Editorial

Poor-quality medical products: time to address substandards, not only counterfeits

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The rapid globalisation of the pharmaceutical market that characterised the two last decades has led to a situation of multiple standards (Caudron et al. 2008): the quality of medicines is not uniform worldwide, but largely depends on the level of income (Newton 2010) and regulation (Editorial, 1852; World Health Organization, 2010; Nishtar 2012) in the country of destination. Poor-quality medicines are generally categorised as either counterfeits, which are deliberately and fraudulently mislabelled with respect to identity and/or source (http://www.who.int/mediacentre/factsheets/fs275/en/), or substandards, which according to the WHO definition of 2010 are genuine medicines produced by the manufacturers authorised by the National Medicine Regulatory Authority (NMRA) but do not meet quality specifications set by national standards (http://www.who.int/medicines/services/counterfeit/faqs/06/en/index.html).

Over recent years, a growing number of global initiatives have been launched to fight the illegal counterfeit medicines (Declaration of Rome, 2006; 13th International Conference of Drug Regulatory Authorities, 2008; Appel de Cotonou contre les faux médicaments, 2009; Council of Europe Convention, 2011), which have become quite a well-known issue, also for the general public and lay press. Conversely, substandards have remained poorly or not addressed, despite being a more widespread problem, highly prevalent in resource-poor settings (Caudron et al. 2008; Newton 2010) and at least as dangerous as counterfeits.

Between 2008 and 2011, the World Health Assembly (WHA) faced persistent difficulties to reach an agreement for adopting a resolution on this matter. However, the 65th WHA approved a resolution on a new ‘Member State mechanism’ (i.e. an intergovernmental mechanism, open to all WHO Member States), proposing international collaboration on ‘substandard, spurious, falsely-labelled, falsified or counterfeit (SSFFC) medical products’. The explicit goal of the Member State mechanism will be ‘to promote the prevention and control of SSFFC medical products and associated activities, to protect public health and promote access to affordable, safe, efficacious and quality medical products’. This creates an opportunity to tackle the problem in a comprehensive, patient-centered approach. But will the Member State mechanism be able to turn the tide? What is the extent of SSFFC, and how should they be approached and fought?

Quality of medicines: a cross-cutting issue

Even if surveys on quality are not generally conducted according to harmonised methods (Newton et al. 2009), there is evidence that poor-quality medicines are widespread in poor countries, with serious and often undetected consequences for individuals and for public health. Problems have been mainly documented in the field of malaria (OMS, 1995; Maponga & Ondari 2003; Minzi et al. 2003; Abdo-Rabbo et al. 2005; Amin et al. 2005, 2007; Alfarad et al. 2006; Atemnkeng et al. 2007; Gaudiano et al. 2007; Bate et al. 2008; Kaur et al. 2008; Tipke et al. 2008; Leslie et al. 2009; WHO, 2011a; Gaurvika et al. 2012), most likely because physicians’ and decision-makers’ awareness has significantly grown because of the spectacular raise in resistance to the traditional molecules. To a minor extent, quality has been investigated and problems have been documented in other therapeutic fields, including tuberculosis (Laserson et al. 2001; Laing et al. 2004; WHO, 2011b), infectious disease (The USP Drug Quality and
Information Program, 2004; Kelisidis et al. 2007), neglected diseases (Sundar et al. 1998; Dorlo et al. 2012), chronic diseases (Laroche et al. 2005; Dorlo et al. 2012), and others (Eichie et al. 2009), as well as in non-disease-specific surveys (Shakoor et al. 1997; WHO 1999; Taylor et al. 2001). Tragically, the presence of poor-quality medicines often comes to light only after the observation of increased resistance patterns or abnormal morbidity and mortality rates, as it recently happened in Bangladesh (Dorlo et al. 2012) and in Pakistan (Arie 2012). To date, the resources mobilised for assuring the quality of HIV-AIDS, malaria and tuberculosis medicines (http://apps.who.int/prequal/default.htm; http://www.theglobalfund.org/en/procurement/quality/pharmaceutical/#General; http://www.fda.gov/InternationalPrograms/FDABeyondOurBordersForeignOffices/AsiaandAfrica/ucm119231.htm) resulted in encouraging results for the medicines covered by international mechanisms such as the WHO prequalification (World Health Organization, 2007; WHO, 2011a,b). No comparable mechanisms exist to ensure the quality of the other essential medicines; nonetheless, poor-quality medicines are not limited to specific diseases, and even simple anti-febrile and anti-cough medicines may cause death if contaminated (Geiling & Cannon 1938; Okuonhgae et al. 1992; Hanif et al. 1995; Woolf 1998; Singh et al. 2001; Rentz et al. 2008; Abubukar et al. 2009).

