

# COUNTERFEIT MEDICINES: A THREAT TO PUBLIC HEALTH AND SAFETY

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## WHAT IS A COUNTERFEIT?

Counterfeit tablets are defined as falsifications that are look-alikes of the genuine medicine, having the correct shape, colour, and imprint. They may or may not contain the same active ingredient as the authentic product. Imitation products are falsifications that do not look like the genuine medicine, but claim or suggest a similar pharmacological effect. They can differ from the genuine product by shape, colour, imprint, or dosage form.

Counterfeits and imitations have been found for various types of medicines from various pharmaceutical companies like Lipitor® (atorvastatin) and Viagra® (sildenafil citrate) from Pfizer for high cholesterol and erectile dysfunction respectively, Zyprexa® (olanzapine) from Eli Lilly for bipolar disorders and Casodex® (bicalutamide) from Astra Zeneca for prostate cancer. The examples used in this article are from Pfizer, who are at the forefront of the battle against counterfeit drugs joined by numerous other companies and authorities across the world.

Figure1 – Counterfeit Viagra® tablets seized in Hungary. Can you tell which is which? The falsification appears on the right, distinguishable by the raised burr around the edge. This particular batch of counterfeits didn't contain any correct active ingredient, instead it was found to contain amphetamine, a stimulant with potent side effects.

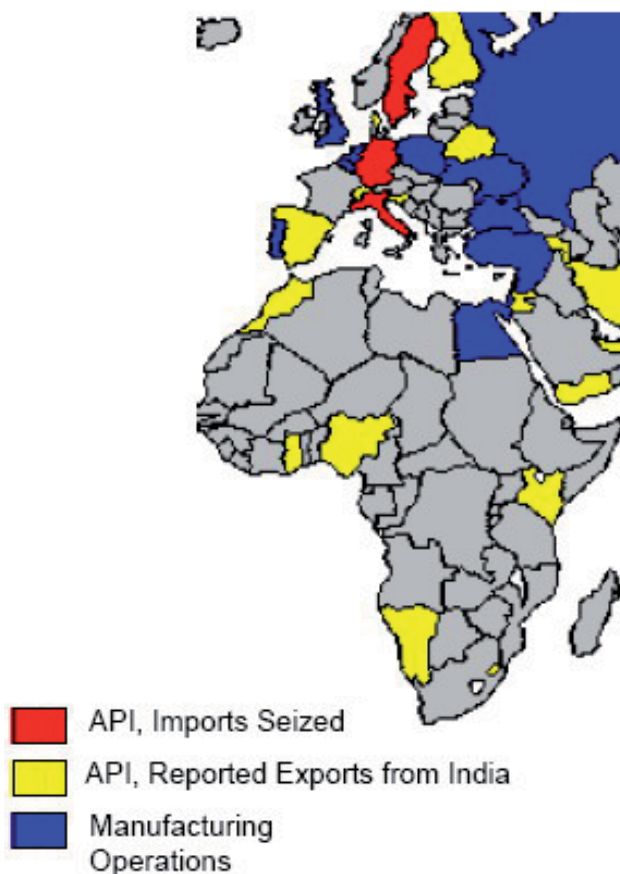


## SCOPE OF THE PROBLEM

As of December 31, 2006, counterfeit Pfizer products had been confirmed in at least 69 countries. The seizure of 100000 counterfeit Viagra® tablets in Zaventem airport on September 4th 2006 is another sign this problem is a growing issue that poses a serious threat to public safety. According to counterfeit experts from the World Customs Organisation the number of counterfeit medicines seized increased with 241% in 2004 compared to 2003 (1), while more up-to-date figures have not yet been published, and a recent study released by the Center for Medicines in the Public Interest, shows global sales of counterfeit prescription drugs are expected to reach \$75 billion by 2010, nearly doubling current levels and outpacing the annual growth rate of legitimate pharmaceutical sales (2).

The countries of origin of many counterfeit medicines include China, India, Pakistan, but production facilities have been found in Europe – including Belgium (3).

Figure 2 – Countries in Europe, Middle East and Africa where counterfeit manufacturing sites have been discovered and counterfeit active pharmaceutical ingredient (API) seized



The main reason for criminals to start copying or imitating prescription drugs is the huge profit that can be made and the low probability of getting caught. The World Customs Organisation estimates the financial loss due to counterfeit to be 5% of global pharmaceutical commerce, equating 20 billion dollars.

