Vademecum

Against falsified medicines, the best medicine

FALSIFIED MEDICINES

Medicines are subject to review and approval before they can be sold legally without harm or endanger public health. They are properly evaluated to check their quality, safety and efficacy - as required by strict EU authorisation procedures.
The presence of counterfeit medicines in the European Economic Area has been detected worldwide.
The World Health Organization (WHO) globally estimates that about 1% of medicines on the market are fake, and some studies demonstrate a growth in the presence of these medicines on the market.
The Competent Authorities have come to join forces and to actively cooperate both at national and international level to combat these medicines trade on the legal distribution chain.

What are they?

Falsified medicines are fake medicines that pass themselves off as real and authorised medicines. A medicine has to be considered as falsified when a misrepresentation of one or more of the following:

- **identification:** including packaging, labelling (the word "counterferit" refers to infringement of intellectual property rights), name or composition/ dosage of any of its components, including excipients;
- **source:** including the manufacturer, country of manufacture, country of origin or the Holder of the Marketing Authorisation (MA);
- **history:** including the records and documents relating to the distribution channels used.

Are counterfeit medicines dangerous?

Counterfeit medicines may present different types of health risks, such as:

- they may contain a higher amount of the active substance that may lead to overdose;
- the active substance may be present in lower doses than the ones existing in the original medicine, or may even be non-existent and thus, not treating the disease;
- these products might contain harmful substances that endanger the health of users.

How counterfeit medicines reach the final consumer?

Falsified medicines can reach consumers through either the legal market or the illegal market. The legal market has an increasingly complex circuit in which the intervention of a large number of stakeholders requires greater control and traceability of the drug. However, there may be flaws that allow the entry of counterfeit medicines, as analysed in *figure 1*.

The legislation aiming at protecting public health indicates that authorized products must be sold through legal channels created for that purpose, such as pharmacies, non prescription medicines sales stores or through authorized online ordering services and regulated by authorized agencies. Channels, other than those lead to an increased risk of getting a counterfeit medicine, since those do not have any authorization to sell medicines or health products. Within the illegal market supply (shops online, sex shops, food supplement stores, ...), the biggest concern is the sale of medicines over the internet, since most of these products have been illegal and the websites where they are sold have not been legitimate. This is a sales channel that is extremely difficult to take action due to its features, making it difficult to identify offenders.

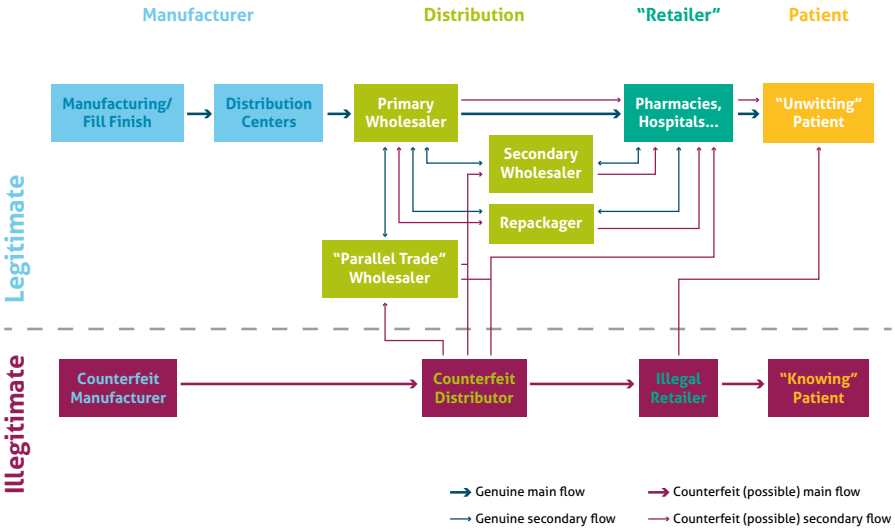


Figure 1 - Product cycle in the legal supply chain with possible action scheme by parallel importers and distributors of counterfeit products. [Source: Shaw, C. J. ,Combating Pharmaceutical Counterfeiting Second Global Congress for Combating. (2005)]

What has been done to combat counterfeiting?

In 2011 the "**European Directive of Counterfeit Drugs**" (Directive 2011/62/EU) was published by the European Union, in order to prevent the entry of counterfeit medicines in the legal supply chain.

The Directive covers key points to brake this phenomenon:

- The adoption of a safety device to be placed individually on medical packaging in order to verify the authenticity and identify individual

packs, and provide evidence of adulteration;
- the adoption of a system that helps a consumer to identify legal websites on the Internet that sell legal medicines at a distance through the creation of a common logo which is recognizable throughout the EU. Online pharmacy websites will be linked to the competent authority webpage, where a list of approved online pharmacies is displayed.

Additional mechanisms to combat counterfeiting were also introduced by this Directive, to be implemented by the authorities, such as the definition of new requirements for import, distribution and manufacture of active substances.

Medicrime Convention

In addition to the publication of the Directive, there are other instruments and initiatives that have been developed in this area. One such example, is the Medicrime Convention, within the Council of Europe, that aims to criminalizing all activities related to counterfeit medicines.

