CAMPAIGN FOR ACCESS TO ESSENTIAL MEDICINES

MEDECINS SANS FRONTIERES

Médecins Sans Frontières briefing note ahead of the February 2011 meeting of Working group of WHO Member States on Substandard / spurious / falsely-labelled / falsified / counterfeit medical products

Time to focus on quality

Both substandard and fake medicines present serious concerns for public health. Médecins Sans Frontières (MSF) comes across many medicines that are substandard or of unassured quality[1] in our activities in more than 60 countries across the world. However, we see or suspect fake drugs or vaccines more rarely.[2]

Although substandard medicines represent the larger problem from a public health perspective (A/SSFC/WG/3, point 24), recent international attention has been paid mainly to counterfeit goods. MSF welcomes the documents prepared by WHO for this working group which describe well the public health problems and current activities and contain a number of useful proposals (A/SSFFC/WG/2-3). What MSF seeks in this policy debate is a better balanced approach that addresses the problem of both substandard and fake medicines in developing countries, instead of one being ignored to the detriment of the other.

The problem of substandard medicines

Substandard medicines are genuine drugs produced by legitimate manufacturers - whether originator or generic - which do not meet the standards set for them with regards to quality, strength, purity and packaging. The circulation of substandard medicines is a neglected problem and hits mainly vulnerable populations in resource-limited countries.

Substandard medicines may have different characteristics: they may not contain the correct amount of the active ingredient; be contaminated; undergo accelerated deterioration because of poor quality packaging; be insufficiently bio-available; be out-of-specification because of impurities or residual solvents; fungal contamination of intravenous fluids; packaging problems; labelling mistakes; and so on.

All these problems can have a direct negative impact on the health of the patient.

They may be caused by inadequate manufacturing practices, due to insufficient technical capacities and competencies. They may also occur because weak regulations and weak

[1] J.-M. Caudron, N. Ford, M. Henkens, C. Mace, R. Kiddell-Monroe and J. Pinel. Substandard medicines in resource-poor settings: a problem that can no longer be ignored. Trop Med and Int Health, Vol. 13 no 8 pp 1062-1072 August 2008. Available from: http://www.msfaccess.org/fileadmin/user_upload/key-publication/Trop_Med_and_Int_Health_vol_13_Substandard%20Meds.pdf

[2] Pécoul B., Chirac P., Trouiller P., Pinel, J. (1999) Access to essential drugs in poor countries. A lost battle? JAMA, 281: 361-367

enforcement do not push manufacturers, seeking to reduce production costs as much as possible, to invest in quality.

Problems with quality of medicines are widespread (A/SSFFC/WG/2, point 3). Among the largest studies into quality of medicines, the WHO-USP study into the Quality of Anti-Malarial drugs in sub-Saharan Africa (QAMSA) assessed the proportion of artemisinin-based combination therapy and sulfadoxine/pyrimethamine products meeting WHO quality standards. The study was conducted in Cameroon, Ethiopia, Ghana, Kenya, Nigeria, Tanzania, Madagascar, Senegal and Uganda and involved laboratory analysis. It found that 44% of samples from Senegal, 30% from Madagascar and 26% from Uganda failed to complete quality control laboratory tests, an alarmingly high failure rate.[3]

What role for National Medicine Regulatory Authorities in importing countries?

The role of the National Medicines Regulatory Agency, or NMRA, is paramount. A major underlying reason for both substandard and fake medicines in developing countries is the weak capacity of medicine regulatory systems in many developing countries (A/SSFFC/WG/3, point 5, 7). The extent of the substandard medicine problem shows that there has been not nearly enough investment in National Medicines Regulatory Authorities, and that a real investment in capacity in least developing countries by national governments and the international community has probably never really been made. NMRAs must be strengthened and have the political support at national level to be autonomous agencies. This should be a national priority with the support of donors and from WHO, and through regional and international initiatives.

In 2010, MSF held a meeting that included participants from regulators, purchasers and civil society organizations from developing countries that mainly rely on importation. The participants shared their concerns about the quality of medicines entering their countries.

In many developing countries, where regulatory authorities are often under-resourced, a medicine may be granted registration after a simple review of the documents provided by the supplier, rather than after a full evaluation involving an audit at the manufacturing site plus in-depth analysis of the product dossier.

A recent WHO assessment report of 26 African countries[4] noted many gaps including in the assessment of products submitted for market authorisation; there is, in many countries, the absence of systems to verify market authorisation on importation or to control exported medicines. While countries usually have structures to inspect production facilities, the lack of qualified inspectors severely limits the number and quality of inspections. Market surveillance was also poor.

