SANOFI FIGHTS AGAINST COUNTERFEIT MEDICINES
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Counterfeit medicines around the world

- One in every 10 drugs sold around the world is fake, and this can reach 7 out of 10 in some countries1.
- The number of identified cases of counterfeit drugs increased by 9% between 2008 and 20102.
- In 2011, medicines ranked first among the list of counterfeit products kept by European customs (24% of total), beating counterfeit cigarettes3.
- U.S. $75 billion in 2010: The profits from counterfeit medicines are higher than the profits from drug trafficking4.
- For every U.S. $1,000 invested, a criminal can garner U.S. $20,000 profits from heroin and U.S. $400,000 from trafficking in counterfeit drugs5.
- In 2012, 100 countries collaborated with Operation Pangea V to fight against illegal online pharmacies. This resulted in 79 arrests and the seizure of 3.75 million potentially deadly medicines worth a total of $10.5 million6.

The Central Anti-Counterfeit Laboratory

- In 2008: creation of the laboratory in Tours.
- The analysis of suspect medicines involves four steps.
- The Laboratory has analyzed about 20,000 suspect products since it began.
- About 3,000 products were analyzed in 2012 with 200 confirmed cases of adulterated products.
- Within five years, the laboratory staff has more than doubled.

1 www.leem.org (décembre 2011)
2 Pharmaceutical Security Institute “2011 situation report”
3 Report on UE customs enforcement of intellectual property rights 2011
4 Institute of Research Against Counterfeit Medicines (IRACM)
5 Institute of Research Against Counterfeit Medicines (IRACM)
6 Interpol - Operation “Pangea V”
Why have counterfeit medicines taken on such importance?

First, we are seeing a geographical intensification of counterfeiting which is no longer focused on one or two parts of the world, but is now global, largely because of the internet. And this touches on every therapeutic class. So it is not just about lifestyle products: drugs for treating chronic and serious diseases such as cardiovascular diseases or cancer can now be counterfeited. These can lead to individual and also collective risks, especially due to the emergence of drug-resistance in the case of treatments for infectious diseases with antibiotics or antimalarials.

Why is it so vital to fight against counterfeiting?

Counterfeit medicines are a real danger to patient health. They don’t contain the expected amount of active ingredient and they don’t meet any of the standard requirements for quality, efficiency and safety. So patients run a number of risks: besides the presence of toxic substances, these drugs can be inactive and cause major adverse effects and complications for patients. Fake drugs can also undermine patients’ confidence in the health system by virtue of the infringement of their legitimate right to be treated with quality medication. So there is a major ethical concern here. When you buy a medicine, you have no reason to think that it is a fake. This means that patients are victims of this trafficking.

Five years after the creation of the Central Anti-Counterfeiting Laboratory, what major advances have been made?

In just five years, the laboratory has constantly expanded its activities and now receives some 3,000 samples each year. The number of employees has more than doubled as we now receive requests about products from all over the world, either from health authorities or from seizures by the police and customs that send us samples for analysis. We have also stepped up our vigilance internally and are working closely with our pharmacovigilance and quality departments to track any medicines that may raise a suspicion of counterfeiting. We have also fine-tuned our technology to recognize and correlate different cases. This means we can compare product profiles, cross check where they came from, and provide valuable information to the authorities.
FIGHTING COUNTERFEIT DRUGS: A MAJOR SANOFI COMMITMENT

» How can we fight against counterfeiting?

In 2007, Sanofi set up a central coordinating unit which brings together internal experts involved in counterfeit medicines from its Industrial Affairs, Security, Medical and Regulatory Affairs, Legal, Public Affairs and Communication teams. By meshing these together operationally, the Group is able to react more quickly and take practical steps against medicine counterfeiting. In 2008, Sanofi created the Central Anti-Counterfeiting Laboratory (LCAC) at the Tours pharmaceutical site to analyze medicines suspected of being counterfeit versions of Group products.

What happens when a product is found to be a counterfeit?

The Security Department makes safety checks on the basis of the evidence. They then cross check this information to prepare a case that is then presented to the police or customs in the relevant countries. This network draws on the expertise of security officials throughout the world, collecting information and evidence to corroborate with the information obtained in the field and then shares it with other pharmaceutical companies. This collaboration operates among members of the PSI (Pharmaceutical Security Institute), which brings together the security directors from 25 pharmaceutical companies.

What is your approach to dealing with the growing influence of the Internet?