After three years of negotiations, it was opened for signature in 2011 and is expected to be adopted by 47 Member States of the Council of Europe and some "observer" countries.

Groups and International Operations: WGEO and PANGEA operation

The Working Group of Enforcement Officers (WGEO), which is under the aegis of the Group of Heads of Medicines Agencies (HMA), at European level, brings together efforts to combat counterfeit medicines and health products. In this group, the police and customs authorities are represented, and it aims at defining best practices, harmonization of action, sharing of information and participation in the coordination of operations, such as the Pangea operation. The Pangea operation is the largest international joint operation for the detection of counterfeit medicines.

It is an operation coordinated by Interpol and that lasts a week, in which all national medicines authorities, police and customs authorities work together, in the detection of illegal sites and import of counterfeit drugs.
The Pangea operation is a good example of "shared model of investigation". All authorities have similar models, related to already performed investigations.
The WGEO group also has the representation of the pharmaceutical industry through the PSI, which is a non-profit association formed by the directors of various pharmaceutical companies. PSI aims at protecting public health and the sharing of information, and is distinguished from others by its statistical work, which has been developed over the years.
Sharing the model of the cooperation would allow other partners to "copy" the good practices; the "food supplements model" could then become a "Fakeshare model", to be simply made available in our bookshelf.
The proposal of using those models could be a good way for starting a cooperation with other (currently non involved) national stakeholders.

Fake or original: small differences, big consequences

In 2010, the Food and Drug Administration (FDA), the American regulatory agency, was faced with a warning indicating that a medicine for weight loss, **Alli**, was forged.
The product contains a substance in its original composition called **Orlistat**, which acts in the peripheral nervous system and inhibits pancreatic and gastric lipase. After some analysis to the drug, it was discovered that what was in the capsules of Alli, was not Orlistat, but **Sibutramine**, a substance that acts on the central nervous system that has already been withdrawn in some European countries due to its side effects.
The differences between the original product and the counterfeit product were few and difficult to detect:

- the counterfeit product had no batch number indicated and the shelf life was composed by the day, month and year, although in the original, it is indicated only by month;

- the original product was sealed with a statement "sealed for your protection", which was not included in the counterfeit product and the packaging had a different slight height;

- finally, when opening the capsule, one could see that the original product contains granules and the counterfeit product contained a powder.

FAKESHARE I – THE PROJECT

What is it?

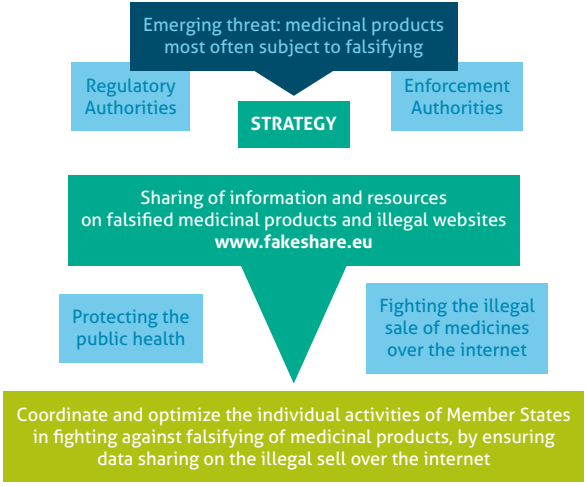
Fakeshare is a European project of cooperation and information launched in 2013, approved and co-funded by the European Commission and coordinated by the Italian Medicines Agency (AIFA). It is inserted in the general context of the **"European Directive of Counterfeit Drugs"** (Directive 2011/62/EU), which intends to protect the health of European citizens against the risks associated with the growing illegal sale of medicines over the internet.

What are the main goals?

The Project aims at encouraging intersectorial and international cooperation between health, police, customs authorities against pharmacrime as for EU Dir. 2011/62 and CoE MEDICRIME Convention.

In details:

- coordinate and optimize the activities developed by individual Member States in



the fight against counterfeiting, thus ensuring a shared management and monitoring of online pharmacies activities by the Information Technology systems.

- implementation of a Web system shared between European Authorities (Regulatory Authorities, Police Forces and Customs) and other entities (industry, academia). This electronic platform with its tools will allow greater cooperation and sharing among involved entities, mainly in the investigation and information management on illegal online pharmacies, which often operate from servers located outside the EU, functioning as entry doors of counterfeit medicines;

Structure

The project has several stages of development, including:

- **PRELIMINARY PHASE.** Data gathering
  - development in the co-beneficiary countries - Portugal, Spain and Italy - of an online survey, in order to characterize the Internet users' profile;
  - Illegal e-pharmacies: classification and performed investigations
  - Illegal medicines and products: investigations, recalls, alerts
  - Existing guidelines and publications
- **WP 1 - PROJECT MANAGEMENT.** Set-up of a restricted multifunctional web platform, to achieve all FAKESHARE objectives:
  - initially, the web platform will be available only to those entities involved by uploading and sharing relevant information in order to optimize and coordinate research and investigative activities;
  - at a second stage the Fakeshare platform will allow public access, through a specific restricted area, thus facilitating the important sharing of information in the protection of public health;

