

WHO Global Surveillance and Monitoring System

for Substandard and
Falsified Medical Products



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EXECUTIVE SUMMARY

Falsification of products that are believed to cure illness is nearly as old as commerce itself. In 1500 BC, Queen Hatshepsut of Egypt hired a team to go out hunting for genuine medicinal plants because the market was flooded with worthless fakes. Tales of falsified medicines have graced the history books and popular culture ever since. Although it is extremely difficult to quantify the problem precisely, recent efforts by the World Health Organization (WHO) and others to support countries in tracking and reporting substandard and falsified medical products suggest the problem is on the rise. This is in part because globalization and e-commerce have increased the complexity of the supply chain for medicines, providing numerous entry points for unethically and illegally produced medical products.

This report, based on data gathered by WHO's Global Surveillance and Monitoring System for substandard and falsified medical products (GSMS) during its first four years of operation, examines the issue in greater detail and it is published together with a WHO study on the public health and socioeconomic impact of substandard and falsified medical products. It outlines the dangers that substandard and falsified medical products present to individuals, communities and countries, and summarizes the information available on the extent of the problem. The report uses case studies from around the world to illustrate the forces that drive the trade in these dangerous products, and provides an overview of the systems and actions that are needed to prevent, detect and respond to the threat posed by substandard and falsified medical products.

What are substandard and falsified medical products?

For many years, the response to this important threat to public health was embroiled in a discussion of complex definitions that meant different things to different people. Reflecting this complexity, WHO used the term "substandard/spurious/falsely-labelled/falsified/counterfeit medical products" (SSFFC). The WHO Member State mechanism on SSFFC medical products was tasked with revising these definitions to ensure that they were focused on a public-health perspective, with no account taken of intellectual property concerns. Based on these deliberations, the seventieth World Health Assembly (2017), which governs WHO, adopted the following definitions:

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.

Source: Appendix 3 to Annex, World Health Assembly document A70/23, 2017.



1. SUBSTANDARD AND FALSIFIED MEDICAL PRODUCTS: THE CONSEQUENCES

Although many millions of people still lack access to the basic medicines they need, the global trade in medicines has increased very rapidly in recent years. Unfortunately, this growth has opened the door not just to quality, safe and effective medicines, but also to medicines, vaccines and other products that do not meet quality standards and that are sometimes toxic.

In the worst cases, medicines that contain the wrong ingredients may kill or seriously harm patients. This report details several cases in which dozens and even hundreds of patients have died after taking such products. Much more commonly, substandard or falsified medical products will fail to prevent or cure a disease, meaning that illness is prolonged and the patient suffers needlessly. In the case of infectious diseases, this can have an especially pernicious knock-on effect. Antimicrobials that do not deliver a full dose because they are badly made or degraded will kill only the most susceptible pathogens. That contributes to

antimicrobial resistance through the development of drug-resistant mutations of the pathogen and its onward transmission.

When people suspect that some medicines are not safe or effective, they begin to lose faith in medicines and the health system in general. Trust and confidence in cost-effective, life-saving interventions such as childhood vaccination can be undermined globally if vaccines that do not meet quality standards are discovered anywhere in the world.

There is an important economic impact, too. Medicines that fail to protect or cure patients strain the budgets of households and health systems, damaging the very fabric of society. Legitimate manufacturers of both generic and innovator pharmaceutical products suffer financially and reputationally when criminals falsify their products.

2. EVIDENCE FOR THE MAGNITUDE OF THE PROBLEM

Systematic efforts to estimate the proportion of medicines that patients take that do not meet quality standards, as well as to track and measure the production and trade of falsified products, are in their infancy. WHO launched the GSMS in July 2013. The system provides national medicine regulatory authorities with an information portal to which they can report suspect medical products, and which they can consult to check if similar products have been found elsewhere. WHO works with national medicine regulatory agencies to investigate suspect cases if necessary, and to issue alerts when warranted. The need for an international data exchange of this type has grown in parallel with the increasing complexity of the pharmaceutical industry. In one case, the lives of patients in South America were saved after the database analysis showed that they were affected

by the same contaminated product that had caused deaths in Asia several months earlier. The antidote was promptly administered, patients' lives saved, alerts were issued, and contaminated products were discovered in other countries and removed from the market.

