Access to Quality Medicines in Developing Countries

An informal selection of scientific literature

Elements added on 14/06/17 are in red

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1. Introduction

Poor-quality medicines are mainly prevalent in low- and middle-income countries (LMICs), where they represent a serious threat to individual and public health[1]. Even medicines whose manufacturing process is not *per se* complex may present serious quality problems: for instance, paracetamol-containing products may be prone to develop the toxic contaminant 4-aminophenol, if manufactured in inappropriate conditions.

Over recent years, a growing attention has been being given to the need of assuring the quality of medicines in LMICs, e.g. in the framework of strategies against resistance to anti-malarials[2] and antibiotics[3], of strategies to improve access to asthma medicines[4], and of general medicines' procurement strategies[5]. The WHO set up a Member State Mechanism for Substandard/Spurious/Falsely-labelled/Falsified/Counterfeit medical products or SSFFC (http://apps.who.int/gb/ssffc/).

Quality of essential medicines should not be pursued in isolation, but always in conjunction with access to essential medicines[6].

In this informal working document, we try to summarize the internationally accepted definitions and to provide a non-exhaustive selection of scientific papers and regulatory documents addressing the subject of quality of medicine, with (non-exclusive) focus on resource-constrained settings.

2. Definitions[7]

Appropriate standards

By "appropriate standards", we mean those set by the World Health Organization (WHO) for pharmaceuticals in the *WHO Technical Report Series 992: WHO Expert Committee on Specifications for Pharmaceutical Preparations, Technical Report Series 996, 49th report, 2015*[8]; the *WHO Expert Committee on Specifications for Pharmaceutical Preparations, Fiftieth Report, WHO 2016*[9]*,* and further updates.

In addition, reference may be done to the *Guide to Global Fund Policies on Procurement and Supply Management of Health Products, July 2016, Geneva, Switzerland*.

Substandard and falsified medical products

On 29 May 2017, delegates at the World Health Assembly have reached new agreement on substandard and falsified medical products. The new definitions are as follows:

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[1] Oxfam. *Eye on the Ball: medicine regulation –not IP enforcement– can best deliver quality medicines* (2011) http://www.oxfam.org/en/policy/eye-ball

[2] Chapter *Removal of substandard and counterfeit drugs* in the WHO document *Global plan for artemisinin resistance containment, 2011*

[3] Section on *Unassured drug quality and irrational use* in the paper of Raviglione et al. *The WHO policy package to combat antimicrobial resistance*. Bulletin WHO 2011; 89:390-392

[4] Macé C, *Access to essential asthma medicines: the response of the Asthma Drug Facility*. Ess Med Mon 2011;5:1-4

[5] Chapters 1.3.2.3 and 1.4.4 in *The World Medicine Situation 2011 - Procurement of Medicine*. WHO, Geneva 2011

[6] R Ravinetto and C. Luyckx. Access to medicines and quality of medicines: always together! Published on International Health Policies on 30/01/2013. http://e.itg.be/ihp/

[7] Various resources on "Legal and Regulatory Aspects of Falsified and Substandard Medicines" are available at http://www.globalforumljd.org/legal-and-regulatory-aspects-falsified-and-substandard-medicines

[8] http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

[9] http://www.who.int/medicines/publications/pharmprep/trs_996/en/

- The new name of “substandard and falsified” (SF) medical products will be used for what had previously been known as “substandard/spurious/falsely-labelled/falsified/counterfeit (SSFFC)” medical products.
- “Substandard” medical products (also called “out of specification”): authorized by national regulatory authorities, but fail to meet either national or international quality standards or specifications – or in some cases, both.
- “Falsified” medical products: deliberately or fraudulently misrepresent their identity, composition or source.
- “Unregistered or unlicensed medical products”: have not been assessed or approved by the relevant national or regional regulatory authority for the market in which they are marketed, distributed or used.

3. Regulatory and policy documents in English

- WHO-IMPACT. Declaration of Roma, 18th February **2006**. Conclusions and recommendations of the WHO “Combating Counterfeit Drugs: Building Effective International Collaboration” International Conference
- Pan-American Network for Drug Regulation Harmonization Anti-Counterfeiting Group, WHO Drug Information Vol.22, N°4, **2008**, p.278.
- ICDRA 3rd International Conference of Drug Regulatory Authorities, Strategies to fight counterfeit medicines, WHO Drug Information Vol.22, N°4, **2008**,pp. 262-263.
- WHO Legal aspects of defining counterfeit medicines: a discussion paper. WHO **2009**. Regional Office for South East Asia, New Delhi.
- WHO Regulatory Harmonization. Updating medicines regulatory systems in sub-Saharan African countries. WHO Drug Information Vol. 24, No. 1, **2010**
- WHO. Assessment of medicines regulatory systems in Sub-Saharan African countries: an overview of findings from 26 assessment reports. WHO **2010**
- WHO. Report of the working group of member states on substandard/spurious/falsely labeled/falsified/counterfeit medical products. A/SSFFC/WG/5, 11th March **2011**[10].
- Moore T et al. Assuring the quality of essential medicines procured with donor funds. Health Nutrition and Population Discussion Paper **2011**. The International Bank for Reconstruction and Development / The World Bank
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- WHO Quality Assurance and Safety Medicines (QSM) Team. Regulator prequalification of medicines: a future concept for networking. WHO Drug Information Vol. 26, No. 3, **2012**
- Addis Ababa Declaration on Combating Pharmaceutical Crime. 12 December **2013**[11].
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- Chowdhury P et al. Indian Council for Research on International Economic Relations. Policy Brief # 1. Administrative Structure & Functions of Drug Regulatory Authorities in India. September **2015**
- Chokshi M et al. Indian Council for Research on International Economic Relations. Policy Brief # 2. Drug Quality and Safety Issues in India. September **2015**
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[10] http://apps.who.int/gb/ssffc/pdf_files/A_SSFFC_WG5-en.pdf

