



World Health Organization (WHO) Combating substandard and falsified medical products

This is the third of a series of special newsletters that describe the context of CIOMS activities and the work of its member organizations and partners. It explains what the World Health Organization (WHO) is doing to ensure that all medicines, vaccines and other medical products circulating on the markets of WHO Member States meet the norms and standards that have been agreed as part of their marketing authorization.

CIOMS thanks the WHO Incidents and Substandard/Falsified Medical Products Team for their support and review of this newsletter. For more information please contact the WHO Team at: rapidalert@who.int.

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The problem

“Every person has the right to expect that when they use a medical product, whether medicine, vaccine or diagnostic kit, it works. But too often, that is not the case.”

From: *The Oxford Statement* [1]

All approved medical products have been scientifically proven to treat, prevent or diagnose disease. But this does not mean that all products on the market conform to approved quality standards. Substandard and falsified products are produced, distributed and sold all over the world. The problem is growing as the products themselves and their distribution chains are becoming more complex.

Definitions endorsed by the Seventieth World Health Assembly [2]

Substandard medical products

Also called “out of specification”, these are authorized medical products that fail to meet either their quality standards or their specifications, or both.

Unregistered/unlicensed medical products

Medical products that have not undergone evaluation and/or approval by the national or regional regulatory authority for the market in which they are marketed/distributed or used, subject to permitted conditions under national or regional regulation and legislation.

Falsified medical products

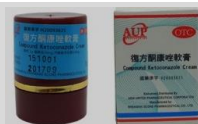
Medical products that deliberately/fraudulently misrepresent their identity, composition or source.

The term “counterfeit” is not used in this context. This term is usually associated with the protection of intellectual property rights, an area which is expressly excluded from the mandate of the WHO Member State Mechanism on substandard and falsified medical products.[2]



Substandard

Left: Manufacturing defect – a partially formed tablet in a blister pack.
Right: Storage – burst tablets kept unpacked at 40°C/75% relative humidity for 5 days.
(From: WHO Prequalification experience, presentation at ICDRA 2010 [3])



Unregistered

“... the above-mentioned product has not gone through the FDA Philippines registration and testing process. ... Thus, the Agency cannot guarantee its quality and safety.”
(From: FDA Philippines Advisory No. 2019-468)



Falsified

A confirmed falsified pack of a product, of which falsified versions were traded globally. The tablets were found to contain paracetamol, instead of the leukaemia medicine ponatinib as stated on the label.
(From: WHO Medical Product Alert No. 2/2019)

>>> The problem

Magnitude

In 2017 WHO carried out a review of 100 scientific papers reporting on testing of medicines samples.[4] Of a total of 48 218 samples of medicines collected in 88 countries, 5 094 (10.6%) failed quality testing. In other words, **one in ten medicines samples tested in these studies did not meet quality standards.**

Pharmaceutical sales in these countries totalled nearly US\$ 300 billion in 2014. Assuming that substandard products accounted for a tenth of that amount, roughly US\$ 30 billion were wasted every year to buy them. [4]



One in ten medicines samples on the market failed quality testing, as reported in studies reviewed by WHO. [4]

Substandard and falsified medical products are notoriously difficult to detect. The problem affects every region of the world. Substandard and falsified products from all main therapeutic categories, including both innovator and generic products, have been reported to WHO. [5]

Impact

“At best, these products do nothing but prolong sickness, waste money and erode hope. At worst, they kill, cause serious harm, and fan the flames of drug resistance.”

Dr Tedros Adhanom Ghebreyesus, WHO Director-General, in his [speech](#) on the launch of report on the public health and socio-economic impact of substandard and falsified medical products, 29 November 2017. [6]



The medical centre set up by Médecins Sans Frontières, where patients affected by falsified diazepam were treated (see [WHO Medical Product Alert No 4/2015](#)).

Photograph from WHO GSMS Report 2017 [7].

Substandard and falsified medicines cause needless suffering for people and their loved ones, and have far-reaching consequences in societies:

- **Health impact:** Falsified and substandard products do not work as intended and can cause serious adverse effects. They also fuel drug resistance, resulting in more infections that cannot be treated with available medicines. And as people lose confidence in health care systems they may not seek needed treatment. All this increases deaths and illness.
- **Economic impact:** Time and money is wasted by patients, their families, health systems, manufacturers and other actors in the supply chain. An increased burden is placed on health care professionals, national medicine regulatory authorities, law enforcement bodies and criminal justice systems, further straining already scarce resources, staff and infrastructure.
- **Socioeconomic impact:** More deaths and prolonged illness result in lost household income, increased poverty, and lost productivity in societies.