Some 1500 products have been reported to the GSMS so far; some cases involve millions of doses of medicines, others a single dose. It is clear that these cases represent only a fraction of the problem. But following careful analysis of the reports, a clearer picture is already emerging.

Table 1 shows examples of medical products reported to the GSMS during its first four years of operation.

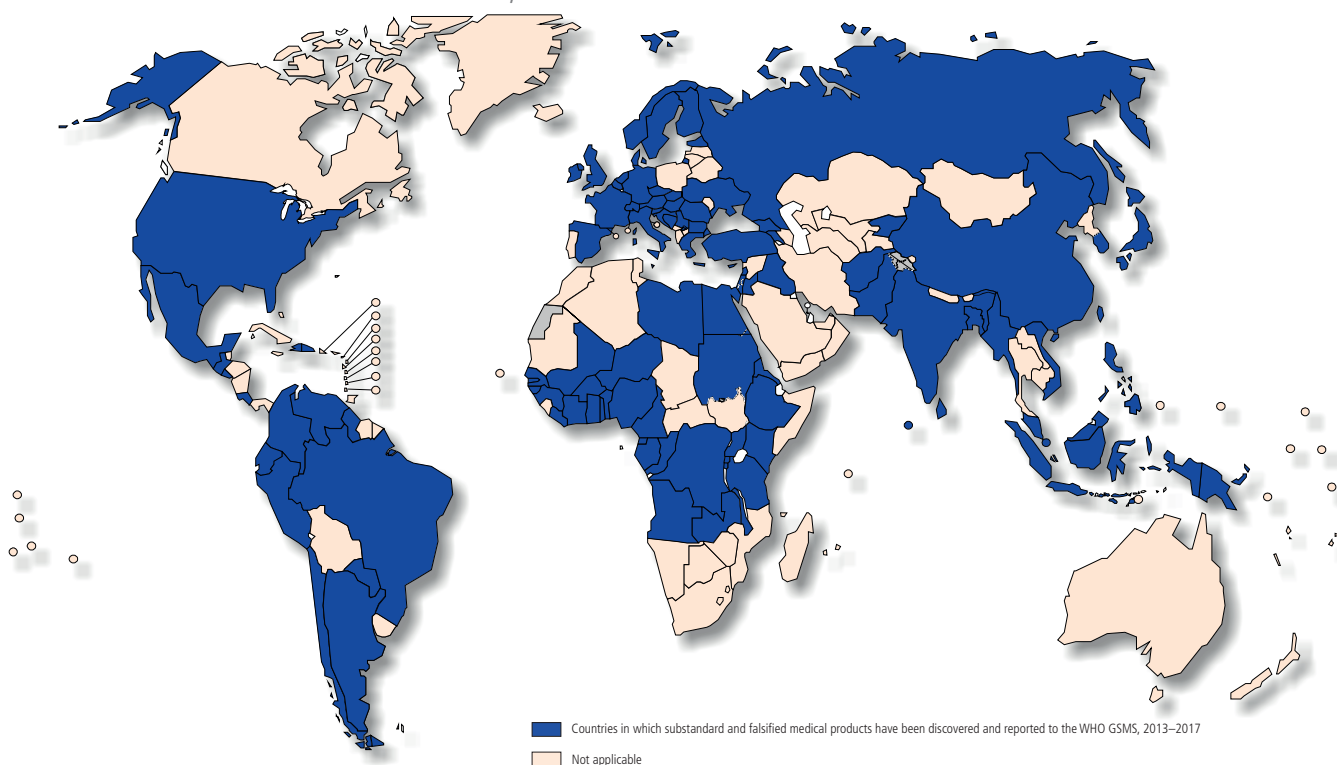
TABLE 1: EXAMPLES OF SUBSTANDARD AND FALSIFIED PRODUCTS REPORTED TO THE GSMS (2013–2017)

Type of product	Number of Member States reporting	Total no. of product reports	Percentage of all products reported to database ^a
Anaesthetics and painkillers	29	126	8.5
Antibiotics	46	244	16.9
Cancer medicines	19	100	6.8
Contraception and fertility treatments	19	29	2.0
Diabetes medicines	7	11	0.8
Heart medicines	22	75	5.1
HIV/hepatitis medicines	9	43	2.9
Lifestyle products ^b	37	124	8.5
Malaria medicines	26	286	19.6
Mental health medicines	19	45	3.1
Vaccines	11	29	2.0

^a Since only selected products are reported in this table, the percentages in this column do not add up to 100%. A table showing the breakdown of all reports using the anatomical therapeutic chemical classification is provided in the Annex to the main report.

