# Raman Spectroscopy used in the Identification of Counterfeit Pharmaceuticals

## COUNTERFEIT DRUG OVERVIEW

The World Health Organization (WHO) estimates that up to 30 percent of branded drugs sold in developing nations are counterfeit which can have profound implications not only for patients, but also on customs and border agencies, legal systems, pharmaceutical organizations. The challenge is to identify and verify the chemical composition of target drugs to determine their exact chemical makeup. Although few definitive studies exist on the exact nature of the problem, governments and organizations across the globe report unsettling trends:

- Counterfeit drugs are $35-$40 billion-a-year global business - *World Health Organization*
- Drug counterfeiting is 10 to 25 times more profitable than drug trafficking. Counterfeiting a 'blockbuster' (medicine generating sales of more than one billion dollars for the pharmaceutical company) can generate a profit of USD500,000 for an initial investment of USD1,000 while the same initial sum invested in the trafficking of counterfeit money or heroin would bring in USD20,000. -*International Federation of Pharmaceutical Manufacturers and Associations (IFPMA)*
- Upon examination of all reported cases of pharmaceutical counterfeiting, 32% of counterfeits have no active ingredient at all, 20% have incorrect ingredients and over 8% have high levels of impurities. Only 1% were copies of the real drug. - *World Health Organization*


www.fakemedicinesrealdanger.com/web/about-counterfeiting

## GEOGRAPHICAL IMPACT

According to researcher Roger Bate less than 1% of medicines are counterfeit in developed countries (United States, United Kingdom, and Europe) and approximately 10% in a large number of developing countries (Russia, China, Cambodia). But the real impact is felt in the underdeveloped worlds of Asia and Latin America. According to the *WHO International Medical Products Anti-Counterfeiting Taskforce (IMPACT)* program:

- In some countries, counterfeit prescription drugs comprise as much as 70 percent of the drug supply.
- One in three medicines is counterfeit in some African, Asian or Latin American countries.
- One in five medicines is counterfeit in the former Soviet Union.
- China, India and, to a lesser extent, Russia are the main producers of counterfeit drugs but Nigeria and the Philippines also have a significant number of illegal factories.
- 30% of drugs in Kenya are no more than just chalk.
- 7% of anti-malarial drugs in India — where 70% of the population faces the risk of contracting the killer disease — are counterfeit. - *Lancet*
- Fake tuberculosis and malaria drugs are estimated to kill 700,000 people a year.- *International Protection Network*

By geographic area, Asia is significantly dominant by number of incidents:

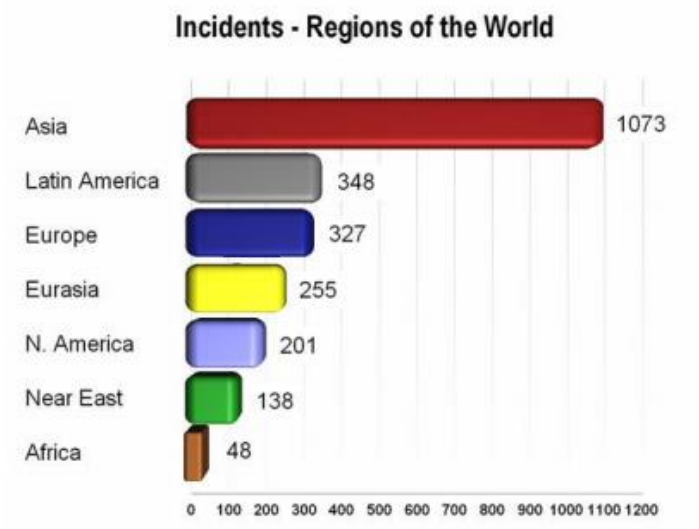


**Figure 1:** Incidents by region. **(**Source: Pharmaceutical Security Institute, Situation Report, 2010**)**

http://hal-ensmp.archives-ouvertes.fr/do 1

## THE DANGERS OF COUNTERFEIT DRUGS

Authorities have been plagued with detecting counterfeit drugs before they reach patients. Dangerous substances are substituted for the active ingredient or products have been tampered with, contaminated, diluted, repackaged or mislabeled in a way that misrepresents the contents, dosage, and origin or expiration date. Identification and elimination is considerable public health challenge.