Left: A child receives anti-malarial medicines in Muna IDP camp, near Maiduguri. (Photograph: P. Utomi Ekpei/ WHO)

Right: Substandard antimalarials distributed in public health centres in a Central African country. More than 8 million doses of these poor-quality medicines had been distributed in sub-Saharan Africa in 2012. (Source: [7])



Taking the example of substandard **antimalarials in sub-Saharan Africa**, the study estimated that these products (defined as containing less than 85% active ingredient):

- account for 7.6% of artemisinin combination therapy (ACT) drugs and 10.4% for other antimalarials.
- cost US\$ 10.4–38.5 million per year to purchase, and
- cause 31 000–116 000 deaths annually.

This estimate does not take into account the broader socio-economic impact.

The WHO response

The WHO Member State Mechanism: “Prevent, Detect and Respond”



In 2012, WHO Member States got together to address the issue of substandard and falsified medical products.[8] They defined objectives for their work (see right) and developed a detailed workplan.

The [WHO Member State Mechanism](#) is a voluntary body open to all WHO Member States' regulatory authorities and ministries of health. The time spent building trust between nations in the early years is now bearing fruit. The body has simplified and clarified definitions of substandard and falsified medical products with a focus on public health (see page 1), and is supporting countries in many technical areas. The Mechanism has become the global forum at which Member States convene, coordinate, decide and organize activities to address substandard and falsified medical products.

Objectives

- 1 To identify major needs and challenges and make policy recommendations, and develop tools in the area of prevention, detection methodologies, and control of SF medical products in order to strengthen national and regional capacities.
- 2 To strengthen national and regional capacities in order to ensure the integrity of the supply chain.
- 3 To exchange experiences, lessons learnt, best practices and information on ongoing activities at National, Regional and Global activities.
- 4 To identify actions, activities and behaviours that result in SF medical products and make recommendations, including for improving the quality, safety and efficacy of medical products.
- 5 To strengthen regulatory capacity and quality control laboratories at National and Regional levels, in particular for developing countries and least developed countries.
- 6 To collaborate with and contribute to the work of other areas of WHO that address access to quality, safe, efficacious and affordable medical products, including, but not limited to, the supply and use of generic medical products, which could complement measures for the prevention and control of SF medical products.
- 7 To facilitate consultation, cooperation and collaboration with relevant stakeholders in a transparent and coordinated manner, including regional and other global efforts, from a public health perspective.
- 8 To promote cooperation and collaboration on surveillance and monitoring of SF medical products.
- 9 To further develop definitions of SF medical products that focus on the protection of public health.

Definitions

Definitions of Substandard, Unregistered/Unlicensed, and Falsified Medical Products

[Arabic](#) pdf, 146kb |
 [Chinese](#) pdf, 799kb |
 [English](#) pdf, 198kb |
 [French](#) pdf, 662kb |
 [Russian](#) pdf, 442kb |
 [Spanish](#) pdf, 99kb

— [More information on definitions is available here:](#)

Detection Technologies

Available authentication technologies for the prevention and detection of SF medical products

[Arabic](#) pdf, 848kb |
 [Chinese](#) pdf, 1.27Mb |
 [English](#) pdf, 864kb |
 [French](#) pdf, 2.44Mb |
 [Russian](#) pdf, 1.17Mb |
 [Spanish](#) pdf, 819kb

— [More information on detection technologies is available here:](#)

Definitions
Detection Technologies
Global Focal Point Network
Internet
National Plans
Registers
Risk assessment
Risk communication and awareness
Socioeconomic and public health impact
Track-and-Trace
Training material
Transit

The WHO Member State Mechanism has developed a wide range of technical tools for use by Member States. All the documents are available in the six UN languages on the Member State Mechanism's webpage at: <https://www.who.int/medicines/regulation/ssffc/mechanism/en/>

>>> The WHO response

WHO Global Surveillance and Monitoring System (GSMS)

The WHO Member State Mechanism has supported the development of a global regulatory focal point network to combat poor quality medicines. Launched in 2013, the WHO GSMS aims to get better data concerning substandard and falsified medical products, and to use that data to improve prevention, detection and response.