^b So-called lifestyle products include products for cosmetic use, erectile dysfunction, body-building and dieting.

FIG. 1: COUNTRIES IN WHICH SUBSTANDARD AND FALSIFIED MEDICAL PRODUCTS HAVE BEEN DISCOVERED AND REPORTED TO THE WHO GSMS, 2013–2017



The numerical distribution of cases is influenced by the roll-out of the GSMS system, which includes training for staff appointed by national medicine regulators to act as focal points interacting with the global reporting system. As of July 2017, staff from 126 WHO Member States had been trained in 17

workshops. There is a striking association between increased training and increases in cases reported, suggesting that the greater the effort made to look for substandard and falsified medical products, the more of them will be found.

Much of the media coverage around “fake” medicines, particularly those purchased over the Internet, has focused on what are known as lifestyle medicines, such as slimming tablets and treatment for impotence. But over the past four years, WHO has received reports of substandard or falsified medical products in all therapeutic categories, covering everything from cancer medicines to contraception, from antibiotics to vaccines. They are not confined to high-value

medicines or well-known brand names; antimalarials and antibiotics are the two most frequently reported medicines in the database, and reports are split almost evenly between generic and innovator products. Table 2 shows the number of countries and the number of reports concerning key antibiotics and antimalarials included in the WHO Model List of Essential Medicines as a percentage of all antimicrobials.

TABLE 2: KEY WHO MODEL LIST OF ESSENTIAL MEDICINES (EML) ANTIBIOTICS AND ANTIMALARIALS REPORTED TO GSMS (2013–2017)

Type of medicine	Number of Member States reporting	Total no. of product reports	Percentage of all antimicrobials reported to GSMS
Key access antibiotics	36	186	30.09
Watch group antibiotics	19	38	6.14
Reserve group antibiotics	2	2	0.32
Antimalarial medicines	25	285	46.11
Any EML product – as per exact dosage and formulation	68	714	Not applicable

^a A list of minimum medicine needs for a basic health care system and essential medicines for priority diseases (<http://www.who.int/medicines/publications/essentialmedicines/en/>).

To assess the true level of substandard and falsified medical products on world markets, a random selection of products from a representative sample of outlets would have to be regularly tested – a near impossible task owing to the expense and human resources that would be required. Currently, field surveys are commonly undertaken in areas where products that do not meet quality standards are most likely to be found, better known as a risk-based approach.

The study estimates the observed failure rates of substandard and falsified medical products in low- and middle-income countries at approximately 10.5%. If this is applied to unweighted estimates of market size in low- and middle-income countries, the estimated spend is in the order of US\$ 30 billion. If this is even approximately correct, it highlights the urgent need to address this problem.

Like any other commerce, the trade in substandard and falsified medical products depends on profit margins. It does best where demand is high, and where there is a shortage of supply; indeed, even very

low-cost products are attractive to those involved in the manufacture and distribution of falsified medical products, as long as the potential sales volume is high enough. The trade is driven by a combination of the ill-informed, the careless, the unprincipled and the criminal, so it thrives in places where the technical capacity is poor and the risk of detection is low.

Substandard and falsified medical products are most likely to be found where:

- Access to affordable, quality, safe and effective medical products is constrained.
- Standards of governance are low, ranging from poor ethical practices through to corruption in both the public and private sectors.
- The tools and technical capacity to ensure good practices in manufacturing, quality control and distribution are limited.



2.1 Constrained access to affordable, safe and quality medical products

Cost pressures are felt throughout the supply chain. Those who cut corners in an attempt to maximize their profit margins can undermine the quality of the medical products that reach patients. And consumers buy what they can afford. Medicine pricing and health policies, including what a health insurance programme will cover, can push people away from the regulated supply chain towards street markets or the Internet. One case in the database involves medical practitioners in the United States of America buying cancer medicines over the Internet after just such a policy change. Attempting to save US\$ 500 on the normal price of US\$ 2400 per dose, 19 medical practices exposed their clients to falsified cancer medicines containing no active ingredients.

