

Understanding the links between access to quality, safe, efficacious and affordable medical products and the emergence of substandard, spurious, falsely-labelled, falsified, counterfeit (SSFFC) medical products

Revised draft concept note prepared by the Secretariat

1. In line with objective 6 of the agreed objectives of the Member State mechanism,¹ subparagraph 8c of the workplan of the mechanism,² and prioritized activity D in the mechanism's list of prioritized activities for 2014–2015,³ this is a revised concept note for a proposed study to deepen the understanding of the links between poor access and the emergence of SSFFC medical products.

Background

2. Since 2011, Member States, through the Member State mechanism, have been engaged in a number of efforts aimed at improving access.

2011

3. An overview of the activities carried out by WHO within the context of measures to ensure the availability of quality, safe, efficacious and affordable medicines was provided during the first meeting of the Working Group of Member States.⁴ During that meeting, Member States made several recommendations, which were included in the report of the Working Group.⁵

¹ See document A/MSM/1/INF/1.

² See document A/MSM/2/6, Annex 2.

³ See document A/MSM/3/3, Annex 3.

⁴ See document A/SSFFC/WG/2.

⁵ See document A/SSFFC/WG/5.

2012

4. Acknowledging the need for improved access to affordable, quality, safe and efficacious medicines as an important element in the effort to prevent and control medicines with compromised quality, safety and efficacy, and in the decrease of SSFFC medical products, the Health Assembly adopted resolution WHA65.19, in which, inter alia, it decided to establish a Member State mechanism to address this issue. Objective 6 of the Member State mechanism's terms of reference¹ mandated the mechanism to work on collaboration with and contribution 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 should complement measures for the prevention and control of SSFFC medical products.

2013

5. The Member State mechanism incorporated paragraph 8 into its workplan.² Subparagraph 8(c) concerns increasing knowledge and understanding in relation to lack of accessibility/affordability and its impact on the emergence of SSFFC medical products, and recommending strategies to minimize that impact.

2014

6. The third meeting of the Member State mechanism decided that a study to increase understanding and knowledge concerning the links between accessibility and affordability and their impact on the emergence of SSFFC medical products and to recommend strategies to minimize their impact would be included on the next provisional list of activities for consideration by the fourth meeting of the Member State mechanism.³ The mechanism incorporated into its list of prioritized activities for 2014–2015 prioritized activity D, under which the WHO Secretariat was engaged to review and report on all WHO activities on access to quality, safe, efficacious and affordable medical products, from an SSFFC medical products approach.³

2015

7. The fourth meeting of the Member State mechanism considered a report by the Secretariat on WHO's work regarding access to quality, safe, efficacious and affordable medical products.⁴ The report reviewed the progress made in several targeted initiatives and examined the links between gaps in the implementation of those initiatives and the emergence of SSFFC medical products. It was agreed that the Secretariat would submit to the Steering Committee of the Member State mechanism at its meeting in March 2016 a concept note and proposed budget for further work on subparagraph 8(c).⁵

¹ See document A/MSM/1/INF./1.

² See document A/MSM/2/6, Annex 2.

³ See document A/MSM/3/3.

⁴ See document A/MSM/4/4.

⁵ See document A/MSM/4/10.

2016

8. In March, the Steering Committee reviewed the concept note and proposed budget, as presented by the Secretariat. It was agreed that the Secretariat would revise the concept note so that it could be agreed upon by the Steering Committee at its next meeting in November 2016. In May, the Sixty-ninth World Health Assembly considered a report on SSFFC.¹ During the discussions that followed, several Member States reiterated the importance of continuing WHO's work on this issue.²

Emerging evidence from the WHO global surveillance and monitoring system

9. WHO's work on access is guided by principles of rational selection and use of a limited range of quality medicines, efficient procurement and effective distribution systems, affordable prices, and the role of good governance.³ Since 2013, when it was first piloted, the WHO global surveillance and monitoring system has received reports concerning over 1250 substandard and falsified products covering all therapeutic categories. The data thus gathered provide compelling evidence of the links between the emergence of SSFFC medical products and access. In particular, the fact that over half the medical products reported to the global surveillance and monitoring system match the product names of WHO Essential Medicines⁴ reflects the urgent need for the proposed study.

10. The following table highlights the growing evidence on the links between access and the emergence of SSFFC medical products.

Table. Incidents reported to the WHO global surveillance and monitoring system

Benzylpenicillin – April 2013
A doctor at a teaching hospital reported the sudden death of an 8-year-old girl who had attended the hospital for her regular injection of benzylpenicillin. There had been a stockout of the medicine at the hospital and the family of the patient had been advised to procure the medication from the local market. They returned with a product that the nurses found difficult to mix prior to injection. The child died suddenly following the administration of the medicine.
Ephedrine – May 2014
A report detailing unexpected adverse drug reactions attributed to a suspect product was received from a humanitarian organization providing medical support in a war-torn country. Owing to shortages, a hospital had been forced to procure ephedrine from an unknown source. Ephedrine is used during surgery to control low blood pressure. Patients had reportedly suffered from adverse reactions and the products were confirmed to be falsified.

¹ Document A69/41.

² See summary record of the Sixty-ninth World Health Assembly, Committee B, fifth meeting.

³ See document A/MSM/4/4.

⁴ Although the reported products may not always match the exact dosages, this data suggests a link between essential, lifesaving medicines and the emergence of SSFFC.

