Sanofi-aventis takes action against counterfeiting
CONTENT TABLE

I Editorial

II Drug Counterfeiting – a plague on public health
   A Definition
   B Some examples
   C A worldwide issue
   D Amplifying factors of counterfeiting
   E Cooperation with official bodies

III Our commitment in the fight against drug counterfeiting
   A A dedicated organization to fight drug counterfeiting
   B Industrial Activities Against Counterfeiting
   C Technologies developed against counterfeiting
   D Examples of counterfeited drugs

Appendix: Tours pharmaceutical site
Drug counterfeiting is a significant public health threat and is rapidly increasing with dozens of new cases being reported throughout the world every day. Drug counterfeiters must be prosecuted as such, since their products can have serious effects on patients. When we talk about counterfeiting, the issue is not profitability or protection of an innovation. We are talking about public health.

A medicine is not like any other product. Before being marketed, a drug must obtain market authorisation (MA) granted by a competent authority. This MA guarantees the product’s safety, quality and efficacy. “Fake medicines” do not meet these requirements and subsequently are dangerous to an individual’s health. At best, a counterfeit product has no therapeutic effect, at worst the patient can die from it.

All pharmaceutical companies are concerned, whether they are research companies or generic producers. For too long we have underestimated the phenomenon of drug counterfeiting which, from small, marginal beginnings is now completely industrialised and global. According to official World Health Organization (WHO) figures in 2006, drug counterfeiting represented approximately 45 billion euros in sales. This represents almost 10 percent of the world pharmaceutical market.

Even though counterfeiting is a global phenomenon which must be combated throughout the world, the European Union must play a leading role in this fight because counterfeiting is also present here, amplified by parallel trade that allows counterfeit products to circulate freely from one country to another, once inside the Union.

As members of the pharmaceutical community, we have a duty to stand side by side with the authorities and join this battle in the Northern Hemisphere, as well as in the Southern Hemisphere, where most of the counterfeit products circulate. By doing so, we will also contribute to the local economic development of the countries in the Southern Hemisphere where, we are convinced the pharmaceutical industry will play a major part in its future.

This is why sanofi-aventis has made the fight against drug counterfeiting a top priority and is committed to being part of all efforts to be made to overcome this plague on public health.
II Drug counterfeiting—a plague on public health

A Definition

In the etymological meaning, counterfeiting is “the fraudulent copy of another’s product without their consent”.

According to the WHO definition, a medical product is counterfeit “when there is a false representation in relation to its identity (e.g. any misleading statement with respect to name, composition, strength, or other elements), its history or source (e.g. any misleading statement with respect to manufacturer, country of manufacturing, country of origin, marketing authorisation holder).”

This applies to the product, its container or other packaging or labelling information.

Counterfeiting can apply to both branded and generic products.

Therefore, counterfeit products may include:

- products with the correct active ingredient(s), in the correct proportions;
- products with the correct active ingredient(s), but with the wrong dosage;
- products without active ingredient(s);
- products with impurities or toxic ingredients.

B Some examples

Counterfeit drugs can have damaging effects on patients’ health, including death.

In 1995, 89 people died in Haiti after ingesting cough syrup manufactured with diethylene glycol (a chemical commonly used as anti-freeze). This particular product was made in China and transported through a Dutch company to Germany, before winding up on the Haitian market.¹ Counterfeit drugs are even more detrimental to public health efforts when health care resources of the country considered are limited.

A recent survey of seven African countries by WHO found that **between 20% and 90% of all anti-malarials failed quality testing**. These included chloroquine-based syrup and tablets, whose failure rate range from 23% to 38% and sulphadoxine/pyrimethamine tablets, up to 90 percent of which were found to be below standard.¹

¹: WHO: http://www.who.int/en/
A worldwide issue

“For too long, we have underestimated the drug counterfeiting situation. It used to be marginal, it is now totally industrialised.”