We have a team in charge of looking for counterfeit goods on the Internet in close contact with subsidiary security managers. The objective is to identify illegal websites selling the Group’s molecules and take appropriate action. For example, this information can be sent to Interpol, which every year carries out large-scale operations to dismantle networks selling medicines illegally online.
How much international collaboration is there?

Sanofi is committed to encouraging governments to implement stronger legal measures to fight counterfeit medicines. In December 2010, the Council of Europe adopted the MEDICRIME convention to criminalize the counterfeiting of medical products, which was signed by 22 countries.

Sanofi has also engaged the United Nations Office on Drugs and Crime (ONUDC). With their global political reach, the United Nations can certainly play an important role as part of the United Nations Convention of 2000 against transnational organized crime by declaring counterfeit medicines to be a criminal activity.

Interpol underpins cooperation between police forces around the world in making illicit international activities a key part of their agenda. In 2012, 100 countries collaborated in Operation Pangea V to fight against the illegal sale of medicines online. This resulted in 79 arrests and the seizure of 3.75 million potentially lethal medicines for a total value of nearly $10.5M.

The World Customs Organization also organizes flash searches of containers in various parts of the world. In 2011, the WCO developed a system for customs information and cooperation, to which Sanofi has subscribed. Customs officers can log into the database and view images of different products so they to identify counterfeit medicines more easily.

“For 1,000 dollars invested, a criminal can garner 20,000 dollars in profits with trafficking heroin and 400,000 dollars by dealing in counterfeit drugs.”
How can medicines be protected against counterfeiting?

The three levels of protection

The Group has developed a three-level approach to protecting its products. Only levels 1 and 3 are enforced by the European Falsified Medicines Directive of July 2011.

**LEVEL 1** Protecting the integrity and inviolability of the box

For Frédéric Bourgeois, Associate Vice President Global Supply Chain Quality at Sanofi, “Level 1 is very important. If you protect your box without ensuring its inviolability, counterfeiters can open the box and insert fake products.” Proof of tampering can be incorporated into different types of protective devices: pre-cut, torn-off glue dots, labels on the box tab, etc.

**LEVEL 2** Authenticating the product

To check the authenticity of its products, Sanofi has developed special high-security labels that contain both visible (for distributors and patients) and invisible identifiers (known only to Sanofi). This level of protection has been introduced for medicines most at risk from counterfeiting and for all of the Group’s new medicines. Others may also be concerned if they are subject to increased counterfeiting in certain countries. Frédéric Bourgeois explains that “when faced with a regional or historic increase in falsified medicines, we can decide to protect certain products by using special high-security labels because for Sanofi the health of patients is absolutely essential.”

**LEVEL 3** Identifying each box using a Data Matrix

Since January 1, 2011 in accordance with the legislation, all Sanofi products sold in France are identified using a two-dimensional bar code printed on each box containing the following traceability information: the product code, the batch number, and the expiry date. By systematically reading the Data Matrix in pharmacies, the traceability of medicines delivered to pharmacies or hospitals can be improved, and it also enables the automatic detection of obsolete batches.

Aiming for better traceability

Sanofi has supported the **mass serialization project proposed by EFPIA** to identify each box. The underlying principle consists in associating a unique random number series with the box’s Data Matrix. This number will be coded and affixed to the product when it is packaged and also sent to a central database. When the pharmacist queries the system, he will know whether that number exists and whether it has already been sold. Frédéric Bourgeois says that “this is the most complex system to implement. The database must be perfectly confidential and reliable, with a rapid response time for the pharmacist. This control will also aid in the fight against reimbursement fraud.” Tests were carried out in Sweden in 2009/2010 and, since early 2013, a pilot project was implemented on a larger scale in Germany. The ultimate goal is for all European Member States to adopt this system, and such identification technology must be harmonized to be fully effective.
Raising awareness among all stakeholders

The general public. "The general public is not really aware of the existence of counterfeit medicines and the risks they incur," says Caroline Atlani. In December 2012 and January 2013, Sanofi launched an awareness-raising campaign targeting more than four million Air France travelers to North America, Latin America, Africa, the Middle East, Asia and the Pacific, by screening a film aboard airplanes and inserting a page of practical tips in the Air France magazine. Sanofi has also published a brochure for Internet users.

The scientific and medical community. The goal is for all healthcare professionals to be integrally associated with promoting the message. In France, pharmacists are being involved as they are well placed to communicate the risks incurred by buying medicines illegally.

