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Health Risks of Counterfeit Pharmaceuticals

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Abstract

Pharmaceutical products are not exempt from the practice of counterfeiting. In recent years, many reports have become available demonstrating the presence of fake medicines on the market. Several studies have demonstrated that they are quite often of bad quality.

It is estimated that 5% of all world trade in branded goods is counterfeit, leading to huge financial losses for the pharmaceutical industry. But much more important, from a public health point of view, is that history has shown that such products may lead to a great health risk. The essence of counterfeit products and the reason they are so dangerous is the complete absence of quality control, since they are often indistinguishable from the genuine product.

The existence of counterfeit drugs has long been ignored both by the pharmaceutical industry and by drug regulatory authorities. At present initiatives are being taken, nationally and internationally, to curb counterfeiting. It is now realised that a strong regulatory agency is essential, but the initiatives can only be successful if all parties concerned actively co-operate.

Any product being manufactured anywhere in the world can, and will be, imitated by someone else. In many instances imitations are sold under the name of the original innovator product. Such products are called counterfeit, fake, phoney, or bogus.

Pharmaceutical products[1] are not exempt from the practice of counterfeiting. In particular, in recent years many reports have become available demonstrating the presence of fake medicines on the market.

This article tries to identify the issues regarding the impact that counterfeit drugs make on public and patient health. It gives a number of striking examples and tries to demonstrate to the reader that counterfeit drugs are a major threat to society.

1. Financial Consequences

Counterfeit products on the market represent a considerable loss of income for the manufacturers of genuine products, in the case of medicines probably in the order of several billions of dollars per year.

1 In this article, the terms pharmaceutical product, medicinal product, medicine, and drug are equivalent.

Nobody has exact figures, but if one accepts the estimate from the International Customs Organisation that 5% of all world trade in branded goods is counterfeit, and if the total annual turnover of the pharmaceutical industry is estimated to be $US400 billion, this would mean a financial loss for the industry of $US20 billion annually.[1]

2. Health Risk

Of great importance, from a public health point of view, is the health risk due to fake medicinal products. Counterfeit medicines[2] may sometimes contain the correct ingredients, in incorrect quantities, but often contain either a wrong active ingredient, which may even be toxic, or no active substance at all.

It can be seen that this is what makes counterfeit pharmaceuticals distinct from imitated fashion articles, and what makes the practice so dangerous. History has shown that toxic components, replacing or adulterating the intended ones, may lead to a great health risk.

The catastrophe in Haiti, now some years ago, is in illustrative example of what can happen. Almost 100 cases of fatal kidney insufficiency in children have been documented, following ingestion of a cough syrup containing glycerine heavily contaminated by diethylene glycol (antifreeze). The actual number of deaths may be much higher.[2]

To give another example: predicting what happens when a patient with potentially fatal falciparum malaria is treated with capsules that only contain trace amounts of chloramphenicol, does not require much imagination. This most serious form of malaria needs to be treated with drugs like mefloquine or chloroquine. Chloramphenicol is an antibiotic inactive in malaria.[3]

Counterfeited vaccines, as have been found in Niger and India, may jeopardise vaccination programmes in countries where health programmes are already heavily tried. It has been estimated that between 60 000 and 80 000 children in Niger have been treated with inactive vaccine, which may have led to more than 100 fatal infections from which the victims would otherwise have been protected.[4]

The essence of counterfeit products is by definition their complete absence from all modalities of quality control: these products carry a disguise that makes them indistinguishable from the genuine product. They may carry names of widely known products, or batch numbers of registered products, but all are fake.

3. Industry and Regulators

The existence of counterfeit drugs has been ignored for many years both by the pharmaceutical industry and by drug regulatory authorities and the situation today is not much different from the early 1990s.[3] Industry does not like to be confronted with imitations of their products for fear that both prescribers and patients may lose confidence in their products. Authorities feel guilty for not having their act together when counterfeit drugs prevail on the markets that they are supposed to control.

Fortunately however, on both sides some change in attitude has been noticeable. Under the aegis of the International Federation of Pharmaceutical Manufacturers Associations (IFPMA), industry has established the Pharmaceutical Security Institute, a special institution to investigate and locate counterfeit, and to report on their findings. However, in general their reports have not been provided to the competent authorities (which could have enabled them to take action), and have not been made public.

2 A counterfeit medicine is one which is deliberately and fraudulently mislabelled with respect to identity and/or source.[1]

They are only available within the pharmaceutical industry.