[11] http://www.interpol.int/News-and-media/News/2013/N20131216

4. Regulatory and policy documents in French

- WHO. Guide pour l'élaboration de mesures visant à éliminer les médicaments contrefaits. WHO/EDM/QSM/**99**.1
- XIIIe Conférence des Chefs d'État et de gouvernement des pays ayant le français en partage. Montreux (Suisse), 23-24 octobre **2010**. Résolution sur le renforcement de la cooperation entre les États pour lutter contre les faux médicaments et les produits médicaux falsifiés.
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- Communauté Economique et Monétaire de l'Afrique Centrale (CEMAC). Conférence des Ministres de la Santé des Etats membres de la CEMAC. Déclaration de Douala. « Mettre un ferme au trafic des faux médicaments et aux circuits illicites des médicaments en Afrique Centrale ». Douala, Cameroun, 23 juin 2016
- Duteil Q et Chemtob-Comc é MC. Le traffic des faux médicaments : état des lieux et moyens d'action. Panorama de droit pharmaceutique **2017**; 4 :97-117

5. WHO Alerts[14] and other Regulatory Alerts

- WHO Pre-qualification Programme. Falsified lamivudine, zidovudine and nevirapine tablets (Zidolam-N) in Kenya. Alert, 22 and 23 September **2011**
- WHO Information Exchange System. Alert No. 125. Contaminated Isotab® (isosorbide mononitrate) incident in Lahore Pakistan. 3rd February **2012**. QSM/MC/IEA.125
- WHO Information Exchange System Alert No. 126. QSM/MC/IEA.126. Contaminated Dextromethorpan Active Pharmaceutical Ingredient. 24 January **2013**
- WHO Information Exchange System Alert No. 127. QSM/MC/IEA.127. Falsified batches of Coartem recently circulating in Western and Central Africa. 3 May **2013**
- WHO Information Exchange System Alert No. 128. QSM/MC/IEA.128. Falsified batches of Postinor 2 recently discovered in Nigeria. 26 July **2013**
- WHO Information Exchange System Alert No. 129. RHT/SAV/MD//IEA.127. Contaminated Dextromethorphan active pharmaceutical ingredient. 17 October **2013**
- WHO Information Exchange System Alert No. 129. RHT/SAV/MD//IEA.130. Falsified batches of Coartem recently circulating in Cameroon. 8 November **2013**
- WHO Information Exchange System Alert No. 131. RHT/SAV/MD//IEA.131. Falsified antimalarial medicines in West and Central Africa. 25 March **2014**
- WHO Information Exchange System Alert No. 133. RHT/SAV/MD//IEA.132. Falsified medicines in West and Central Africa. 10 October **2014**
- WHO Information Exchange System Alert No. 1/2015. RHT/SAV/MD/1/2015. Falsified antimalarial medicines circulating in West Africa. February **2015**
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- WHO Information Exchange System Alert No. 3/2015. RHT/SAV/MD/3/2015. Falsified meningitis vaccines circulating in West Africa. UPDATE. May **2015**

[12] http://www.fondationchirac.eu/le-conseil-des-ministres-acp-a-adopte-une-resolution-contre-les-faux-medicaments/

[13] www.fondationchirac.eu

[14] All available in English and French at http://www.who.int/medicines/publications/drugalerts/en/

- WHO Information Exchange System Alert No. 4/2015. RHT/SAV/MD/4/2015. Adverse reactions caused by Falsified Diazepam in Central Africa. July **2015**
- WHO Information Exchange System Alert No. 5/2015. RHT/SAV/Alert 5.2015. Falsified emergency contraceptive circulating in East Africa. November **2015**
- WHO Information Exchange System Alert No. 1/2016. RHT/SAV/Alert 1.2016. Falsified phenobarbitone tablets circulating in West Africa. February **2016**
- WHO Information Exchange System Alert No. 2/2016. RHT/SAV/Alert 2.2016. Falsified AMARIL yellow fever vaccines circulating in South East Asia. February **2016**
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- WHO Information Exchange System Alert No. 3/2016. RHT/SAV/Alert 3.2016. Falsified Hepatitis C medicines circulating in South East Asia. February **2016**
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