Police and customs. Sanofi recently signed a partnership with Interpol together with 29 major pharmaceutical companies. The three-year agreement for a total cost of €4.5M covers the creation of the Interpol Pharmaceutical Crime Program, focusing on fighting counterfeit medicines. It will combine training with targeted enforcement actions.

Governments and institutions. Sanofi is participating in a number of working groups and conferences, such as the UNODC conference held in February 2013 with representatives from Interpol, WCO, WHO, Member States and pharmaceutical companies. The aim is to mobilize countries to strengthen any laws that provide for insufficient penalties. The issue was also raised at the G8.
In 2008, Sanofi created the Central Anti-Counterfeit Laboratory (LCAC) in Tours to centralize all Sanofi products requiring verification about their counterfeit status. The aim is to deploy a dedicated team of experts and technologies to detect fake medicines. This laboratory is part of Sanofi’s Industrial Development and Innovation division and addresses the need to anticipate innovation in a rapidly changing field.

» Who sends suspect products to the laboratory?

The largest proportion of the products received by the laboratory comes from Sanofi’s own market surveillance operations through test purchases in high-risk countries and tests on sensitive products, both on the Internet and in pharmacies. Other products come from customs, the police, health authorities and health workers. Patients can also report a suspect product to a Sanofi subsidiary.

» What is the laboratory’s agenda?

» Perform technical reviews of the packaging and usage leaflet as well as the most advanced chemical analysis of suspected samples of the most commonly counterfeited products.

» Develop analytical methods and disseminate them globally to allow each Group industrial site anywhere in the world to examine and analyze all suspect products corresponding to those made by the Group, using the same criteria.

» Centralize "identity cards" corresponding to a list of identified counterfeits in a single, central database, which is the only way to spot links between the various counterfeits.

The LCAC is one of the most successful approaches taken in any major pharmaceutical company. The process has driven the search for the protection of medicines into a new dimension, especially with the formation of identity cards.

The LCAC helps train customs agencies around the world by means of the IPM (Interface Public Members) portal of the WCO, supplying useful information to customs officials to detect counterfeit products. It gives customs services concrete evidence in the field and enables them to detect counterfeit products more effectively.
How to detect a fake medicine in four steps:

**STEP 1** Traceability

The first level of evaluation is to search for information in the database to see if the product has been manufactured in a Sanofi site. Everything from the batch number, date of manufacture, and packaging is analyzed. If an error is spotted, an action is immediately triggered.

**STEP 2** Visual scrutiny

The product is given a microscopic examination: print fonts, printing techniques, packaging, engravings, glue tabs on boxes can all be compared using imaging techniques.

**STEP 3** General chemical analysis

The chemical fingerprint is examining using spectroscopic techniques that give a first level analysis of the product’s composition and allows the characteristics to be compared against the reference products stored in databases.

These three steps will, in most cases, quickly identify whether or not it is a counterfeit medicine.

**STEP 4** Detailed chemical analysis

If it is clear that it is a counterfeit product, the final step is to extend the chemical analysis to determine whether the product contains the active ingredient, or toxic compounds, etc. This step applies gas or liquid chromatographic techniques to identify unknown components as traces or in larger quantities.
What do you do with this information?

A report containing all the results on the product is drafted and sent to the coordination unit that will make the appropriate overtures to the relevant authorities.

Since 2008, the Laboratory has analyzed about 20,000 suspect products. The outcomes of these analyses have been used to build a solid foundation for mobilizing local authorities, conduct legal actions, and also set up proactive programs to fight counterfeit medicines in countries where cases of counterfeiting have been identified.

How can you deal with the diversification of counterfeit products?

In just five years, the laboratory workforce has more than doubled from five to twelve people. "Apart from the actual volume of our activity, the most important aspect is the development of this new profession and the emergence of new skills," says Nathalie Tallet. "When we started in 2008, we were rather focused on standardized quality control techniques. But since then, we have developed much more specialized skills." These make it possible, for example, to work much faster and develop new techniques to handle higher volumes. What is driving our development is more the need for a more varied skills base and more structured teams rather than the sheer volume of analyses.

Some 3,000 products were analyzed in 2012 with 200 confirmed cases of counterfeit products. While the number of analyzed medicines remains stable, the nature of the products analyzed is expanding considerably. Nathalie Tallet stresses the need for the laboratory to be at the forefront of technology innovation to meet the challenges of the growing diversity of products. "Every therapeutic class is involved in counterfeiting, and our portfolio of products to be analyzed is growing almost by the day."