Cost is not the only constraint on access to quality-assured medicines. Adequate supply can be undermined by chronically poor infrastructure coupled with poor planning, or by unpredictable surges in demand, for example in the case of a disease outbreak, a conflict or a natural disaster. Such situations disrupt the flow of legitimate medical products, leading to shortages that are sometimes exacerbated by thefts from stockrooms. Where shortages of quality-assured medicines arise, falsified medicines frequently flow in to fill the gap. The breakdown of planning and regulatory systems and communication between health, customs and law enforcement officials, which is common in these disturbed settings, increases the challenge of keeping the supply chain safe.

Sometimes, access to safe and cost-effective medical products is restricted due to cultural reasons or patient preference. People sometimes demand a particular product or brand even where an affordable, effective, quality-assured alternative is universally available. One case reported to WHO involved the falsification of so-called imported brands of vaccine in Indonesia. Although the Indonesian Ministry of Health provides universal access to domestically produced vaccines for free, health care workers had been supplementing their own incomes by providing imported brands at a charge, promoting them to parents as having fewer side-effects. This created a demand that was quickly

filled. National regulators found that at least 37 hospitals and health centres were injecting children with vaccines that had no active ingredients. Several arrests and convictions followed.

2.2 Lack of good governance

Falsified and substandard medical products often reach patients because of a failure of governance. In this context, governance does not refer to the technical aspects, such as oversight of manufacturing procedures or temperature-controlled warehouses; rather, it refers to the laws that underpin existing rules and regulations, and the institutions that enforce those laws. The term includes poor ethical practice through to corruption in both the public and private sectors.

The pharmaceutical trade has become a complex web of international exchange, and is set to become yet more complex. Regulatory structures have to some extent struggled to keep up with this global interconnectedness. Many national regulators have no explicit authority to regulate the quality of products made for export, leaving the onus for quality control on importing countries whose regulatory capacities may be even more strained. Often, regulators finance their work by charging for product registration, which, in some cases, may cause conflicts of interest. Cross-border collaboration between police forces and judicial systems is not always effective, even though a significant proportion of cases reported to the GSMS database involve several countries.

In most cases, the first line of defence against falsified medicines is due diligence – does the manufacturer exist, is the wholesaler registered, does the package look genuine? Simple steps, but the systems needed to follow them – open registers of manufacturers and, wholesalers – are not always available. And sometimes there is no incentive to check up on products. Health workers who know that their supervisors are cutting corners on pharmaceutical supplies are often reluctant to report suspicious products for fear of reprisals.

Falsification (including the deliberate production of medicines that do not contain enough active ingredient) is sometimes difficult to spot, and very often difficult to trace back to its origins, reducing



the chance of successful prosecution. According to the international police organization INTERPOL, organized criminal networks that once specialized in the illicit drug market are now targeting the medicine trade because profits are high, the risks of detection and successful prosecution are low, and the penalties, if prosecution does succeed, are almost negligible compared with those incurred for large-scale drug trafficking.

2.3 Weak technical capacity and tools

Substandard medical products are usually the result of a technical deficit coupled with poor oversight. Good manufacturing practices; well-equipped laboratories; field detection technologies; transport and storage systems that keep products at the right temperature while accurately tracking their whereabouts; competent oversight of production and supply chains – all depend on having the right equipment and well-trained staff. In many countries, some or all of those things are already in short supply. It is in those places that the need for strong technical oversight is greatest, but that is also where the capacity to provide them is most strained.

In general, there is more regulatory oversight over the production of medical products than there is over their shipment and distribution – times at which even well-made medicines can easily degrade. Often, the basic infrastructures needed to maintain and check quality throughout the supply chain are lacking. Simple field testing technologies that allow for quality to be screened close to the patient are in particularly short supply. Sometimes, a handful of regulatory staff are tasked with overseeing hundreds of factories and thousands of wholesalers and retail outlets. Even without the additional complication of e-commerce, the challenge is formidable.

While a functioning national regulatory agency is a key component in ensuring that patients receive quality medical products, there is also a responsibility to improve the technical capacity of health care workers and those involved in the supply chain. All need to be aware of the risks and how to avoid them, including the identification and reporting of suspected substandard and falsified medical products to the appropriate authorities in their respective countries.