There are, however, a number of developing countries that have achieved significant progress that could serve as an example for others to follow. Another possible avenue for progress is through regional and sub-regional cooperation to pool resources. This includes the harmonisation of procedures between countries through regional initiatives (such as the EAC and UEMOA[5]), as well as a system of mutual recognition of evaluation of products done by

[3] Survey of the Quality of Selected Antimalarial Medicines Circulating in Madagascar, Senegal, and Uganda, November 2009; http://www.usaid.gov/our_work/global_health/hs/publications/qamsa_report_1109.pdf

[4] Assessment of medicines regulatory systems in sub-Saharan African countries. An overview of findings from 26 assessment reports. WHO/EMP/QSM/2010.4. WHO 2010 http://www.who.int/medicines/publications/assesment_africa/en/index.html

[5] East African Community (Kenya, Uganda, Tanzania, Rwanda, Burundi) and Union Economique et Monétaire Ouest Africaine (Bénin, Burkina Faso, Côte d'Ivoire, Guinea-Bissau, Mali, Niger, Sénégal, Togo)

other regulatory authorities or by fast-tracking national registration based on WHO prequalification.

Regional harmonisation between different countries' regulations can be closely linked to another objective – that of preventing medicines from entering a country through unwanted channels from neighbouring countries.

What role for National Medicine Regulatory Authorities in exporting countries?
Highly-regulated countries can play a double-edged role in this field. Many such countries have less stringent enforcement of regulatory requirements for products intended *solely for export*. This deceives many purchasers, who may be under the false impression that the products purchased meet the producing country standards, when in fact this is not the case. Exporting countries (both developed and developing countries) need to ensure that medicinal products produced and exported from their territory meet WHO quality, safety and efficacy standards.

What role for the World Health Organization?
The support given by WHO to NMRAs over many years has been important, be it through normative work or through direct support such as assessment, training, participation in Good Manufacturing Practices (GMP) audits, consulting activities and so on (A/SSFFC/WG/2, point 20-24). In addition, the prequalification of health technologies ensures the quality of HIV, TB, malaria and reproductive health products (A/SSFC/WG/2, point 25-26) for various actors, and enables countries to fast track national registration. Throughout these activities, WHO performs a series of essential functions for developing, establishing and promoting international standards for pharmaceuticals, fulfilling its mandate under the WHO Constitution (A/SSFFC/WG/2, point 4).

This support now appears under threat. MSF is concerned that the priority given to the Department of Essential Medicines and Pharmaceutical Policies (EMP), a WHO flagship programme, is declining. Its resources are down to the bare bones necessary to perform essential functions (except maybe for the pre-qualification programme), after decreased funding from WHO's regular budget over the past few years.

WHO's normative work in the field of pharmaceuticals is essential and will be badly impacted if it is not adequately supported. This role should therefore be reinforced and adequately resourced.

In this respect, WHO guidelines must not become 'me-too' guidelines, or those based on guidelines from other countries or organizations like the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)[6]. WHO has a responsibility to set standards that are international in scope, reflecting the disease burden and the risks and benefits faced globally, instead of simply reflecting the position of selected regions.

Member States that are not yet doing so should take the opportunity to contribute more actively to the setting of norms, standards and guidelines for the quality, safety, and efficacy of medicine by the WHO Expert Committee on Specifications for Pharmaceutical Preparations, so that measures addressing public health problems are adopted in an objective and reliable way. Those guidelines must be properly informed by international experts and needs to take into

[6] ICH brings together the regulatory authorities and pharmaceutical industry of Europe, Japan and the US.

consideration the risk and benefit implications for availability of medicines when introducing new standards.

WHO also has a key role in establishing and revising the text of *The International Pharmacopoeia* and preparing the international reference materials for the essential medicines, included in the International Pharmacopoeia. It is crucial that this guidance continues to be done in an independent scientific way, at an international level, and be made publicly available in different languages so that all Member States can benefit from it.

It is essential that additional practical and direct support is offered by WHO to countries to strengthen their NMRA so that they can implement WHO guidelines. The WHO Medicines Regulatory Package (A/SSFC/WG/2, point 22) is a first step in the right direction, but this needs to be further developed and implemented at country level.

What role for donor countries and organisations?
Donors have a key role in reinforcing the work of WHO and in establishing programmes to support national medicine regulatory agencies.

In addition, donors have a responsibility in their health programmes to set clear quality assurance policies for the selection and purchase of the medicines bought with their funds. For many donors, this is not the case today. For example, the World Bank has strict financial and managerial rules set for medicine purchases but does not provide clear guidance on how to procure quality medical goods. A notable exception is the Global Fund, which has developed a sound quality assurance policy for antiretroviral, anti-tuberculosis and anti-malarial medicines, and is working on establishing a policy for other essential medicines.

Donors should set a clear quality assurance policy in accordance with WHO standards to ensure that their health programmes in countries with weak regulatory capacity have access to quality medicines.