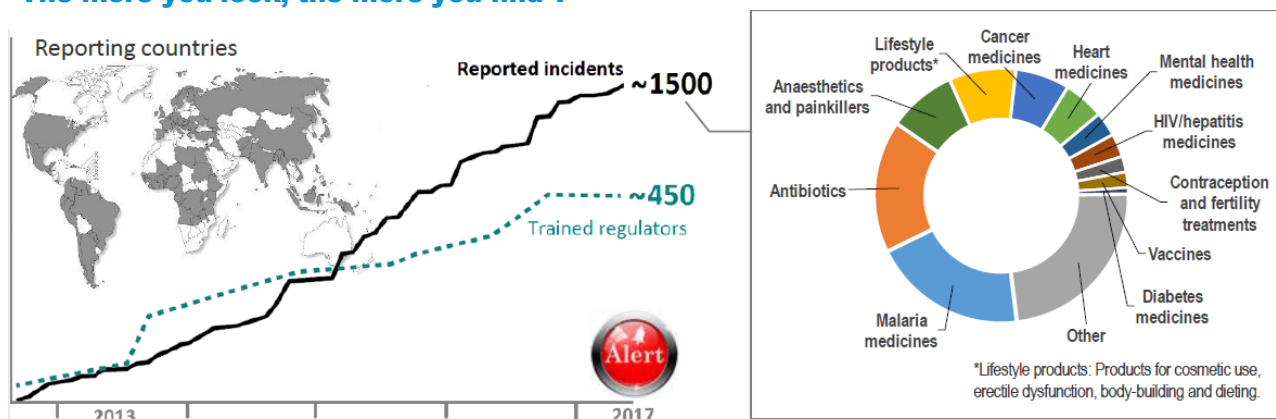
The system works as follows: Trained focal points at national medicine regulatory authorities report suspected or validated substandard and falsified products to WHO via an electronic rapid alert form. Incoming reports are automatically uploaded to a secure WHO database, and an alert is sent to other focal points that have reported the same issue. This

enables regulators to share information, for example laboratory testing results.

WHO will contact the reporting focal point within 72 hours (within 24 hours if adverse reactions in patients have occurred) and provide technical support where requested. In emergencies this may take the form of facilitating urgent laboratory analysis or in extreme and complex cases deploying experts in the field.

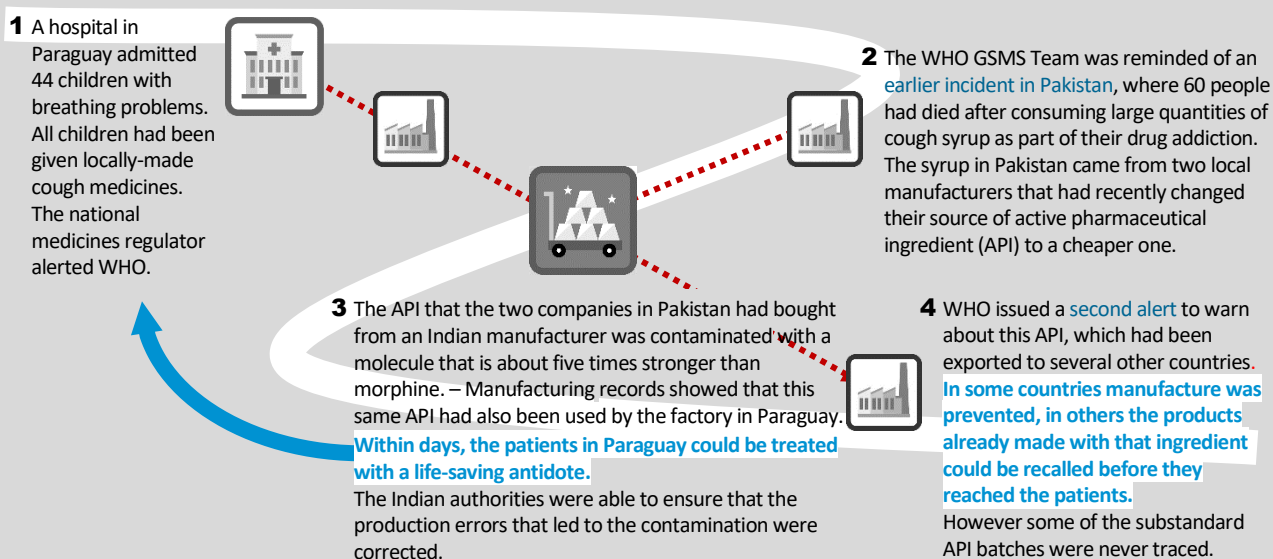
If there is a serious threat to public health with potential wide geographic impact, WHO will consult with the reporting focal point to assess the need of issuing a WHO medical product alert. Since 2012 35 alerts have been issued globally, of which 11 in 2019 alone.