Jean-François Dehecq

The United States Food and Drug Administration estimates that counterfeits make up more than 10% of the global medicines market.¹

Many developing countries of Africa, parts of Asia, and parts of Latin America have areas where more than 30% of the medicines on sale can be counterfeit.²

European statistics show in particular a strong increase of drug counterfeit seizures at the European customs, with a total of 2.7 million of drugs seized in 2006, representing a growth of 384% compared to 2005.³

¹: FDA: http://www.fda.gov/
No country is free of drug counterfeiting. Most developed countries with effective regulatory systems and market control (e.g. USA, EU, Australia, Canada, Japan, New Zealand, etc.) currently have a low proportion of counterfeit drugs, less than one percent of market value. However, trends point to a shift and there has been an increase in the prevalence of counterfeit medicines even in developed countries.¹

Recently published WHO analysis shows that counterfeiting is greater in those regions where regulatory and legal oversight is weaker. The problem is further exacerbated by a number of other factors: scarcity and/or erratic supply of basic medicines, uncontrolled distribution chains, large price differentials between genuine and counterfeit medicines, lack of effective intellectual property right protection, lack of regard for quality assurance and corruption in the health-care system.

Today, the most counterfeit branded pharmaceuticals include innovative treatments for severe diseases (anticancers, heart diseases, anticholesterol and antihypertensive drugs, psychologic disorders and infections) whereas before, counterfeit had more to do with lifestyle drugs such as erectile dysfunction.

¹: WHO: http://www.who.int/en/
**D Amplifying factors of counterfeiting**

1 **Parallel trade**

Parallel trade in pharmaceutical products represents a significant volume within the European Union, owing to the price differences fixed by national governments. The European Commission recognises the legality of parallel trade in pursuance of the free circulation of goods.

Nevertheless, in making it easier to distribute medicines within Europe, parallel trade also encourages the development of counterfeiting. As soon as a counterfeit is introduced in one country of the EU, it is then very difficult to prevent it circulating within the EU, due to the absence of customs borders. This amplifies the difficulty of the product’s tracking.

2 **Commerce on the Internet: e-commerce**

In industrialised countries and to some extent in developing countries, Internet-based sales of pharmaceuticals are a major source of counterfeit medicines, threatening those who seek cheaper, stigmatised or unauthorised treatments.

Some Internet pharmacies are completely legal operations, set up to offer clients convenience (Germany, Netherlands, Portugal, United-Kingdom, United-States). These pharmacies require patient prescriptions and deliver medications from government licensed facilities. Some countries, such as the United-Kingdom, have set up a validation system to secure the Internet pharmacies where patients can buy drugs.

Nevertheless, illegal Internet websites sell medications without asking for prescriptions and use unapproved or counterfeit products. In some cases, these Internet websites are operated internationally and sell products that have an unknown or unclear origin. On 31 March 2008, a man was fined over £ 5.000 for illegally selling unlicensed medicines through his website called www.evopharmacy.com. Samples from the tablets showed that they contained sildenafil and tadalafil which are found in erectile dysfunction medication.

According to the WHO, medicines purchased over the Internet from sites that conceal their actual physical address are counterfeit in over 50% of cases.

---

1: WHO: http://www.who.int/en/
2: MHRA: www.mhra.gov.uk
E Cooperation with official bodies

There is no simple or quick solution or remedy that can be applied to eliminate counterfeit medicines, nor can the problem be solved by any individual company or government.

The problem has reached a global dimension and needs a global approach and collaboration. The different players of the fight against counterfeiting emphasize the need for an international regulatory framework.

International Medical Products Anti-Counterfeiting Taskforce (IMPACT)
The WHO launched IMPACT in 2006, in response to the growing public health crisis of counterfeit drugs.
IMPACT is a taskforce of the WHO, exclusively dedicated to drug and medico-surgical material counterfeiting. IMPACT aims to set up guidelines into models to help countries in their fight against drug counterfeiting.

PEI (Protect health, Exchange information, Initiate actions in collaboration with the dedicated authorities)
PEI is a non profitable professional organization, whose missions consist in fighting against theft, illegal misappropriations and drug counterfeiting.
PEI is an organization made up of 27 members, based in Washington DC, assembling pharmaceutical companies, to of which sanofi-aventis became a member on January 1st, 2006.