Remarkably, similar concerns about a north–south quality gap, leading to serious consequences for the health of vulnerable populations, have been expressed about in vitro diagnostics and medical devices, where substandards seem to be a more widespread problem than counterfeits (Mori et al. 2011).

**Inadequate definitions?**

The 2010 WHO definition of substandard medicines – ‘genuine medicines produced by the manufacturers authorised by the NMRA which do not meet quality specifications set for them by national standards’ – (http://www.who.int/medicines/services/counterfeit/faqs/06/en/index.html) differs from the previous one\(^1\) in that the reference to quality specifications set in official pharmacopoeias has been replaced by the reference to quality specifications set by national standards, without taking into account that according to the WHO itself, only approximately 20% of countries have fully operational regulatory mechanisms for medicines. Of the remaining countries, 50% have NMRA of varying capacity and 30% have either no or very limited capacity for medicine regulation (African Medicines Regulatory Harmonization Initiative, 2008), for example, limited capacity to obtain the minimal information needed to thoroughly assess products’ dossiers before registration. In the case of countries with underresourced NMRA, setting the national standard as reference leads to a normative framework that de facto accepts a multiplicity of standards, including inadequate standards. This contrasts with the previous definition, which promoted the reference to the internationally recognised and harmonised standards of official pharmacopoeias. The inadequacy of the current definition of substandards enables many manufacturers to sell poor-quality medicines with no risk to be sanctioned, just because these products have been registered by NMRA with limited capacity. The current status quo further the interests of companies with poor technical capacity or with poor ethics, but it certainly does not serve the interests of the patients.

**Opportunities and threats for the Member State mechanism**

The difficulties that caused the delay of agreement at WHA level were mainly because of the sometimes almost exclusive emphasis on ‘counterfeits’, and to the tensions between the ‘intellectual property approach’ and the ‘public health approach’ (Newton et al. 2011). A constructive dialogue for developing measures that ensure universal access to medicines of proven quality is now rapidly required to achieve the human right to health (Universal Declaration of Human Rights 1948, art. 25) as well as one of the Millenium Goals (target 8.E, ‘in cooperation with pharmaceutical companies, provide access to affordable essential medicines in developing countries’).

As the SSFFC definition encompasses medicines, vaccines, medical devices and in vitro diagnostic tests, the new Member State mechanism has now the opportunity to shape evidence-grounded policies for protecting vulnerable men, women and children from the plague of poor-quality medical products as a whole, thus addressing the problem comprehensively rather than product by product or disease by disease, and without prioritising counterfeits over substandards. This may only be achieved...
by a complex set of measures that are needed to prevent the appearance of poor-quality medical products and that include:

- Strengthening the national and international regulatory oversight – without putting the responsibility exclusively on the authorities in the ‘territory of use’;
- Increasing transparency on quality information;
- Adapting the procurement policies of all the major donors and procurement agencies, to promote a uniform reference to WHO standards (WHO, 2011c; http://www.who.int/medicines/areas/quality_safety/en/).

It is hoped that the Member State mechanism will manage to overcome those ideological, economical and commercial interests that have so dramatically delayed this issue at the WHA over the last six years. The interest of the patient and the protection of his/her health should be central. Any other considerations are peripheral.

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