New pharmaceutical forms are also affected by counterfeiting. In 2008, the main focus was on solid forms, whereas now injectables (for treating cancers and serious diseases) play a major role in counterfeit drugs.

"Since 2008, the Laboratory has analyzed some 20,000 suspect products."
How can counterfeit medicines be defined?

For the World Health Organization (WHO), a counterfeit medicine is one which is deliberately and fraudulently mislabeled with respect to identity and/or source.

For the new directive of the European Parliament and of the Council published in the Official Journal on July 1, 2011, a counterfeit medicine is defined as a medicinal product bearing a false representation of:

- Its identity, including its packaging and labeling, its name or its composition, with respect to any of its components, including excipients, and the dosage of these components;
- Its source, including its manufacturer, country of manufacturing, country of origin or the holder of the marketing authorization;
- Its history, including records and documents relating to the distribution channels used.

Falsification may involve both branded and generic products.

The risks incurred in counterfeit medicines involve:

- the safety and health of patients;
- public health in general;
- damage to the environment;
- a breach of ethics.

A counterfeit medicine can be a product containing:

- uno trace of the active ingredient;
- the right active ingredients, but the wrong dosage;
- impurities or toxic substances;
- other active ingredients than those found in the genuine product.

"Counterfeit drugs can be dangerous to health."
The market for fake medicines

According to the WHO, the incidence of counterfeit drugs is very low in most industrialized countries with regulatory systems and effective market controls (Australia, Canada, Japan, New Zealand, United States and most of the European Union). It represents less than 1% of the value of the market.

The proportion of counterfeit medicines is much higher, however, in many African countries, parts of Asia and Latin America and in emerging countries, with up to 20-30% of the market. The distribution channels in these regions are less controlled, and it is more difficult to prevent counterfeiters from infiltrating supply networks.

Counterfeiting circuits manage to cross all borders. Falsified products can be manufactured in China and exported to Britain and infiltrate the legal distribution chain via a wholesaler into or be purchased on the Internet anywhere in the world.

The Internet has become a major platform for circulating counterfeit medicines. According to the WHO, in more than 50% of cases medicines purchased from Websites that conceal their physical address are counterfeit.

Counterfeiting according to the law

In many countries counterfeiting in general, and especially the counterfeiting of medicines, is not a criminal offense. When it is, penalties are usually not specific to the falsification of medicines, but common to all cases of counterfeiting, especially the infringement of intellectual property rights.

Penalties vary from country to country and may include fines, imprisonment, the confiscation and destruction of counterfeit goods, loss of civil rights or of the right to exercise certain professions. Counterfeiters can also be ordered to pay damages.

How does Sanofi recommend?

In legal terms, Sanofi’s approach is to look for criminal penalties to neutralize counterfeiters rather than seek compensation if the law allows this.
The international framework

The MEDICRIME Convention
The Council of Europe has developed the first international legal instrument in criminal matters that is specific to counterfeit medical products: The MEDICRIME Convention was adopted on December 8, 2010.

This international convention qualifies criminal offenses including the manufacture of counterfeit medical products and their marketing. This text is open for signature by the 47 Council of Europe and all other States that wish to work with the Council of Europe in the fight against counterfeit medical products. Twenty-two countries have signed to date (including three that are not part of the Council of Europe). Only Ukraine has ratified this agreement.

http://conventions.coe.int/Treaty/Commun/ChercheSig.asp?NT=211&CM=8&DF=&CL=FRE

The Cotonou Agreement
Launched at the initiative of former French President Jacques Chirac on October 12, 2009. Sanofi supports the Cotonou Agreement to encourage the international community to develop a comprehensive legal response and strengthen collaboration between civil society and national public services against trafficking in counterfeit drugs.

The European Directive on Falsified Medicines
Adopted on June 8, 2011, this Directive aims to make the legal supply chain for medicines fully secure.

It refers specifically to the issue of counterfeit medicines rather than to the infringement of intellectual property rights. Sanofi was actively involved in the work groups that led to the adoption of this Directive.
ADVICE FOR PATIENTS
ON THE INTERNET AND WHEN TRAVELING

What are the risks on the Internet?