Regulatory authorities equally seem to realise that they have to be more forthcoming with their information, as was recently demonstrated in Brazil. The Ministry of Health shut down a pharmaceutical plant on the suspicion that it was guilty of manufacturing fake contraceptive pills that were reaching the market, and provided the media with ample details on the issue.

The UK has even produced guidelines on dealing with counterfeit drugs,[5] and recently The Copyright etc. and Trademark (Offences and Enforcement) Act was passed, designed to protect the position of patent and copyright owners.[6]

In addition, the European Commission, through its Economic and Social Committee expressed in an "Opinion" its concern, and it suggested a formal political act. Unfortunately the document is very much economically oriented, and does not go into health aspects of drug counterfeiting.[7]

The US FDA recently contracted with New Mexico State University Physical Science Laboratories, and with the consultancy firm, Reconnaissance International as a subcontractor, to undertake a series of Industry/Agency Working Groups, in order to identify areas of risk and opportunities for enhanced security in the US drug supply.[8] The same consultancy firm, together with the WHO, organised a global conference on counterfeiting in Geneva, Switzerland, towards the end of 2002. Participants included the pharmaceutical industry, the WHO, several drug regulators and the anti-counterfeiting industry. Notwithstanding, the activities mentioned above, this conference concluded that there is still a glaring lack of political will to tackle this seriously underestimated problem.[9]

4. The WHO

Notwithstanding the rather indifferent position of industry and regulatory authorities, the Governing Bodies of the WHO reacted to concern about counterfeit medicines at an international conference on the rational use of drugs, held in Nairobi, Kenya, in 1985, and as early as 1988, it adopted a resolution at the World Health Assembly requesting the WHO to initiate programmes for the prevention and detection of the export, import and smuggling of counterfeit, spurious or substandard pharmaceutical products.

However, due to lack of funds it was 5 years before the WHO, together with the IFPMA, was able to organise an international workshop.[10] This meeting identified the relevant issues and formulated recommendations to all parties concerned, including the industry, the authorities and the WHO.

In 1995 Japanese governmental support enabled the WHO to start a project on counterfeit drugs. Apart from a second workshop[6] three major activities characterised the project. Consultations were organised to discuss relevant subjects and to formulate guidelines directed to national Drug Regulatory Authorities in order to assist them in the combat against counterfeit drugs. The database that the WHO had started several years before was reviewed, and two country studies on the prevalence of counterfeit drugs were undertaken. Furthermore, a network (currently comprising some 120 people) was created consisting of responsible individuals in the Ministries of Health in member states. Their role is to provide each other, and the WHO, of any relevant information concerning counterfeit drugs.

The results of the consultations were combined in a comprehensive manual, which contains information and recommendations on the assessment of the size of the problem at country or region level, guidelines directed to governments on the education and training of drug inspectors and analytical laboratory technicians.[11] It describes simple analytical methods for testing suspected samples, and thin-layer chromatography was identified as the most appropriate simple method. Guidelines for countries on

the implementation of an anti-counterfeiting programme were also included.

5. The Size of the Problem

5.1 How Big is the Problem?

What are the odds that a patient buying a drug receives an imitation? Reliable data are hard to obtain. Studies have been carried out in a few countries, but results are not easy to compare because of differences in design, in particular sampling methods. However, within large margins of uncertainty, some conclusions can be drawn.

The investigations by Réseau Médicaments & Développement (ReMeD) in France, carried out in francophone Africa, found that 17% of samples were below official standards, and some 4% were counterfeit.[12] The Pharmaceutical Security Institute has done extensive unpublished studies in the Philippines, comprising some 700 samples. They found that 7% of the products marketed were definitely counterfeit. Two studies done by the WHO in Vietnam and Myanmar obtained similar results, but somewhat lower incidences.[13]

One important aspect to come out of all studies is the often abominable quality of drugs available in uncontrolled street markets: ReMeD found that 17% did not conform to official standards i.e. were substandard, but a study by Poole in Nigeria concluded even higher figures.[14] In some cases the quality of the products was not too far from the standard; however, the provenance of the product was completely unknown. Unknown origin of a pharmaceutical product implicates absence of any guarantee of quality.

The WHO database of cases of counterfeit drugs was started in the 1980s, and is based on anecdotal reports from the literature and on reports from industry and regulatory agencies. Inevitably, the information it contains is diluted by unconfirmed and nonvalidated reports. In the framework of information received through an established network of counterfeit drugs officers in the national Ministries of Health, the database was extended and reorganised.