The exportation of Active Pharmaceutical Ingredient (API) from India plays an integral role in the manufacture of counterfeit medicines around the world. During the six months from January to July 2005, for example, large quantities (> 250kg) of sildenafil citrate, Viagra®'s active ingredient, were exported from India to Europe, with destination such as Spain, United Kingdom, Netherlands, Germany, Switzerland, Turkey, Ukraine and Belarus. It is important to note that out of one kilogram sildenafil citrate, approximately 14,000 tablets of counterfeit Viagra-pills could be produced. If these are sold at the normal market price of genuine Viagra® a profit of up to 2000% could result. This gain in profit is roughly 10 times higher than trading with heroine. The probability of being caught trading illegal medicines is lower compared to dealing with opioids and if caught the penalties are also often less than those of the illicit drugs trade, with most convictions based on Intellectual Property or Copyright infringement. These might be reasons which contribute to the fast and uncontrolled growth of this dangerous business.

## FROM BACK ALLEYS TO PHARMACY SHELVES - COUNTERFEITS IN LEGITIMATE SUPPLY CHAINS

It's a well known fact that prescription drugs bought through the internet are more often than not falsifications or imitations of the genuine products, since they can be obtained without prescription and their origin is difficult to retrieve. But counterfeit drugs have also been found infiltrating the legitimate supply chain in the past decade (4). It's become more difficult to guarantee the integrity of the supply chain due to its increasing complexity. The expansion of the European Union and the dramatic growth in the number of parallel traders are at the basis of the supply chain's complexity.

## PARALLEL TRADE AND ITS DANGERS

The process of parallel trading involves medicines originally intended for use in one country e.g. Spain, being diverted to another country e.g.

the UK. Pricing and reimbursement is a prerogative of the member states hence prices vary from member state to member state (5). The parallel traders exploit this for their own commercial gain. The consequential cross border trade is legal due to the free movement of goods principle within the EU and is safeguarded under the Treaty of Rome.

Parallel traders import 140 million medicine packs across borders every year within the EEA (6) and each of these can travel through as many as 20-30 pairs of hands before finally reaching the patient (7).

By its nature, parallel trade potentially compromises the integrity of the supply chain which is essential to protect patient safety. The repackaging process, which is integral to parallel trade, can provide a potential vehicle for counterfeit medicines to enter the legitimate supply chain and thus pose a serious threat to patient safety. This process involves the repackaging of individual medicine packs, including the removal of any tamper-proof safeguards, possibly the removal of other security features, and the replacement of the original patient information leaflet (PIL) by a PIL in the language of the country of destination.

Figure 3 – The complexity of the medicines supply chain.