There are legal online pharmacies that have been created to facilitate access to medicines for patients (e.g., in Germany, USA, France, Netherlands, Portugal, and the United Kingdom). Fifteen European countries have legalized the sale of medicines on the Internet. However, a large number of websites operate illegally offering prescription-free medicines that are normally sold on prescription, as well as selling unapproved or counterfeit products. Run by illegal organizations, these outlets function as a network, hiding their true identity or lying about their location.

The European Directive on Falsified Medicines contains a special chapter on the Internet, including the establishment of a system of lists of online pharmacies approved by the competent Member State authorities, the use of a common logo, and an information campaign targeting patients about the risks of medicines sold illegally on the internet.

In France, Sanofi is a signatory of the Charter on the Fight Against Cyber-Counterfeiting of December 16, 2009. By virtue this charter, intellectual property holders and ecommerce sites undertake to implement concrete measures to fight against the sale of counterfeit goods on the Internet.

Sanofi works closely with the relevant authorities, technical operators, financial organizations and e-commerce sites to take effective action against illegal pharmacies and counterfeit medicines on the Internet.

What can I do in practice?

Never respond to email spam messages offering medicines as they are often from a fraudulent source.

Don’t give out information about your personal health online.

In France, since the decree published in the Official Journal of January 1, 2013, the sale of medicines on the Internet is legal under certain conditions. It does not apply to medicinal products subject to medical prescription: the list of drugs that can be sold online is published on the website of the MSNA (French National Security Agency for Medicines and Health Products).

It is mainly pharmacists who are authorized to open an online pharmacy, subject to meeting a set of specifications managed by regional health agencies. The list of approved French online pharmacies is available on the website of the National Council of the College of Pharmacists and the Ministry of Health.
Before your trip

Prepare a travel kit suited to your destination and take enough medication for your entire trip. If you have a chronic disease, you should take more medicines than you actually need for the trip, in case of a postponed return. Your prescriptions (with the name of the molecules and the manufacturers’ names) must be kept in your hand luggage, as well as essential medicines or your first-aid kit. For other medicines, half can be put in your luggage and the other half in your carry-on bag so you don’t run out of medicines if your luggage is lost or stolen.

During your trip

If a patient has a health problem, they should consult a physician (a list is available in embassies) before buying any medicines, which must be done through official distribution channels (usually pharmacies). When buying medicines, make sure that the packaging has not been tampered with and that there are no visible abnormalities on the box, instructions, blister pack, or the actual medicines. Report any discrepancies to the pharmacist and the manufacturer (hotline number on the box). Be careful: very cheap products could signal a fake medicine! If you suffer from any adverse effects, see a doctor because this might be due to a counterfeit product. Finally, only purchase enough for your personal needs as importing and exporting medicines are subject to border controls.

Coming home again

When bringing in medicines, France has the following import conditions:

» From non-EU and extra-Schengen countries, the quantity transported must correspond to the duration of the treatment. The doctor’s prescription must be presented to customs.

» From EU countries: the quantity transported must relate to your personal use. An administrative medical certificate must be presented to customs.
Employees: 337 people

Established in 1967, the Tours pharmaceutical plant has managed to adapt to the new challenges of the pharmaceutical industry. It has transformed in recent years with the arrival of new products requiring investments in buildings and equipment, including a large-volume workshop and a new micro-grains facility.

The site produces tablets (multilayer and programmed release) and capsules (powder and programmed micro-granule release). These are packages in blisters, jars and tubes.

Tours has a reputation for high quality, evidenced by the excellent results of FDA inspections in 2010 and 2012, its expertise in the control of complex processes for demanding markets, and its impressive customer service levels.

Passionate about their job, Tours’ highly-qualified people are also focused on improving the site’s overall performance. Starting in 2011, the production teams began to implement LEAN, which is now deeply embedded in the site culture.

The site exports 80% of its production to Europe, Asia, Africa, the Middle East, Latin America, the United States, Australia and Japan.

Tours is part of the Pharmaceuticals Solids operational unit, and also houses a Centre for Industrial Development and Innovation (ID&I) and the Central Anti-counterfeiting Laboratory.

Production
Amaryl®, Allegra®, Allegra D24®, Aprovel/Co-Aprovel®, Cardizem®, Mizollen®, Tildiem®, Telfast/Allegra®, Stilnox/Ambien®, Xatral®

Regulatory Status
Approved by: MSNA, EMA, FDA, PMDA (France, EUROPE, USA AND JAPAN)
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)
http://www.mhra.gov.uk/home/idcplg?IdcService=SS_GET_PAGE&nodeId=217

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/