A Case for including Substandard and Falsified (SF) Medical Products in the African Union Smart Safety Surveillance (AU-3S) System

SF Medical Products

The seventieth World Health Assembly (WHA 70, 2017), adopted the definitions of three classes of medical products that qualify as Substandard and Falsified (SF) Medical Products. Substandard medical products also called "out of specification", are authorized medical products that fail to meet either their quality standards or their specifications, or both. Unregistered/unlicensed medical products have not undergone evaluation and 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 are those that deliberately/fraudulently misrepresent their identity, composition or source[i].

Substandard and falsified medical products are by their very nature difficult to detect. They are often designed to appear identical to the genuine product and may not cause a visible adverse reaction. They, however, often fail to properly treat the disease or condition for which they were intended and can lead to serious health consequences, including death.

SF Medical Products affect Safety of Patients

SF medical products pose a public health danger as they may contain no active ingredient, the wrong active ingredient or the wrong amount of the correct active ingredient. They are also found to contain corn starch, potato starch or chalk commonly. Some SF medical products are toxic with either fatal levels of the wrong active ingredient or other toxic chemicals. They are often produced in deplorable and unhygienic conditions by unqualified personnel and contain unknown impurities and are sometimes contaminated with bacteria.

Substandard and falsified medical products may cause harm to patients and fail to treat the diseases for which they were intended. They lead to loss of confidence in medicines, healthcare providers and health systems. Substandard and falsified medical products from all main therapeutic categories have been reported to WHO including medicines, vaccines and in vitro diagnostics. Anti-malarials and antibiotics are amongst the most commonly reported substandard and falsified medical products. Both generic and innovator medicines can be falsified, ranging from costly products for cancer to very inexpensive products for the treatment of pain. They can be found in illegal street markets, via unregulated websites through to pharmacies, clinics and hospitals. Substandard and falsified medical products contribute to antimicrobial resistance and drug-resistant infections.

SF and Vulnerable Populations

Monitoring SF becomes even more compelling as substandard and falsified medical products are most likely to reach already vulnerable patients in situations where there is constrained access to quality and safe medical products, poor governance and weak technical capacity.

Low- and middle-income countries and those in areas of conflict, or civil unrest, where health systems are weak or non-existent bear the greatest burden of substandard and falsified medical products. SF medical products, thus pose the same safety concerns that authorized medical products may pose. Hence, their

safety surveillance must be of prime concern to authorities in Africa as an estimated 1 in 10 medical products in low- and middle-income countries is substandard or falsified.[ii]

AU-3S

Safety, including access to safe medical products and other health technologies (such as medicines, vaccines, diagnostics and other health interventions), is a fundamental human right. Yet for the people in Africa, access to safe medical products continues to be elusive.

The launch of medical products for diseases that are endemic to Africa may no longer benefit from safety data from high-income countries (HICs) as such products are not of concern in HICs. It has, therefore, become necessary for Africa to create an effective fit-for-purpose safety surveillance system to support the safe launch of medical products in Africa.

The AU-3S programme will be a smart fit-for-purpose continental safety surveillance system (encompassing both passive and active surveillance approaches) for priority products that will support African Union Member States, at the continental level, to safeguard the health of their citizens. The system will cover the entire product life cycle from clinical trials through product approval to post-approval monitoring for safety and effectiveness. Priority diseases will inform criteria and selection of products including innovative and emerging products/technologies and emergency response needs. The AU-3S programme will be guided by the principles of an African continental approach, prioritization, reliance and sustainability. The programme will employ an integrated approach that will define the required principles and structures that need to be in place for AU Member States to enable informed and appropriate decision making in the context of safety data collection, analysis, signal detection, and appropriate regulatory action.

Objectives of AU-3S

Countries with stringent PV systems have strengthened warnings on or completely withdrawn several medical products from use following marketing authorization due to safety concerns[iii].); a situation which is likely to continue especially in the era of faster approval of medical products. Whilst PV capacity is available and relatively strong in the developed countries, the same cannot be said of developing countries. PV capacity in the developing countries is weak hence reducing their ability to monitor the safety of products after product approval and widespread use[iv].

An assessment of medicine regulatory systems in 26 sub-Saharan African countries showed that in relation to PV, only 8 (30%) countries collected reports on adverse events with only 3 programmes being sufficiently established to contribute a sizeable number of reports. Of the 8 countries collecting adverse events, 7 were members of the WHO Programme for International Drug Monitoring (PIDM). In those countries where a PV system existed, it was not well integrated with other regulatory activities World Health Organization. Assessment of medicines regulatory systems in sub-Saharan African countries: An overview of findings from 26 assessment reports. 2010, Geneva.

A subsequent review of the specific features of PV in Africa suggests the presence of health systems that are weak and lacking in basic infrastructure, personnel, equipment and facilities.[v]

Value proposition

The WHO in 2013 launched the Global Surveillance and Monitoring System (GSMS) to encourage countries to report incidents of substandard and falsified medical products in a structured and systematic format, to help develop a more accurate and validated assessment of the problem of SF.[vi]

Collecting, aggregating and analyzing data on SF in Africa through 3S will complement the global public health efforts and at the same time, focus on a comprehensive safety profile of priority medical products for Africa.

It is reasonable to argue that all the gains made in improving the safety profile of priority medical products in vulnerable populations of Africa will be negated if the safety profile of an authorized medical product is monitored and the availability of SF copies of same are not.

Countries already collect data on SF. Reporting such data into the same data warehouse as safety data of authorized products may not pose a big challenge. The SF data will go into a registry of SF in Africa. Such data put side-by-side with other safety data of authorized products will yield useful information to give a more comprehensive view of the safety of medical products for the African population.

To ensure that there is no duplication of effort, portals for collecting such data will be interoperable with SF portals. Other similar SF databases, both regional and global, can then interface with 3S for collaboration.

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[i] WHO Global Surveillance and Monitoring System for Substandard and Falsified Medical Product" https://www.who.int/medicines/regulation/ssffc/publications/GSMS

[ii] https://www.who.int/medicines/regulation/ssffc/publications/GSMS_ExecutiveSummary_EN.pdf?ua

[iii] Lasser KE, Allen PD, Woolhandler SJ, Himmelstein DU, Wolfe SM, Bor DH. Timing of new black box warnings and withdrawals for prescription medications. JAMA. 2002 May 1;287(17):2215-20

[iv] Olsson S, Pal SN, Stergachis A, Couper M. Pharmacovigilance activities in 55 low- and middle-income countries: a questionnaire-based analysis. Drug Saf. 2010 Aug 1;33(8):689-703.doi

[v] Isah AO, Pal SN, Olsson S, Dodoo A, Bencheikh RS. Specific features of medicines safety and pharmacovigilance in Africa. Ther Adv Drug Saf. 2012 Feb;3(1):25-34. doi:10.1177/2042098611425695

[vi] https://www.who.int/en/news-room/fact-sheets/detail/substandard-and-falsified-medical-products