3. TACKLING THE PROBLEM

Tackling the challenges posed by substandard and falsified medical products requires three interconnected approaches. The first focuses on preventing the sale and consumption of substandard and falsified medical products; the second on implementing systems to detect any substandard or falsified products that are already in the supply chain; and the third requires authorities to respond quickly and proportionately to any incidents that are detected.

Within WHO, this work is coordinated by the Member State mechanism on substandard and falsified medical products. This group works to strengthen the evidence base around substandard and falsified medical products, and provides technical guidance to WHO and its Member States as they build their capacity to

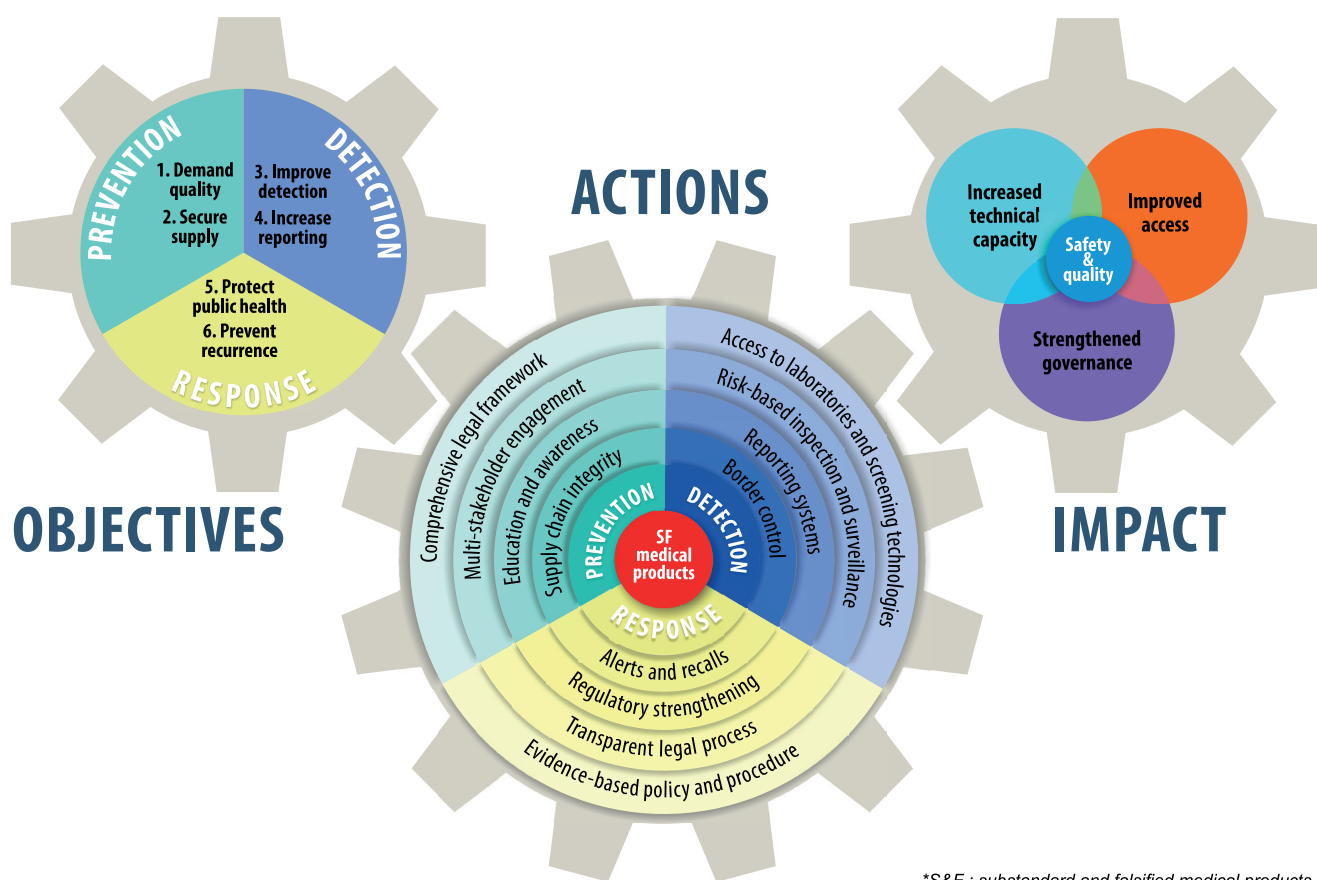
meet the growing challenge. The GSMS provides an important part of that evidence base.