In spite of the deficiencies of the database, some conclusions can be drawn. Of the 751 cases reported, indications about the quality of the active ingredients contained were supplied only for 325 cases. Of these, about 59% contained no active ingredients, 7% contained the correct amount of active ingredients, 17% contained the incorrect amount of active ingredients and 16% contained different active ingredients. No indication was given about the quality of the active ingredients of the remaining 58% of the case reports.[13]

The majority of cases came from the South Eastern and the Western Pacific (SEARO), and from the African Region (AFRO). Fewer reports were logged in from the American Region (AMRO) and from Europe (EURO) [figure 1]. It may be expected that the number of reports from the AMRO will increase in the near future, now that the Haiti catastrophe has alerted people to this problem. The recent activities by the government of Brazil, resulting in the adoption of new legislation specifically referring to counterfeiting medicinal products may also be the heralds of a more open attitude.

5.2 Which Products Are Most Often Counterfeited?

The database distinguishes between developing and developed countries. In industrial countries the reports refer to all classes of drugs in almost equal frequencies. Contrary to what one would expect, it is not always the most expensive drugs that are most often faked (figure 2).

Note that in the developing world, antibiotics and antiparasitics, the drugs that are most needed there, are the counterfeiters' favourites. Other pharmacotherapeutic groups were represented in almost equal frequencies.

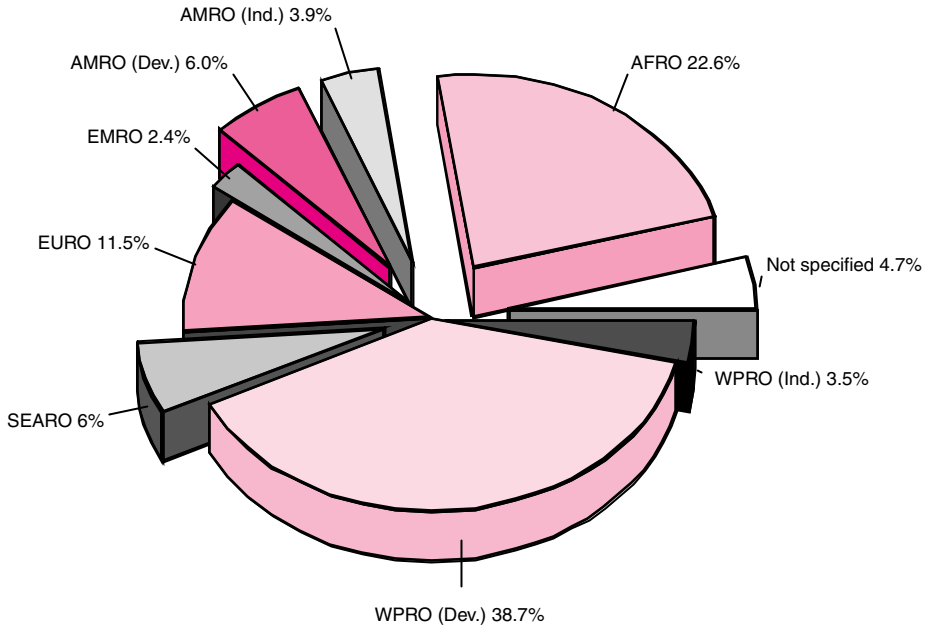

Fig. 1. Geographic origin of reports of counterfeited drugs (WHO regions). **AFRO** = African Regional Office; **AMRO** = American Regional Office; **Dev.** = developing; **EMRO** = Eastern Mediterranean Regional Office; **EURO** = European Regional Office; **Ind.** = industrialised; **SEARO** = South East Asian Regional Office; **WPRO** = Western Pacific Regional Office.

A more precise estimate of the incidence of counterfeit drugs is difficult to make, but one thing is certain: in countries with a weak regulatory system the odds of a patient receiving a drug that does not comply with the standard are often unacceptably high. One dreads to think of the consequences of the fact that in more than one out of ten cases a patient receives a drug that is not up to standard, be it due to counterfeiting or simply incompetence!

6. What Needs to Be Done

A simple remedy does not exist. Those who think that counterfeiting will ever be banned will be disillusioned. The world of counterfeiters of medicines is as opaque as that of narcotic drugs, and eradicating criminal counterfeiting is as difficult to realise as containing narcotic drugs. But this should not lead to despair, on the contrary, concerted action is required from all parties concerned.

