an important step in ensuring wholesalers and pharmacists are able to verify the authenticity of a product based on overt, covert or forensic means.

On the negative side, the proposed Directive does not cover the internet medicines market. More and more products will be purchased over the internet and tighter regulation is needed to protect brands and ultimately consumer safety.

Significantly, at the same time, a number of tracking systems are being trialled to monitor pharmaceuticals through the supply chain.

The BRIDGE project is a three-year initiative to examine the feasibility of a tracking system across Europe's complex and multi-layered medicines supply chain. Another pilot is trialling a data matrix product coding system with medicines distributors and pharmacists in Sweden.

Taken in isolation, tracking is just one element of the fight against counterfeits. However, when the product is also authenticated—as the proposed EU Directive is striving for—a comprehensive deterrent against counterfeits exists. It's therefore significant that steps to develop tracking systems are taking place at the same time as efforts to make authentication features compulsory.

Another key initiative from the EU is a new €210m (A\$313m) 'Citizen Protection' research fund, and one of the subjects to be covered under this fund is 'Tackling counterfeit medicines and related criminal networks'. This will be a collaborative research project involving at least three organisations in EU member states or accession countries.

Similarly, the US Counterfeit Enforcement Act, which has just been introduced, is set to increase penalties for the sale of counterfeit and contraband drugs. The US Food and Drug Administration has also issued draft guidance on Incorporation of Physical-Chemical Identifiers into Solid Oral Dosage Form Drug Products for Anti-counterfeiting. The guidance note is a mechanism by which the FDA is simplifying the process of incorporating taggants into pharmaceuticals, in an attempt to strengthen supply chain security.

These developments illustrate the growing international and political momentum to tackle the problem and are the latest in a line of tools being employed around the world to improve regulation and control of medicines.

The WHO has been worried about the 'silent epidemic' for a number of years and has put in place an International Medical Products Anti-Counterfeiting Taskforce—IMPACT. The agency is focusing on strengthening anti-counterfeiting technology, harmonising legislation, tougher enforcement, better regulation and public information.

This is an important aim as, tackled collectively, this can be hugely effective. Nigeria is a good role model. Nearly a decade ago, Nigerian health authorities indicated that more than 60% of drugs in the country were fake or adulterated. But a vigorous anti-counterfeiting campaign, including stiffer penalties and banning several dozen Chinese and Indian companies, has reduced this number to 10–16%.

To differentiate between acceptable and counterfeit, or substandard, products is no easy-task. However, as is the case in Nigeria, an effective strategy that incorporates a mix of authentication technologies, backed up by political will and ammunition, can have a big impact. The end result is a significant improvement in product safety and security. ■