

# Controlling Counterfeit medicines in Southeast Asia – Science and Collaboration

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In 2001 Paul Newton and colleagues in Lao

PDR published a letter in the Lancet detailing the extent of the problem associated with counterfeit artesunate in the Mekong countries.<sup>1</sup> Artesunate is the key ingredient in antimalarial treatment. Dr Newton had discovered that the ampoules he was using for the treatment of severe malaria were not effective and tests proved that they actually contained no artesunate. They were counterfeit. Further investigations showed that of 104 shop bought 'artesunate' samples from the region, 38% did not contain artesunate.

Other dangers of fake antimalarials are that some contain small amounts of active product, to fool chemical detection systems, and exposure to low levels of a drug promotes the development of resistance - a particular concern in malaria. Signs of resistance to the leading antimalarial drugs - artemisinin-based compounds - have been seen in south-east Asia.<sup>2</sup>

Fakes also include many other types of medicines. In 2004 it was estimated that 10% of the medicines available in South-east Asia were counterfeit.<sup>3</sup>

The issue of counterfeit medicines has sometimes been clouded by confusion with generic medicines and substandard medicines. Several countries have introduced legislation to control counterfeits but lack of awareness of the difference has meant that the laws have also affected the import of legitimate generic medicines.<sup>4</sup> Customs misunderstanding led to blocking transit of good generics through Schipol airport.<sup>5</sup>

Generic medicines are legitimate copies of patented (branded) pharmaceuticals. They

can be produced after patent protection has expired or under certain flexibilities of Intellectual Property law. The same GMP and quality standards apply to generics as to branded medicines.

## What are counterfeit pharmaceutical products

Counterfeit products are deliberate imitations of legitimate products that are meant to deceive buyers. They demonstrate several criteria.

- They are deliberately and fraudulently mislabeled with respect to identity and/or source
- They can be branded and generic
- They can include products:
  - With correct ingredient(s)
  - With wrong ingredient(s)
  - Without active ingredient(s)
  - With insufficient quantity of active ingredient(s)
  - Or with fake packaging
- Worse – products may contain other ingredients that are harmful eg in 2001, diethylene glycol in paracetamol preparation led to some 200 000 deaths in China; in the USA, fake heparin may have led to more than 60 deaths in 2008.<sup>6</sup>

In 2005 Prof Mohamed Ibrahim Izham presented the details of the WHO Rapid Alert system that was being introduced, to the HAIAP Regional Consultation in Penang.

## Rapid Alert System for Combating Counterfeit Medicines

This system serves as a rapid alert mechanism for WHO, Member States, and partner organizations for combating counterfeit medicines in the Western Pacific Region. When counterfeit medicines are detected in the Region and reported through the Rapid Alert System, relevant authorities

<sup>1</sup> Newton P et al. Fake artesunate in southeast Asia. The Lancet Vol. 357 June 16, 2001

<sup>2</sup> Dondorp AM et al. Artemisinin resistance in Plasmodium falciparum malaria. N Engl J Med 2009;361(5):455–67.

<sup>3</sup> WHO Fact Sheet

[http://www.wpro.who.int/media\\_centre/fact\\_sheets/fs\\_20050503.htm](http://www.wpro.who.int/media_centre/fact_sheets/fs_20050503.htm)

<sup>4</sup> Court ruling in Kenya a victory for access to medicines

<http://www.essentialdrugs.org/edrug/archive/201004/msg0036.php>

<sup>5</sup> India may drag EU to WTO on seizure of drugs in transit

<http://www.essentialdrugs.org/edrug/archive/200903/msg00057.php>

<sup>6</sup> Izham M. Combating Counterfeit Drugs: Counterfeits

Kill. Presentation to HAIAP Regional Consultation Penang, April 2005.

are alerted immediately and time-sensitive actions are taken.

The system was to be used only for reporting cases of counterfeit medicines and to discuss and share information on the particular case of counterfeit medicine. All reported cases would be delivered to the Public Health unit in WPRO for confirmation with the country focal point; and the report sent to all members in the electronic communication network. This initiative intensified surveillance – upgrading it from a passive to an active surveillance system. It would detect cases of counterfeit drugs and help know the magnitude and nature of the problem.

It was found that reporting had a significant effect - products immediately disappeared from the market after being identified.

The system was not easy to implement fully, largely due to the difficulties in stimulating reporting from within member countries.

Since 2005 significant developments have resulted in more successful control of counterfeit pharmaceuticals. In 2005 WHO had teamed up with Interpol and the world customs organisation to develop multi country operations in collaboration with the health Ministries, Customs, Drug Regulatory authorities and the Police in each participating country.

### **Operation Jupiter – South America**

Operation Jupiter conducted in collaboration with Interpol in South America between November 2004 and April 2005 led to thousands of arrests; and seizures of millions of counterfeit cigarettes, hundreds of thousands of counterfeit or recordable CDs and DVDs and thousands of fake pharmaceutical products, computers and electrical goods.

<http://www.inta.org/INTABulletin/Pages/InterpolReportonOperationJupiter.aspx>

## **Operation Storm in Southeast Asia**

**Operation Storm** was initiated to build on ‘the intelligence dividend’ that arose from Operation Jupiter for conducting investigations concerning counterfeit pharmaceuticals in southeast Asia. Counterfeit medicines are a much more serious issue than CDs or T Shirts.