Countries with weak regulatory systems are more likely to have counterfeit products on their markets. Drug control systems therefore need to be strengthened and sufficient, competent drug inspectors should be controlling the market. Countries should have access to an operational analytical laboratory to check suspected samples. Drug regulators should collaborate with customs and the police force to detect illegal imports of medicines and take proper action on the basis of legislation that provides the possibility of punishment with sufficient deterrent effect. Experience from Pakistan[15] and Vietnam[16] has shown that impressive results can be obtained.

These and other measures cost money that is often not available in countries that need it most. But both governments and industry should realise that funds used to curb the counterfeiting of drugs is money well spent. Industry should support governments and help them to train inspectors and analytical chemists. Pharmaceutical companies should

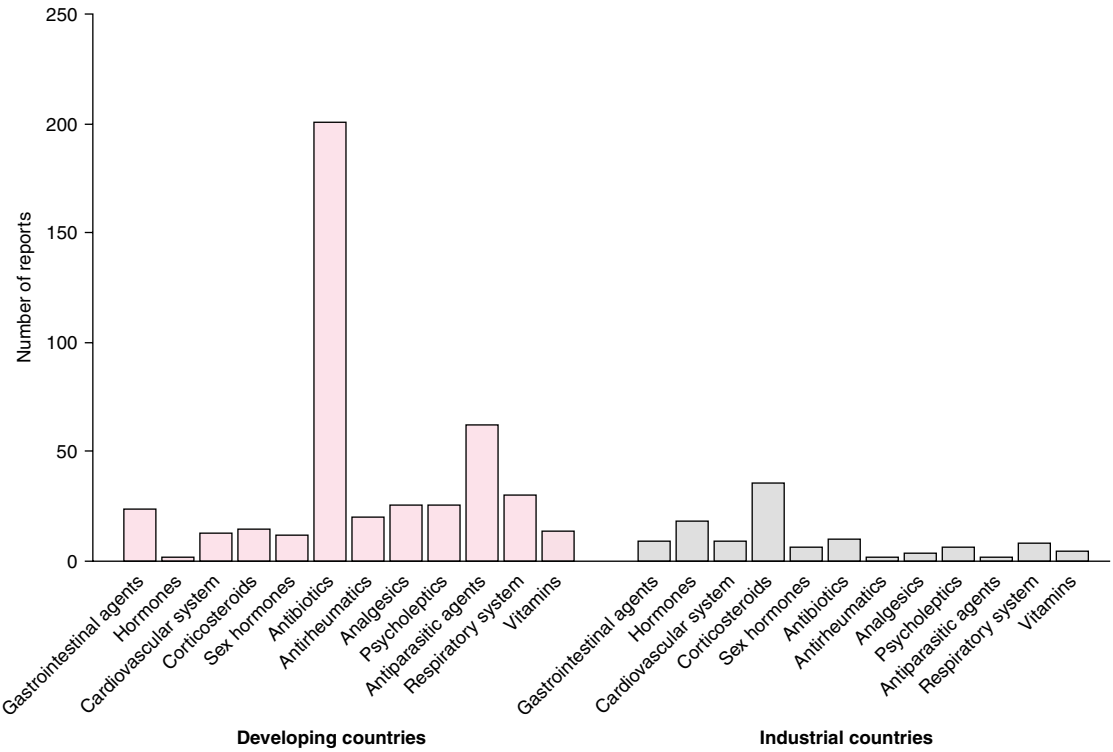

Fig. 2. Comparison of anatomical therapeutic chemical (ATC) classification of counterfeited products in developing and industrial countries.

monitor their customers and do business only with accredited wholesalers, and share their information with the governments in order to facilitate proper legal action.

Doctors and pharmacists should also be alert. When they are confronted with ineffectiveness of a commonly effective therapy they should wonder about the quality and origin of the medicine. Ineffectiveness should be reported to the national adverse drug reactions monitoring system and be registered as an adverse effect.

All parties concerned must know that counterfeit drugs cost money to society at large – a lot of money. But, more important, they are dangerous, sometimes life-threatening. Everyone who has anything to do with medicines should be alert. Only with intensive collaboration by all concerned, can society be spared more disasters, either overt such as the Haiti intoxications, or hidden when a patient does not recover from his illness because of ineffective medicine.

Counterfeiting of medicines has to be eradicated because counterfeit medicines can kill!

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