- **WP2 - SHARING OF DATA.** Investigations, studies
  - sharing case studies of falsified medicinal products' detection through the web platform;
  - identification, translation and sharing articles and alerts concerning medicines counterfeiting, through the web platform;
- **WP3- ANALYSIS OF DATA.** Involvement of experts and scientists
- **WP4 - DEVELOP EXPERTISE AND NEW INVESTIGATION METHODS.** Reference documents (investigative/communication models) and web tools for sharing investigation on regular basis:
  - science-based intersectorial investigation projects and models for communication, available to all authorities for launching joint police operations or campaigns to the general public.
- **WP5 - DISSEMINATION AND FEEDBACK.** Models to be used in cooperation between stakeholders

Stages

- management / coordination;
- sharing of information / data:
- analysis of information;
- development of expertise and new research methods;
- dissemination and feedback.

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COORDINATOR

Agenzia Italiana del Farmaco AIFA

CO-BENEFICIARIES

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ASOP Alliance for Safe Online Pharmacies

COMMUNICATION IN THE FRAMEWORK OF COUNTERFEIT MEDICINES

As part of the activities to combat counterfeit drugs, communication and alerts for the general public have a key role.
In this sense, Regulatory Authorities in several countries have also played an active role in communication about counterfeit medicines, through advertising campaigns and other activities to alert the general public.
In the framework of the Fakeshare activities, communication against counterfeit medicines will be strengthened, not only through the dissemination of the project to the direct stakeholders, but also through the communication aimed at professionals and at the general public.
"Risk" is usually defined as a harm that may occur and the probability that it will occur. Perception of risk can change even if the actual risk can not, that means that the perception we have to deal with, is the reality.
Communication of risk needs to involve not only disseminating information but also communicating the complexities and uncertainties associated with risk perception, assessment and management.
Well-managed efforts will help to ensure that messages are constructively formulated, transmitted and received, and that they correspond to actions perceived to be meaningful and justified.

PROTECTIVE MEASURES AGAINST COUNTERFEIT MEDICINES

On 24 June 2014 the European Commission adopted the new **common logo** through the **Implementing Regulation 699/2014**. The logo helps identify the websites which are operating legally. Buying from a legally operating pharmacy or retailer guarantees the safety of the products.
Member States have one year from this date to ensure that provisions on the common logo are applied. Therefore, by July 2015, all online pharmacies or retailers legally operating in the EU should display the logo.
It will be possible in all the European Union (EU) to purchase medicinal products online through the websites of the persons (natural or legal ones) already authorised or entitled to supply medicinal products to the public.
Without prejudice to national legislations prohibiting the offer for sale at a distance of prescription medicinal products to the public, each Member State (MS) has to regulate the online sale of medicinal products not subject to medical prescription to the following conditions:

- the natural or legal persons offering medicinal products online through their own website must have an **authorization or be entitled to supply medicinal products also at a distance** to the public in accordance with national legislation of the MS in which they are established
- the **data of natural or legal persons offering medicinal products to the public at a distance** must be public: name or corporate name, address of the place of activity, starting date of the activity, address of the website used for selling medicinal products and the classification of medicinal products offered for sale
- the person has to comply with the current legislation of the MS of destination of the medicinal products

The **Directive 2011/62/EU**, whilst allowing each MS to impose additional conditions for public health protection, provides indications on the minimal contents that the persons' websites must have:

- the contact details of the competent authority that issued the authorization to supply medicinal products to the public and to which the person notified the starting date of the online sale activity
- the hyperlink to the website of the competent authority of the MS where the person is established. Such website shall provide all the information on the national legislation in force, a description of the legislative differences between the MMSS, the list of the persons authorized in offering medicinal products for sale at a distance to the public and their website addresses, background information on the risks related to medicinal products supplied online to the public illegally.

How does the common logo look like?

The European Commission implementing regulation no. 699/2014 provides the **common logo technical standards** and model for its proper use.
Only logos that exactly match the requirements established by the regulation will be deemed as authentic.

What is the purpose of the logo?

The purpose of the logo is to allow consumers, that are interested in safely purchasing online medicinal products, to distinguish between legal and illegal websites. The logo must be **clearly displayed on all webpages** of the authorized websites and allow consumers to immediately identify the MS where the person is established.

The presence of the logo on a website offering medicinal products to the public at a distance guarantees that the person offering medicinal products for sale at a distance is properly authorized to sell them in the MS of establishment and, as a consequence, that the medicinal products sold online are safe.

How does the logo work?

The logo links to the website of the national competent authority of the MS of establishment and, in particular, to the detailed list of all authorized persons offering medicinal products to the public at a distance. This list must be always updated, reporting the date of the latest updating.

Only pharmacies listed on the National Agency webpage are allowed to take orders over the internet. Thus, when you are dealing with a selling web-page that is not in the aforementioned list, do not take the risk, because the probability of getting a counterfeit medicine and put your health at risk is very high.