Counterfeit drugs post many different threats to patients:

1. Failure to provide effective treatment: As patients think they are addressing their disease, insufficient active ingredients put children and the elderly at severe risk.

2. Adulterants with toxic chemicals: Often leading to death or injury, contaminated drugs are one of the most dangerous threats. In 2008 contaminated Heparin from China killed 62 people in the US. The same year, there were numerous deaths due to cough syrup contaminated with anti-freeze, including 84 Nigerian children.

3. Drug resistance: When drugs contain too little of their active ingredients to kill all of the disease, it can lead to the emergence of drug resistant strains. Asia and Africa are seeing major problems with drug resistant strains of tuberculosis, malaria, and HIV.

4. Loss of confidence in the pharmaceutical industry: Even a single case of a counterfeit drug undermines the entire credibility of the pharmaceutical supply chain.

5. Diversion of funds to organized crime: Pharmaceutical products are attractive candidates for illegal trade, especially in developing countries. This has enticed criminal organizations to become involved, some with links to the narcotics trade or other forms of organized crime.

Figure 2: In addition to wrong, diluted, or even toxic ingredients, counterfeit drugs are produced in facilities without high pharmaceutical industry manufacturing standards.

## Methods of Detection

Methods of detection range from low-tech chemical-reagents to high-tech nanoparticle tags embedded into the drugs. Some of the competing solutions to address counterfeit drugs include:

1. Color based chemical kits: There are several color-based chemical kits that authenticate certain drugs. They are designed for specific drugs like MDMA and antimalarial drugs. To test for authenticity, a portion of the drug in mixed the chemical kit and observed for a specific color change based on the presence of the active ingredients. These kits are inexpensive, however they are designed for specific drugs only and are not general purpose and destroy evidence during testing.

2. Serial Number Authentication Software: Cloud-based authentication software to authenticate product barcodes and serial numbers. This approach requires all manufacturers to tag product barcodes into a database. The consumer would then verify the product barcode on a website or a mobile app. There are also SMS based serial number authentication services. These approaches still rely on the use of barcodes and serial numbers for authentication, but not necessarily the ingredients in the package.

3. Radio frequency identification (RFID) tags: RFID tags are electronic chips embedded in the packaging of the drugs and the integrity of supply chain is validated along the way by verify the tag code at several points in the supply chain. However, RFID tags have not become common practice as they are expensive and manufacturers, distributors, retailers and governmental agencies do not necessarily agree on who should bear the additional cost burden to implement the technology. Besides cost of implementation, this technology can become very critical to monitor and might be impractical for Brazil, Russia, India, and China (BRIC) nations as well as other developing nations.

4. "Track and trace" technologies: Nanoparticle tags embedded into drugs and tracked and verified by associated readers. This approach requires that manufacturers change their processes to incorporate these tags and would require the approval of FDA and other drug regulators on the use of these tags. Additionally, the tags would be ingested by users and would need to be verified as safe by users.

5. Raman spectroscopy: In the end, the key authenticator for a tablet or capsule is its actual chemical composition. Today, Raman spectroscopy, a decades-old, proven technology, is emerging as the go-to tool for the rapid, non-destructive detection of counterfeit drugs.

## About Raman Spectroscopy

In Raman spectroscopy, a laser is directed at a substance. The laser excites the molecules in the substance and emits energy or wavelengths of light that can be captured.