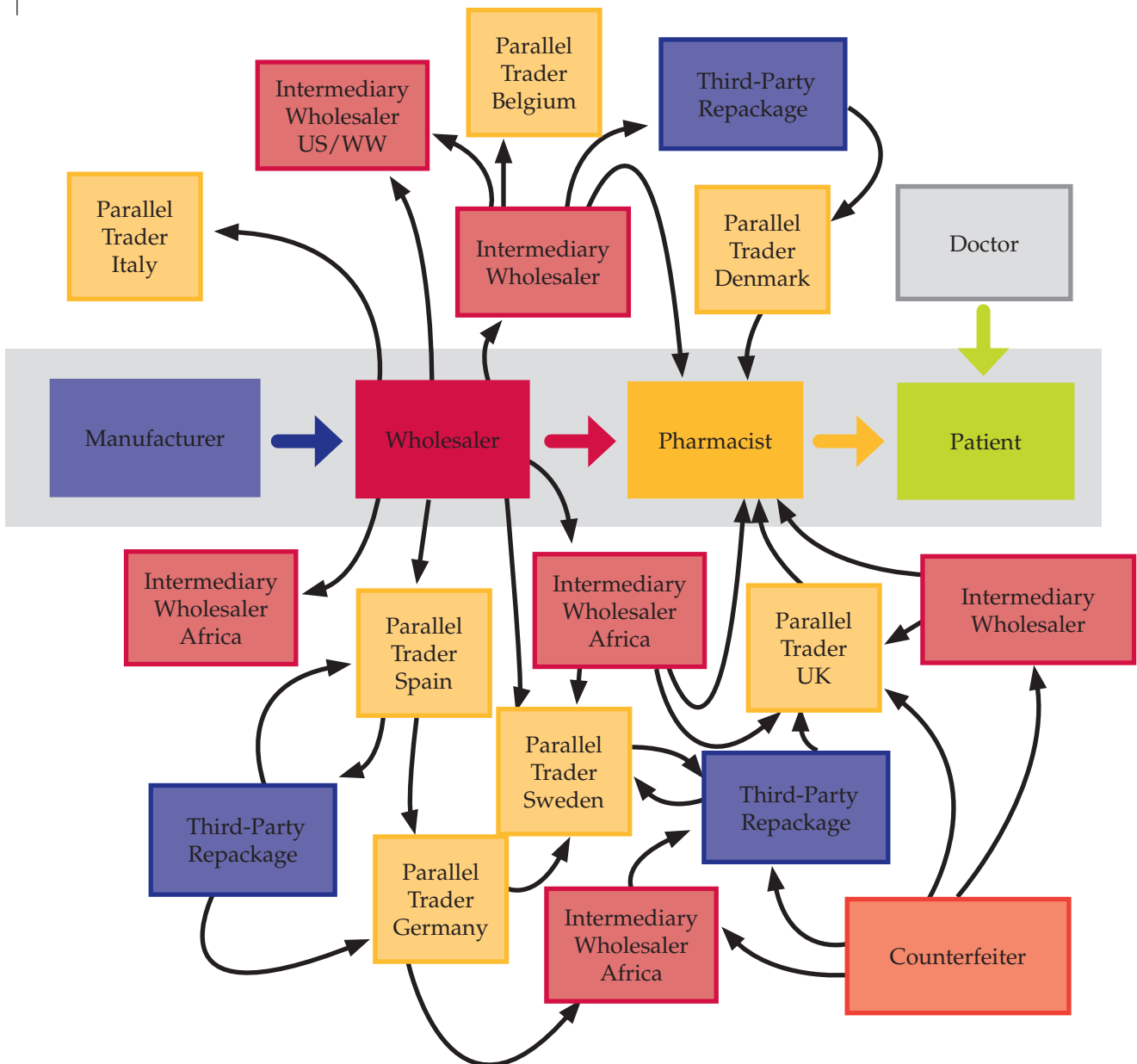


Figure 4 – Counterfeit drug manufacturing device from Egypt.



The process also entails the removal of blister strips and the addition of stickers indicating the name of the product in the destination market, the name and address of the parallel trader. After all this is done, the repackager then reinserts the

blister strips, together with a new PIL, in a new box or the original manufacturer's box, in which case another sticker is applied to the outside, identifying the product in the local language of the country of destination.

The ability of parallel traders to remove the original manufacturers' packaging is leading to a number of problems which are undermining the integrity of the supply chain and posing a potential risk to patient safety. The introduction of counterfeit drugs in the packages is just one, the introduction of human error such as the expiry date and batch numbers on the medicine boxes not matching the expiry date and batch numbers on the medicines inside and patient information leaflets that are in the wrong language or are out of date, is another. Also a full and effective batch recall may be impossible since there is no requirement to record the batch numbers of imported or exported medicines with regulatory authorities across the EU. There is no unified system of track and traceability of medicines, which leads to a concern about how effective a cross border recall could be. Last but not least stock issues arise both in countries exporting and in countries importing via parallel trade.

Figure 5 – Counterfeit packaging in Egypt.



Figure 6 – And storage ...



## A THREAT TO PUBLIC SAFETY

A recent publication from the Dutch National Institute for Public Health and the Environment, reports on analyses of counterfeits and imitations of erection pills seized between 2000 and 2004 (8). This report summarizes the threat to public health posed by falsifications and imitations of prescription drugs and is based on the analytical result of about 400 samples sent in by governmental inspectorates. Most of these samples were confiscated by the governmental bodies and some samples were obtained via the internet.

For Viagra® falsifications, the samples varied from genuine Viagra®, obtained under suspicious circumstances, via look-alikes (counterfeits) to products claiming or suggesting a similar effect, but which could be distinguished from the genuine Viagra® by simple visual inspection (imitations).