“The more you look, the more you find”:



Above: From 2013-2017 approximately 1500 incidents of suspected or confirmed incidents were reported to the WHO GSMS database. As more regulators are trained, the number is increasing. Source: [7]

How WHO Drug Alerts save lives



Source of illustrations: [7].

More information is found at: <https://www.who.int/medicines/regulation/ssffc/surveillance/en/>

>>> The WHO response

Understanding the causes

The data collected through the Global Surveillance and Monitoring System enables WHO to identify the medical products most at risk, vulnerabilities in supply chains and weaknesses in capacity and health systems.

In a globalized world, regulation of medical products is becoming more and more challenging even for the best-equipped regulatory authorities. In many countries, the regulators are not only under-resourced to perform these tasks, but they also operate in an environment where the police, justice and other systems suffer from similar constraints. Any loopholes affect the control of medical products globally.

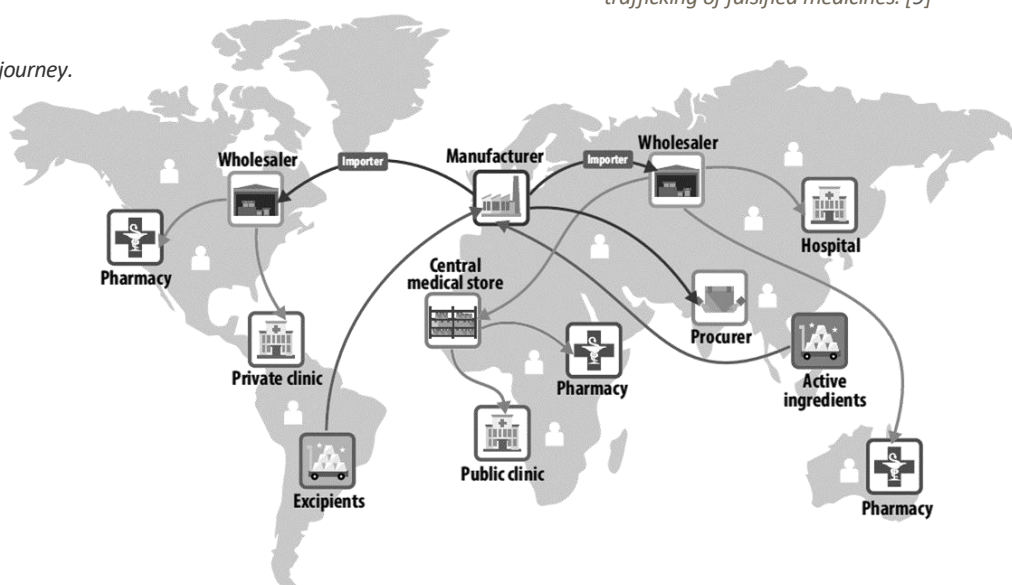
“Lack of access to affordable medicines forces desperate people to buy medicines from unreliable sources.

Lack of good governance allows corruption to penetrate health systems and leaves loopholes for criminal groups to exploit.

Lack of technical capacity undermines the integrity of supply chains and limits the ability of countries to safeguard the health of their people.”

The WHO Director-General in his [speech](#) on 18 January 2020 at the launch of the Lomé Initiative, where African Heads of State signed the Lomé Declaration on criminalizing the trafficking of falsified medicines. [9]

A medicine's journey.
Source: [7]



Lack of access to affordable medical products: Medicines in a street market in West Africa.

The problem can also affect the legal supply chain. Pharmacists in some African countries have declared that in order to compete with the illegal street markets and hawkers of medicines they are compelled to source their products from the cheapest but not necessarily the safest suppliers in order to keep their business afloat. [7]



Lack of good governance: Falsified anti-cancer medicine that penetrated the supply chain and reached patients.