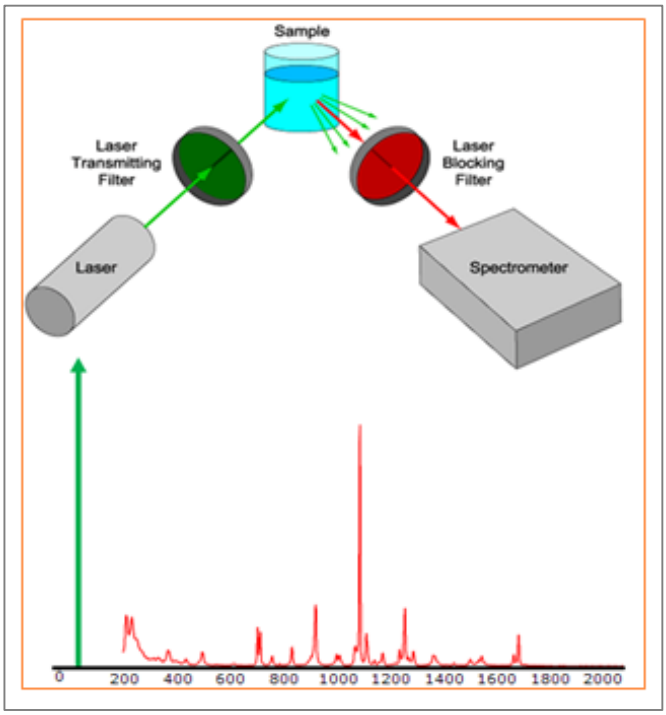


Figure 3: Raman Spectrum – the green line is the laser and the red line is the Raman spectrum (fingerprint) of the sample.

The resulting data on the wavelengths represents the unique "signature" of the substance. This information can be displayed as a graph and can be matched to known graphs of drugs.

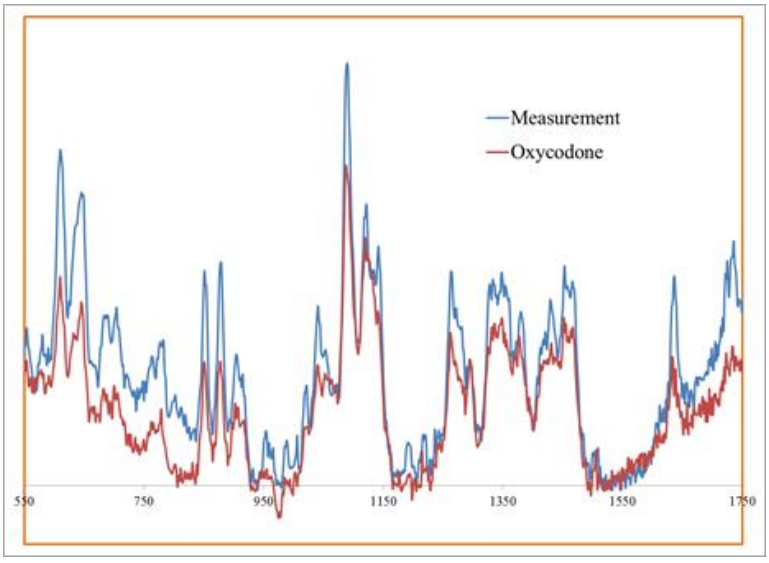


Figure 4: By comparing the spectral fingerprint of a sample to the known spectral fingerprint of a substance, Raman spectroscopy can identify whether a drug is pure or counterfeit.

## Benefits of Raman Spectroscopy

- Simplicity: Easy place, measure, and view results process is performed with minimal training.
- Non-destructive testing: No chemical solvents are needed and no evidence is destroyed when identifying a substance.
- Measurements through glass and plastics: Results are accurate even through glass, plastics, and gel capsule casings allowing tamper-free analysis of the sample.
- Capability for large libraries: Raman spectra are rich with information allowing large spectral libraries to be created with unique entries spanning many substances.
- Identification of diverse formats: Raman spectroscopy can identify chemicals that have been altered, including powders, liquids, and broken, crushed, or partial pills.
- Scientific and legal acceptance: The Department of Justice and affiliated agencies are familiar with Raman spectroscopy and consider it a valid science for confirmatory evidence analysis.

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