Look-alikes were analysed containing sildenafil in the right amount, sildenafil in a much lower amount or other active pharmaceutical ingredients. Imitations were analysed containing sildenafil, sildenafil in combination with another active ingredient; no sildenafil, but another active ingredient or no active substance at all. In most cases the identified compounds were not declared on the label package. In herbal products new sildenafil analogues, of which information about action and side effects is not available, were identified. It's important to note that only 3% of the analysed samples were genuine Viagra® and by the year 2003 all samples obtained from the internet were falsifications.

The report confirms these illegal medicines represent a serious risk to public health and cites the following reasons: the production of the substances and the manufacturing of the products is neither regulated nor supervised by European authorities; the information on the package about the composition of the products is often incorrect or incomplete; the presence of other pharmaceutically active ingredients than the one declared or suggested can lead to unexpected and undesired effects; especially the herbal products with pharmacologically active substances cause extra risks, because consumers tend to believe that herbal products are harmless, and therefore will not attribute the effects to the products.

## THE RESPONSE

Faced with such a highly organised and widespread criminal activity the response from stakeholders has varied tremendously. Regulators such as the MHRA in the UK have done great work with very limited resources but the potential scale of the growing problem demands a better funded and more coordinated and effective national and international approach. All stakeholders need to play their part to secure the supply of medicines, protect patient safety and keep the counterfeiters out. The W.H.O, European Commission, OECD and other international bodies are acting, but when and how this action will translate in to effective policy and well funded regulation and enforcement has yet to be seen. In the meantime, companies like Pfizer have taken action by themselves by introducing security measures on its medicines and providing a more direct and secure supply where pharmacists and patients can better guarantee their medicine's authenticity.

## ACKNOWLEDGEMENTS

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## REFERENCES

Viagra® and Lipitor® are trademarks of Pfizer Inc.  
Zyprexa® is a trademark of Eli Lilly and Company  
Casodex® is a trademark of Astra Zeneca

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## EXAMPLES OF PFIZER'S RESPONSE TO COUNTERFEIT MEDICINES AND SAFE MEDICINES IN PARALLEL TRADE

Pfizer's Global Security Department has undertaken many investigations of on-line pharmacies purporting to sell genuine Pfizer medicines. Many of these cases have subsequently been referred to national regulators or law enforcement bodies who have taken appropriate action. In February 2007, following information provided by Pfizer, the Swedish authorities arrested two people trading through 89 websites selling counterfeit medicines.

Pfizer is partnering with health regulators, global customs and trade organisations to uncover counterfeiters and those who undermine the integrity of genuine medicines, and highlight the threat they pose to patient safety

- Pfizer is a member of the WHO IMPACT group on anti-counterfeiting and regularly contributes to and supports the work of many national and international organisations working to eradicate counterfeits and raise standards in the safe supply of medicines
- Pfizer actively supports the development of independent research to help develop everyone's understanding of the threat to patient safety from counterfeit and substandard medicines
- Pfizer works with many national regulators in investigating counterfeiters and those involved in supplying sub-standard medicines

Pfizer is attempting to render its medicines supply chain more secure through new strategies and new technologies to better protect patients

- Pfizer has introduced direct to pharmacy supply (DTP) of medicines in the UK as a direct response to the threat posed to patient safety from counterfeit medicines
- Pfizer has introduced tamper evident packaging on all its medicines. For those medicines known to be the target of counterfeiters Pfizer has introduced a colour-shifting ink logo that is extremely difficult to copy or reproduce. This is the same technology used on Euro bank notes
- Pfizer is a member of the EFPIA distribution and anti-counterfeiting groups and is active in the joint development of an industry position on the coding of medicines

Figure 7 – The V-tag program in the USA: a unique tag is placed on each bottle of Viagra® during production and a web-based system permits pharmacist to verify authenticity.



Pfizer has built a team of trade and security experts to investigate, monitor and tackle counterfeiting in every region and has invested in state of the art forensic facilities

- Pfizer has a team of five security specialists in Europe who have extensive experience of investigating serious and organised crime. They work closely with law enforcement agencies and regulatory authorities from all over the EEA
- Pfizer's forensic facility at Sandwich in the UK is responsible for analysing over 400 suspected counterfeit medicines from all over the European region each year. They regularly support on-going investigations by law enforcement agencies and regulatory authorities from across the EEA

As the world's largest pharmaceutical company, Pfizer is a leader in raising awareness of the risks from counterfeit medicines and is committed to ensuring all patients receive safe medicines.