Distributors in the U.S. had acquired the medicine via an Internet-based pharmacy from a subsidiary wholesaler based in the UK, who bought it from a company in Denmark, which in turn had purchased it from a Swiss company supplied by an Egyptian businessman. He told a news agency that he had bought the medicines (thinking they were genuine, made in Turkey) from a Syrian dealer, who signed a hand-written sourcing document with his thumb-print because he could not write. [7]



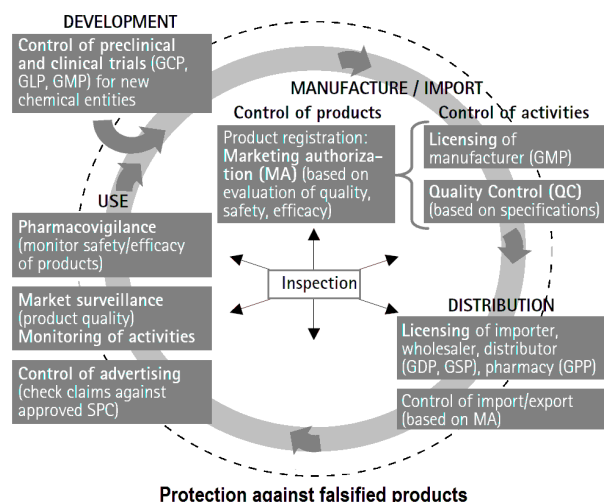
Lack of technical capacity: Expired meningitis vaccine awaiting destruction at a private pharmacy.

Many countries do not have technical capacity to control the medicines circulating in their territories. Sometimes, a lack of simple equipment such as incinerators prevents health centres from following correct protocols for disposing of expired products, empty vials and other packaging. [7]

Source of illustration and photographs: [7]

>>> The WHO response

Strengthening regulatory bodies



Functions of a medicines regulatory system. Adapted from: [10]

Combating substandard and falsified medical products requires a fully functioning regulatory system (see above). Given the complexity of medicines regulation in a globalized world, it is crucial for regulators in all settings to collaborate and to use their resources as efficiently as possible. In alignment with the WHO Member State Mechanism's [Guidance for national plans](#), the global strategy includes twelve strategic actions for countries to prioritize (see right).

These efforts are underpinned by other WHO initiatives to promote [good governance](#) for medical products, strengthen [supply systems](#), and support good quality standards for example through [WHO prequalification](#) of medical products.

Strategic actions for regulatory authorities to combat substandard and falsified products

Prevent

- ☐ Education and awareness
- ☐ Comprehensive legal framework
- ☐ Multi-stakeholder engagement
- ☐ Supply chain integrity

Detect

- ☐ Border control
- ☐ Reporting systems
- ☐ Risk-based inspection and surveillance
- ☐ Access to laboratories and screening technologies

Respond

- ☐ Alerts and recalls
- ☐ Regulatory strengthening
- ☐ Transparent legal process
- ☐ Evidence-based policy and procedure

Source: [7]

The bottom line

The Oxford statement, of which CIOMS is a signatory, calls for making access to quality medical products an immediate global priority [1]. Effective global coordination mechanisms, including the WHO Member State Mechanism, are working on many fronts to safeguard medicines quality standards. Governments and other decision-makers should sustain these efforts and resource them appropriately in the interest of public health.



References

- 1 Newton PN, Bond KC. [Global access to quality-assured medical products: the Oxford Statement and call to action](#). Lancet Global Health. 2019 Dec;7(12):e1609-e1611.
- 2 Annex 12. In: [Seventieth World Health Assembly](#). Geneva, 22-31 May 2017. Resolutions and Decisions; Annexes: pp. 266-269.
- 3 Van Zyl A. [API inspections: WHO Prequalification experience](#). Presentation at the 14th International Conference of Drug Regulatory Authorities (ICDRA), Singapore, 2010.
- 4 [A study on the public health and socioeconomic impact of substandard and falsified medical products](#). Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.
- 5 WHO. [Substandard and falsified medical products \[Fact Sheet\]](#). 31 January 2018.
- 6 [Launch of report on the public health and socio-economic impact of substandard and falsified medical products](#). Speech by the WHO Director-General. 29 November 2017.
- 7 [WHO Global Surveillance and Monitoring System for substandard and falsified medical products](#). Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.
- 8 [World Health Assembly Resolution 65.19](#). 26 May 2012.
- 9 [Launch of the Lomé Initiative](#). Speech by the WHO Director-General. 18 January 2019.
- 10 [Assessment of medicines regulatory systems in sub-Saharan African countries](#). An overview of findings from 26 assessment reports. Geneva: World Health Organization; 2010.

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