ACTA (Anti counterfeit Trade Agreement)
In October 2007, the United States, the European Union, Japan, South Korea, Mexico and New Zealand announced a multilateral agreement plan, so as to establish stronger measures and reference standards in order to guarantee the enforcement of protection rules and intellectual property.

The European Federation of Pharmaceutical Industries and Associations (EFPIA) represents the pharmaceutical industry operating in Europe. In Europe, EFPIA supports the call for greater cooperation between the various authorities and for the creation of an international convention to fight the curse of medicine counterfeiting.
The Medicines and Healthcare products Regulatory Agency (MHRA) has a pre-eminent role in Europe since it is the only European Drug Regulatory Authority (and one of very few worldwide) that has its own dedicated Unit responsible for criminal investigations. The strategy sets out a three year plan to combat counterfeit medicines and devices through a sustained programme of communication, collaboration and regulation.

Business Action to Stop Counterfeiting and Piracy (BASCAP)
In response to the growing threat of counterfeiting, the International Chamber of Commerce has launched BASCAP with the aim of gathering all business sectors and cut across all national borders in the fight against counterfeiting and piracy. This global approach is designed to support individual company and organizational efforts and amplify business messages with national governments and intergovernmental organizations.

Sanofi-aventis works in close collaboration with these agencies, with the European Commission and the European Council, as well as with International Organisations such as Interpol, International Customs Organisation (ICO), and with ministries, customs, police, pharmacists, wholesalers and other pharmaceutical companies to investigate suspected counterfeiters.
III Our commitment in the fight against drug counterfeiting

A A dedicated organization to fight drug counterfeiting

The anti-counterfeiting department is composed of a team of expert investigators who have worked with the police, secret service and customs agencies. The Paris-based department coordinates a network of local and regional agents across the world.

This operational network makes it possible to react quickly and efficiently against increasingly well-organised and professional counterfeiters who now have better smuggling routes, more sophisticated means of manufacturing counterfeit goods and the support of organised crime.

To combat the counterfeiting plague, the anti-counterfeiting department has developed a multi-faceted strategy:

- Gathering and analysing information;
- Pooling skills and know-how with competent national authorities such as police and other law-enforcement agencies, customs, health officials, etc.);
- Participation in operational efforts to combat counterfeiting such as the World Customs Organization’s ‘Secure’ group, the World Health Organization’s ‘IMPACT’ group, Interpol and the World Intellectual Property Organization;
- Active partnerships with other sanofi-aventis departments (assistance in recognising products).
Even more importantly, the anti-counterfeiting department is involved in concrete actions to stop counterfeiters by:

- Monitoring internet activity;
- Monitoring distribution;
- Instigating and carrying out investigations;
- Identifying networks so that responsible parties can be brought to justice, their organisations dismantled and counterfeit products seized and destroyed.
Industrial Activities Against Counterfeiting

In the context of the sanofi-aventis anti-counterfeit programme, a new Central Anti-Counterfeit Laboratory has been set up on the Tours (France) production site.

Its assignments are as follows:

- To help protect the assets of the sanofi-aventis group;
- To ensure pooling of the analysis results and guarantee protection of the data generated.

To achieve this, the laboratory, equipped with the latest technology, consists of a team of 5 experts and a network in Industrial Affairs.

The procedures introduced to ensure the success of the previously-mentioned assignments are:

- Visual inspection of counterfeit samples, copies or generics;
- Routine chemical analyses;
- Management of specific requests for additional analysis from expert laboratories;
- Drafting of analysis and traceability reports on suspect products;
- Management of the central counterfeit, copies and generics analysis database;
- Cooperation with the legal/brands management through the collection of information for customs files.

The Laboratory Good Practices standards represent a benchmark in terms of guaranteeing the reliability of results and their possible acceptance in the case of legal action.
Functioning process of the Central Anti-Counterfeit Control Laboratory
Technologies developed against counterfeiting

Sanofi-aventis is actively fighting counterfeiting at several levels, through packaging protection programs intended for making them more difficult to copy and easier to authenticate.

- Tamper-proof systems
- Visible and hidden authentication systems.