“Prevent, detect, respond” encompasses actions and systems that are mutually reinforcing. They involve many partners (including patients, health ministries, politicians, regulators, law enforcement, customs officials, industry, health care professionals, nongovernmental organizations and academia), so careful coordination is vital.

Fig. 2 sets out the objectives, actions and impacts of tackling substandard and falsified medical products using the three-pronged strategy of prevention, detection and response.



FIG. 2: SETTING PREVENTION, DETECTION AND RESPONSE INTO MOTION



*S&F : substandard and falsified medical products

3.1 Prevention

Since a large part of the trade in substandard and falsified medical products is made possible by a shortage of affordable, quality products combined with patient choices, the first step is to reduce those shortages and inform those choices. Providing accurate and balanced information on the risks of substandard and falsified medical products, how to avoid them, how to spot them and how to report them is critical to encourage rational use of medicines and help drive consumers away from informal markets towards safer outlets. Such information may also increase reporting and the likelihood of detection. Rational selection and pricing policies for pharmaceuticals contribute to their greater affordability and more streamlined planning of the supply chain can reduce stockouts and other shortages.

The second step is to prevent the manufacture of substandard medicines by increasing the technical capacity to implement and oversee good manufacturing practices, and avoid degradation of

medical products through poor conditions during storage and distribution.

Minimizing the manufacture and trade in falsified medical products can only be achieved through better coordination between agencies and stronger deterrents, including the enforcement of legal penalties, an example of which is enshrined in the MEDICRIME convention.

3.2 Detection

Detecting substandard and falsified medical products requires a keen awareness of the likely risk factors (including product shortages), a culture that promotes the rapid exchange of information, and the technology and trained personnel needed to follow up suspicion with appropriate action. The WHO GSMS helps by training regulators and people involved with the procurement and provision of medical products, in order to heighten their awareness. The system provides evidence about likely risk factors, as well as concrete information in close to real time about



suspect products that may penetrate national supply chains or cross borders. These systems have already led to targeted surveillance and seizure of falsified products in several markets. Greater integration of information systems increases the efficiency of this process; pharmacovigilance data and information on suspected antimicrobial resistance may point to areas of heightened risk, while customs and law enforcement data can also be revealing.

Field detection and reporting systems need to be improved and their use expanded. WHO is currently testing a smartphone-based reporting system that encourages front-line service providers to instantly report products that they suspect are not working correctly to national regulatory authorities. Packaging features are also helping retailers and consumers verify the provenance of their medical products.

3.3 Response

The first duty of response is to safeguard public health. That sometimes involves quarantining or recalling products during an investigation, and issuing

alerts as necessary. This work is usually undertaken by national medicine regulatory authorities, but WHO is able to respond with support for investigations when requested, and can help to issue international alerts where appropriate.