As part of the Operation, Inter-country and country trainings were undertaken on GMP, quality assurance and surveillance techniques. Officials from Customs, Drug Regulatory Agencies and the Police (who have basic or no experience dealing with crime

involving counterfeit pharmaceuticals) were trained and key people from focal points were trained in sampling. Communities were also provided with information about counterfeits and education on what to look for.

- A protocol was established so that countries would be able to submit samples for testing through the INTERPOL Liaison Office in Bangkok (LOBANG).
- The Health Science Authority (HSA) Criminalistic Laboratory in Singapore offered their forensics analysis services (including forensic botany) to participating countries.

Meetings were held to design the plan and get approval and cooperation for involving the necessary participants and the private sector. Representatives from national agencies, together with the Operation Storm Coordination Team, established protocols for lines of communication. It was also agreed that countries should aim for medium-level targets. These were realistic targets that were achievable during the first year of Operation Storm.

The overt phase of Operation Storm would last for six months, commencing on 15 April and closing on 15 September 2008.

Priority focus drugs were chosen

- Anti-Malaria medication;
- Anti-Tuberculosis medication;
- Anti-HIV drugs;
- Antibiotics, specifically those for pneumonia and child-related illnesses

A total of 110 samples from 20 million pills were submitted to the HSA Criminalistic Laboratory in Singapore for testing. These samples came from 6 countries (Cambodia, Indonesia, Laos, Myanmar, Thailand and Vietnam) Twenty million seized pills included antimalarials (22 different kinds) representing 66% of the samples; erectile dysfunction drugs - 16% of the samples; and antibiotics, antipsychotics and antiplatelets made up 18% of the samples.

Of these 20 million pills, more than 12 million were counterfeit, while nearly 8 million pills were expired, not registered or diverted medical products. 240,000 blister packs of fake artesunate were found.

### **Use of Forensic Science**

Minute quantities of foreign materials can be found within the packaging as well as anomalies within the product itself. Forensic testing was able to identify the probable source of pollen grains and plant materials

that were found in the seized products and results led to factories in southern China, their subsequent closure and arrests of owners.

More than 100 pharmacies and illicit drug outlets closed and at least 33 suspects arrested.

Interpol Flagship operations<sup>7</sup> – Storm (Southeast Asia), Mamba (Eastern Africa) and Pangea (targeting the Internet) – continue to go from strength to strength.

Successive raids on licit and illicit markets have shown improved results in terms of seizures, arrests, convictions and the closure of illicit websites.

In addition there have been strengthened

- Network for regulators & law enforcement agencies
- Technical support for medicines registration China, Cambodia, Mongolia etc.
- Pharmaco-vigilance centre Cambodia, Viet Nam

There have been Inter-country and country training courses on pharmacovigilance - Manila (Sept 08), Singapore, Hanoi (Dec 2010), Cambodia; Medicines surveillance involving consumers Malaysia and Philippines; and training on GMP in China, Laos and Viet Nam.

Customs authorities have been trained and supplied with rapid detection devices. Although Customs points cannot be the only solution - some countries have many border points - Customs operations are a key component and need to be part of multiagency teams tackling the counterfeit medicine trade. Customs must know the difference between generic and counterfeit.

Regional focal points have been strengthened with mobile laboratory units (Minilabs) for the identification of counterfeit drugs provided to trained and supported focus health workers. Suspect samples are sent for forensic testing.

A total of 270 laboratory units for protection from counterfeit drugs are already in operation in 65 countries worldwide, mainly in Africa and Southeast Asia.

## **Some other outcomes of Operation Storm:**

Intelligence from Myanmar led to the discovery that counterfeit antimalarials sold in Myanmar were produced in Thailand and that the cross border area was also a transit point for amphetamine-like stimulants and other common cough remedies produced in the same area.

Similarly, in Vietnam it was learnt that counterfeit pharmaceuticals are usually bought and sold in the border areas.

Through the private sector, large quantities of counterfeit Duocotexcin and Cotexcin (antimalarials) were found in Kenya and traced to southern China. There is a strong belief that there is a link with Chinese Taipei and further investigation is underway.

## **Conclusion**

The final report of Operation Storm concluded that the operation was able to use the intelligence gained from previous operations and to convince countries in the greater Mekong region of the importance of banding together to control the danger counterfeit pharmaceuticals pose to public health and safety.

‘Operation Storm is unprecedented at both the national, regional and international level. This is the first time that three national agencies – Customs, the Drug Regulatory Agencies, and the Police – are working together to conduct joint operations for counterfeit pharmaceutical crimes. Also for the first time, seven Asian countries have recognized the common threat that counterfeit pharmaceuticals pose and have come together to tackle this problem. Also unprecedented, at the international level, is the cooperation among INTERPOL, WHO and WCO to fund and to coordinate operations’.<sup>6</sup>

In countries that have no drug registration system, quality assurance measures must be built into the procurement process to ensure safety, efficacy and quality of pharmaceutical products. In addition, a system for monitoring and maintaining product quality throughout the product’s shelf life should be in place. If these procedures are followed counterfeit products will be excluded.

*It is worth reading ‘A Collaborative Epidemiological Investigation into the Criminal Fake Artesunate Trade in South East Asia Newton P, Fernandez F et al in PLoS Medicine | www.plosmedicine.org 0218 February 2008 | Volume 5 | Issue 2 | e32. The author’s summary follows the references.*

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<sup>7</sup> Operation Storm final report  
<http://www.interpol.int/Crime-areas/Pharmaceutical-crime/Operations/Operation-Storm>