

“Pill Pirates” Gaining Ground

**The sale of counterfeit drugs becomes an ever stronger global threat.
FT-NIR spectroscopy helps to detect the counterfeits.**

Many products of our daily life are nowadays traded over the internet. Whether it is televisions, cars or houses, almost all items for our personal needs can be ordered by a mouse click. Even medicines can be ordered on the internet with a delivery directly to your doorstep within days.

The drug prices of e-pharmacies are usually much cheaper than in the pharmacy "around the corner". The pharmacies on the internet do not offer a personal customer service, so that they can process the orders without considerable selling expenditure. Furthermore they buy their drugs in large volumes and therefore obtain better purchase prices.

The dark side of the internet drug trade is the ever growing trademark piracy. The recently published study of the "Columbia University's National Centre on Addiction & Substance Abuse" stated that of 185 online portals for drugs in the US, only 11% of the pharmacies asked for a prescription to process the order. In other words: 89% of the examined online portals work illegally. The resulting risks are enormous.

In almost all cases the source of an illegal drug is unknown. And the counterfeiter usually has neither the pharmaceutical nor the technical knowledge on how to copy a certain preparation accurately. The correct polymorph form of an active substance and its dosage is determined in complex clinical studies. Furthermore are homogeneous mixing and accurate proportioning of active ingredient and fillers of crucial importance for the effect (and the danger!) a tablet. By an inappropriate handling there can be no active ingredient in one batch and a lethal dose in the next. One should assume that the user of the counterfeit drug should hope it better contains no active substance than an overdose. The situation is however more complex: A study conducted in South-East Asia in 2001 showed, that 38% of the tested 104 anti-malaria drugs did not contain any active ingredient, and thus led to a huge number of preventable deaths.

Still: illegal tablet production sites flourish. According to current estimations, 25% of all spam emails advertise for counterfeit drugs. That corresponds to approximately 15 billion emails per day globally and requires only a tiny success rate to generate an enormous market. The pharma giant Novartis estimates that in the US alone more than one million patients per year order their drugs over the internet. The World Health Organisation (WHO) estimates that counterfeit drugs make up around 10% of all produced and distributed drugs on the European markets and in some countries as much as 12%. The market value of counterfeits world-wide amounts to roughly 30 billion € and grows substantially faster than the market for legal drugs.

Especially for so called life-style medicines, the internet is a welcomed source. The drugs can be purchased anonymously without any inconvenient questions by the doctor. Today approx. 40% of all Viagra tablets world-wide are counterfeits. Not included in this figure are the so called "natural drugs", where Viagra is mixed with ground tea leaves in order to pretend the impression of a purely natural and well compliant preparation.

In addition, the sourcing of the classical medicines via illegal internet pharmacies flourishes. And this is particularly true in countries and/or social classes, which are often not health-insured. Here the use of an internet pharmacy is the only way to get over illness fast - with the mentioned risks. Often the personal circumstances of the patients require a fast recovery even if the product description "Our product is not U.S. FDA approved" bodes ill.

The problems are well-known by the industry. Nevertheless a prosecution of the pirates and the control of the illegal drug trade are extremely difficult. Even if counterfeiters are convicted in the US or Europe, they are in most cases safe of legal actions in their home countries. In this context it appears useful to invest into the education of the consumer only to use legal sources for their drug purchases. Unfortunately, in Europe there is no recognized central reference point for the surveillance, trend analysis and policy recommendations in the field of counterfeit drugs. Therefore, the legal suppliers must attend their duty by proving the authenticity of their offered products.

Currently the established distribution channels in the US, Europe and Japan are judged as "relatively" safe by the experts. To state the authenticity of their product, large pharma companies often use labels with holographic patterns - similar to a cash note. Also a marking via barcodes or RFID (radio frequency identification) is possible. Unfortunately in recent times even counterfeits of such labels emerged and it appears generally questionable whether the labelling of the package is sufficient for authenticity examination.

Many customers and authorities examine at present whether a more global testing of the drugs is possible (instead of only their packing). Analytical technologies like liquid chromatography (HPLC) and near infrared spectroscopy (NIR) appear to be most promising. Both technologies are already well established in the pharmaceutical industry. The benefit of HPLC is the detailed analysis, but however it destroys the tablet and is relatively time-consuming. The NIR technology is less selective, but convinces by a non-destructive analysis within seconds. In addition also the mobile use of the spectrometer is possible. It is therefore outstandingly suitable for the screening of drugs.

By using mobile units, networks can be built up for an area-wide fight against counterfeit drugs. Such a network was now established for the first time in China. In 2001 the Chinese "State Food and Drug Administration" (SFDA) initiated a research project to evaluate the NIR technology for this task. Shortly after, extensive feasibility studies were carried out. Finally, the decision to go ahead with FT-NIR spectroscopy was taken and hundreds of thousands of dosage forms were measured. A large network of NIR spectrometers was set up and validated. The first instruments are in the field since December 2005. In total, there will be more than 300 spectrometers, built in small vans scrutinizing drugs in China by the end of the year. This way it should be ensured that legal providers of drugs (pharmacies, hospitals, wholesalers...) have no counterfeits in their portfolio.



Figure 1: Fleet of vans for the NIR analysis of counterfeit drugs

The concept of the SFDA can be described as follows: For a long-range and mobile use, the FT-NIR spectrometers (MATRIX-F, Bruker Optik GmbH, Germany) are installed in a small vans. The van drives to all relevant locations as for example pharmacies or hospitals and looks for counterfeit drugs. The screening takes place by pressing a hand-held fiber optic probe directly onto the tablet, and recording a spectrum. This spectrum is then compared with a spectrum of the original (non-counterfeit) drug. If both spectra do not match, the tablets are put aside and brought to a central laboratory for further testing, e.g. with the help of HPLC technology. The use of the NIR spectrometers is very easy. The operator selects via a software menu the substance to be determined and starts the measurement at the push of a button. The analysis starts automatically and only few seconds later the result is displayed on screen. If desired, analysis certificates can also be printed out directly.



Figure 2: Tablet testing at the push of a button

This first network of NIR spectrometers for tracing counterfeit drugs has become a large success from the very beginning. Already on day one, the first counterfeits were found in legal (!) pharmacies. Innumerable more followed since that time. And further countries will follow the example of China. With the help of modern analytic technologies at least the legal distribution channels can be made substantially safer - for the well-being and the security of the patients.

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