Meningococcal meningitis vaccines – May 2015¹
A shortage of vaccines was experienced, following the largest recorded outbreak of meningococcal meningitis in West Africa. Manufacturers were unable to meet the demand for increased supplies. Two falsified versions of the vaccine rapidly emerged on the market and were used by more than 2000 people. One of the vaccines had expired and its date had been altered to give the impression that it had a longer shelf life.
Diazepam – July 2015²
In July 2015, WHO was informed of over 1000 hospitalizations involving patients with paralysis of the neck and upper limbs. The patients had been taking diazepam, which is used to treat anxiety disorders, for the treatment of malaria. This irrational use of the available products was found to be due to access issues and the unavailability of the appropriate medicines. An investigation was conducted by a nongovernmental organization and further analysis supplied by WHO. It was discovered that the cause of the paralysis was falsified diazepam containing dangerous levels of haloperidol, an anti-psychotic medicine.
Phenobarbital – February 2016³
Faced with shortages in the supply chain and price differentials, community-based epilepsy services changed their source of supply. Within one month, health care workers were reporting a lack of efficacy. The products were confirmed to be falsified.
Artemether + lumefantrine – 2013–2016^{4,5,6}
Artemether + lumefantrine is an artemisinin-based combination therapy that is recommended by WHO as a first-line treatment against malaria. The products concerned are prequalified by WHO and are a part of the Global Fund's Affordable Medicines Facility - malaria programme. The programme was initially piloted in seven African countries, where it enabled the products to be purchased at a lower price than other less effective monotherapies. This created a high demand for these products, and falsified versions of artemether-lumefantrine, in its branded and generic forms, have been discovered across Africa in public and private health facilities. There have been occasions when millions of doses of products have been seized together in near perfect packaging but containing no active pharmaceutical ingredient.

11. The WHO global surveillance and monitoring system is providing growing evidence of an initial link between access and the emergence of SSFFC medical products, but more work needs to be done to answer outstanding questions.

¹ Medical Product Alert No.2/2015 (available at: http://www.who.int/medicines/publications/drugalerts/AlertWHO2.2015MENCEVAX_EN.pdf?ua=1, accessed 12 October 2016).

² Medical Product Alert No.4/2015 (available at: http://www.who.int/medicines/publications/drugalerts/Alert4_2015DiazepamEN.pdf?ua=1, accessed 12 October 2016).

³ Medical Product Alert No.1/2016 (available at: http://www.who.int/medicines/publications/drugalerts/Alert1_2016_Fev_FalsifiedPhenobarbitalWestAfrica_EN.pdf?ua=1, accessed 12 October 2016).

⁴ Drug Alert No.127 (available at: http://www.who.int/entity/medicines/publications/drugalerts/Alert_127_Information_Coartem.doc?ua=1, accessed 12 October 2016).

⁵ Drug Alert No. 130 (available at: http://www.who.int/medicines/publications/drugalerts/Alert_130_Information_Coartem_VF.pdf?ua=1, accessed 12 October 2016).

⁶ Medical Product Alert No.1/2015 (available at: <http://www.who.int/medicines/publications/drugalerts/Artemether-LumefantrineENversion.pdf?ua=1>, accessed 12 October 2016).

Goal

12. In line with subparagraph 8(c) of the workplan, the proposed study aims to deepen the understanding of the links between access and the emergence of SSFFC medical products.

Proposed research questions

13. The study will attempt to respond to the following research questions:

- (a) Is there evidence of an increased risk of circulation of SSFFC medical products in the absence of access to affordable products?
- (b) Is there verifiable evidence that SSFFC medical products are circulating in the public sector?
- (c) To what extent can increased public provisioning of medicines contribute to reducing the circulation of SSFFC medical products in the local markets?
- (d) What are the emerging best practices for increasing the access to affordable medicines?

Constraints

14. It is acknowledged that there is a need for capacity-building in order to enable national regulatory systems to verify medicines, detect those that are SSFFC medical products, and take the necessary action to respond effectively to the complex challenge that such products pose. However, it is vital to note that the understanding on the links between access and circulation of SSFFC medical products is limited and there may be information gaps in the literature. Therefore, in order to ascertain and compare their relative effectiveness in controlling the prevalence of SSFFC medical products, there is an urgent need to analyse both the purely stepwise 'regulatory approach' focusing on surveillance and detection and a more comprehensive 'health systems approach' that emphasizes improving public access to safe, quality and affordable medicines.

Approach and costs

15. Two approaches have been proposed by the Steering Committee for consideration by the Member State mechanism.

With limited resources

16. If only limited resources are available to the Secretariat, the following stepwise approach is proposed:

- (a) Complete preliminary survey of the literature
- (b) Complete review of cases reported to the WHO global surveillance and monitoring system
- (c) Complete WHO Secretariat report to be published.

With full funding of approximately US\$ 60 000

17. With full funding available to the Secretariat, the following stepwise approach is proposed:

- (a) An experienced lead researcher/writer will be recruited
- (b) A systematic review will be conducted of the published scientific literature, related information in the public domain, and data generated by the WHO GSMS
- (c) Structured interviews will be undertaken with key informants (to be determined) who are active in delivering pharmaceutical services in countries
- (d) A draft working document will be prepared
- (e) A core group of experts from different regions will be approached by the lead researcher/writer and invited to provide a technical review of the working document. The lead researcher/writer will also serve as the focal point to enable the Secretariat to manage the discussion on this topic on WHO's MedNet collaborative platform.

18. **Budget.** The breakdown of estimated cost to the Secretariat of employing this approach is as follows:

Lead writer/consultant (30 days) – US\$ 18 000
Research assistant (10 days) – US\$ 3500
Secretariat costs (one full-time equivalent staff member at grade P.3 for one month) – US\$ 25 000
Teleconference costs (direct costs from the provider) – US\$ 2800
Total net estimated cost – US\$ 49 300
PSC at 15% – US\$ 7395
Total – US\$ 56 695

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