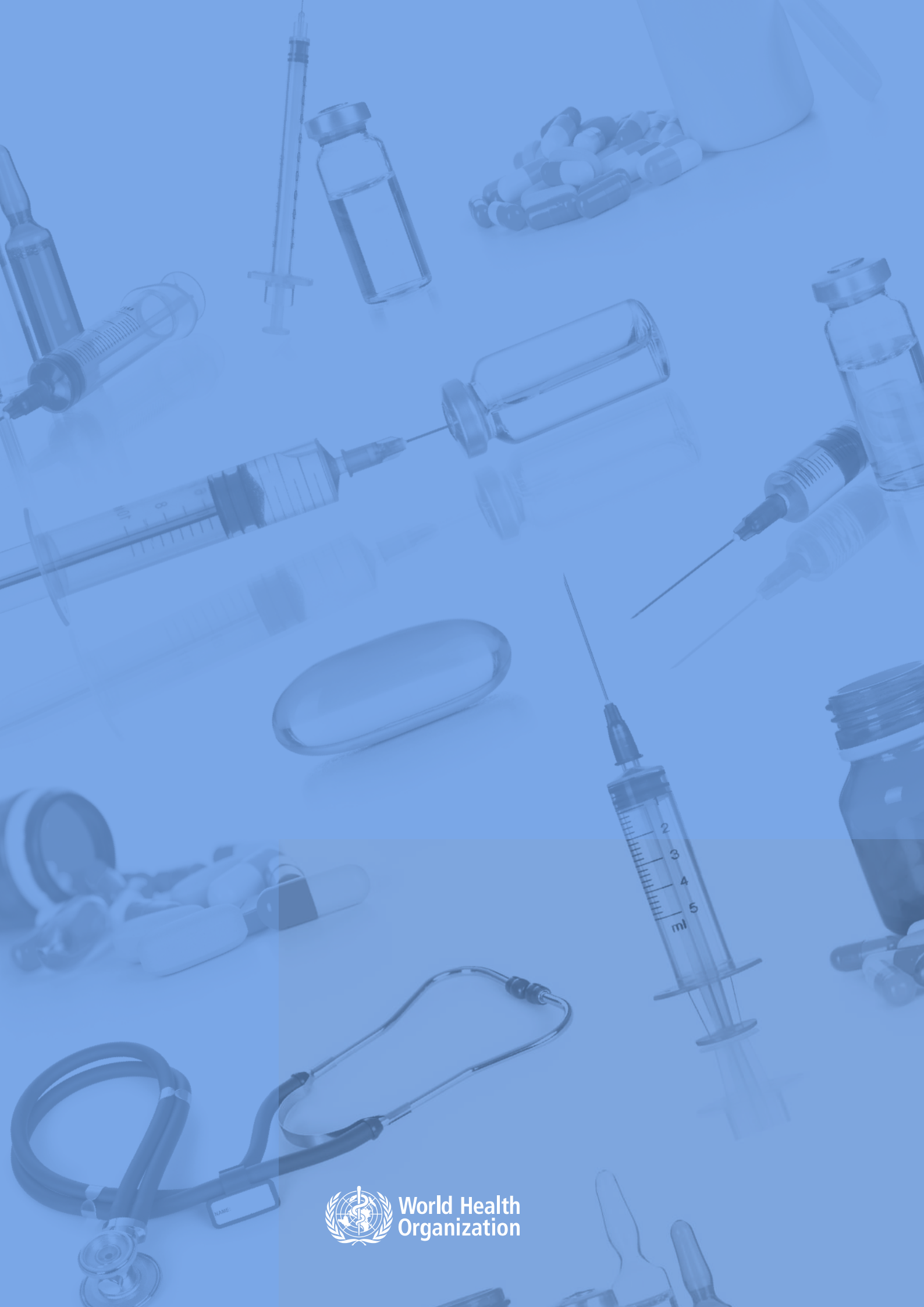
Similarly, criminal prosecutions are the responsibility of national governments in the case of proven falsification, although global bodies can assist by providing contacts in cases where cross-border investigations are necessary. Eventually, however, international regulatory frameworks must be strengthened to cope with the growing challenge for governance systems posed by globalized manufacturing processes and supply chains combined with fragmented national markets. The WHO Regulatory Systems Strengthening team work with national and regional institutions to develop harmonized regulations that reduce duplication, are proportionate to current circumstances, and lighten the load of individual national regulators. They also support the sharing of knowledge, skills and systems at the regional level.

4. CONCLUSION

The world is changing rapidly—advances in technology, a step-change in communications and access to information, low-cost transport and the growth of huge, transnational corporations are all reshaping the global landscape, including the pharmaceutical trade. Unfortunately, some of these changes favour the production and sale of medical products that do not meet quality standards, either because they have been carelessly made or stored, or because of criminal intervention.

The nearly 1500 cases reported to the WHO GSMS over its first four years of operation provide many graphic examples that illustrate the forces that underpin

and facilitate the manufacture, sale and distribution of substandard and falsified medical products. As understanding of the patterns of risk grows, so does the ability to prevent, detect and respond to those risks. The world has never been better equipped to tackle the problem of substandard and falsified medical products. If governments and other decision-makers increase their efforts and resource them appropriately, the rising tide of falsification can be reversed and quality standards increased globally to ensure that people all around the world have reliable access to medical products that work as they are supposed to.



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