**Sanofi-aventis security label (SASL).**
Developed exclusively for sanofi-aventis by one of the world’s leading manufacturers of security paper (bank notes, ...), this security label is a tamper-proof security label, measuring 25x15 mm, attached to the packaging of high-risk products.

As of January 2011, traceability technology based on bar codes (Datamatrix) will be put in place in France and in Europe. The final objective for having set up this code is to ensure traceability of each box in its supply chain to the pharmacist until the end-user, the patient.
Examples of counterfeited drugs

Some counterfeit products will be reasonably obvious to the naked eye; they may display poor packaging or spelling errors. Other examples can however be more difficult to detect.

The following photographs illustrate how easy or difficult it can be to detect counterfeit medicines:

Plavix® from sanofi-aventis

Counterfeit Plavix®

Counterfeit rimonabant®

The names of the compounds have been blurred
Useful links

- World Health Organization (WHO)
  http://www.who.int/topics/pharmaceutical_products/en/
  http://www.who.int/mediacentre/factsheets/fs275/en/

- International Medical Products Anti-Counterfeiting Taskforce (IMPACT)
  http://www.who.int/impact/en/

- European Federation of Pharmaceutical Industries and Association (EFPIA)
  http://www.efpia.org/

- International Pharmaceutical Federation (FIP)
  http://www.fip.nl/www2/

- International Federation of Pharmaceutical Manufacturers and Association (IFPMA)
  http://www.ifpma.org/index.aspx

- U.S. Food and Drug Administration (FDA)
  http://www.fda.gov/oc/initiatives/counterfeit/default.htm
  http://www.fda.gov/opacom/7alerts.html

- Reporting Unlawful Sales of Medical Products on the Internet
  http://www.fda.gov/oc/buyonline/buyonlineform.htm

- Medicines and Healthcare products Regulatory Agency (MHRA)

- Pharmaceutical Research and Manufacturers of America (PhRMA)
  http://www.phrma.org/

- National Association Boards of Pharmacy (NABP)
  http://www.vipps.info/

- World Health Professions Alliance
  http://www.whpa.org/

- INTERPOL
  http://www.interpol.int/
Opened in 1967, the Tours industrial site is mainly dedicated to the production and packaging of oral solid forms of compounds (tablets and capsules) including several of the Group’s major drugs, such as Stilnox®/Ambien®, Aprovel®, Amaryl®, Xatral®, Acomplia®.

With an annual production of **61 million boxes** (i.e., 2.5 billion units) in 2007, this sanofi-aventis site is a major economic player in the ‘Centre’ region of France.

The site employs **450 people**, working in production units, industrial development, and business support activities and covers **65,000 m²**.
# History of the Tours Site

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>1967</td>
<td>Site inauguration (Dausse Laboratories)</td>
</tr>
<tr>
<td>1970</td>
<td>Dausse Laboratories and Robert &amp; Carrière Merger: Birth of the Synthelabo Group</td>
</tr>
<tr>
<td>1984</td>
<td>Launch of Stilnox®</td>
</tr>
<tr>
<td>1986</td>
<td>Launch of Xatral®</td>
</tr>
<tr>
<td>1999</td>
<td>Sanofi-Synthelabo Merger</td>
</tr>
<tr>
<td>2000</td>
<td>Launch of Xatral® o.d.</td>
</tr>
<tr>
<td>2004</td>
<td>Acquisition of Aventis</td>
</tr>
<tr>
<td>2005</td>
<td>Launch of Ambien® CR</td>
</tr>
<tr>
<td>2006</td>
<td>Launch of Acomplia® in Europe</td>
</tr>
</tbody>
</table>

## Main drugs produced on the Tours site

- **Stilnox®/Ambien® (zolpidem) - Insomnia**
- **Xatral® (alfuzosine) - Benign Prostatic Hyperplasia**
- **Aprovel® (irbesartan) - Hypertension**
- **Telfast®/Allegra® (fexofenadine) - Allergy**
- **Tildiem® (diltiazem) - Angina (pectoris)**
- **Kerlone® (bétaxolol) - Hypertension**
- **Mizollen® (mizolastine) - Allergy**
- **Ditropan® (oxybutynine) - Urinary voiding**