What role for procurement agencies?
Many donors and countries with weak a NMRA delegate the quality assurance function to procurement agencies. Procurement agencies may have the technical knowledge to assess the quality of the medicines but often come under pressure to buy medicines of the lowest possible price and their commercial interests may conflict with quality assurance policy.

Procurement agencies, distributors and purchasers, as the main actors purchasing medicines on behalf of developing countries, should be 'prequalified' by a centralised neutral body, potentially hosted by WHO, on the basis of existing WHO standards[7]. This could bring short-term improvements in the quality of medicines in developing countries where the capacity of their NMRA is currently low.

The problem of counterfeit/falsified/fake medicines

Fake medicines present a serious threat for public health that needs to be appropriately addressed. For example, the presence of fake anti-malarials in South East Asia where resistance against artemisinin drugs has already emerged, is a serious concern.

[7] A Model Quality Assurance System for Procurement Agencies
http://whqlibdoc.who.int/hq/2007/WHO_PSM_PAR_2007.3_eng.pdf

However anti-counterfeit laws, under the laudable guise of fighting to eradicate the public health problem of fake medicines, must not be used by pharmaceutical companies and developed countries as a tool to enforce intellectual property rights, and clamp down on legitimate competition from quality generic medicines.

Confusion has been created by the use of the overly-broad term 'counterfeit medicines'. A new term and clear definition is needed to ensure activities address public health concerns; as such, we strongly support the WHO proposal to replace this with the term 'falsified medicines' (A/SSFFC/WG/3, point 27). The problem with the existing term is twofold.

First, 'counterfeit' is a trademark term defined in the TRIPS Agreement covering a brand name, or in some jurisdictions the shape or colour of a medicine. Yet not all fake medicines infringe a trademark. A fake medicine may, for example, falsely claim to contain a pharmaceutical ingredient against malaria, without copying an existing trademark. Any initiative that aims to clamp down on trademark infringements will therefore do nothing to address this problem.

Second, existing counterfeit medicine definitions make no distinction between wilful trademark counterfeiting (when there is a deliberate intention to deceive) and civil trademark infringement (when two brand names or packages are too similar from the rights holder's perspective). This lack of precision has led to a state of affairs whereby legitimately registered generic medicines could be accused of being 'counterfeit', solely because a civil trademark law suit might be ongoing, on the basis, for example, of a similar-looking pill or a similar-sounding name.

The exclusion of patents in the 'Hammamet definition'[8] of IMPACT has been helpful, but civil trademark infringements should also be explicitly excluded from any definition. Neither patents nor civil trademark disputes have anything to do with falsified medicines.

It is important that the issue is resolved, both because it prevents further discussion of the public health concerns, but also because overbroad definitions can defeat the aim of deterring counterfeit medicines. Indeed, trade in fake medicines is encouraged when quality affordable medicines are not available. However much commercial level trademark counterfeiting may be one aspect of the overall problem, applying an intellectual property framework to address the public health problems of substandard and fake medicines is not the appropriate response.

Strengthening NMRAs is again critical. It makes little sense to strengthen customs and enforcement agencies if regulatory authorities continue to lack the resources for surveillance and control of the pharmaceutical market; some even lack resources to examine suspected drugs that have been seized by enforcement agencies.

In developed countries, policies to fight fake medicines have been built on and are additional to existing strong drug regulatory systems. This is not the case in developing countries, where such policies risk becoming a substitute focus and diverting funding away from NMRAs. Enhanced NMRAs will help control substandard and fake medicines and, in resource-limited settings, it is important that policies maximise the potential benefits of investments rather than divert resources.

WHO should collaborate with other intergovernmental and national agencies to address the public health problem of falsified medicines in terms of "advocacy, norms and standards, and technical support" (A/SSFFC/WG/3, point 21) and as appropriate strengthen its own

[8] http://www.who.int/impact/resources/IMPACTthirdgeneralmeeting_%20report.pdf

programme to fight falsified medicines (A/SSFFC/WG/3, point 20). The International Medical Product Anti-Counterfeit Taskforce (IMPACT) is however not the appropriate forum for this. Created in 2006, it includes various stakeholders, including the private sector, lacks a mandate from WHO's governing bodies and presents serious conflicts of interest. For example, the working group on technology (A/SSFFC/WG/4, point 41) is chaired by the pharmaceutical industry trade group IFPMA, although the introduction of new technologies to identify and trace legitimate products, also referred to by WHO (A/SSFC/WG/3, point 11), should be considered very carefully and independently for its potential to create disadvantages to the production of affordable, generic medicines and whether such technologies are feasible to use in resource poor settings.

While there is a need in some circumstances to gather information and evidence from the private sector, there must be a clear separation between two distinct functions; on the one hand consultation, and on the other setting policies and endorsing solutions. Instead, WHO should have its own programme on falsified medicines and collaborate with other government agencies as appropriate.

Conclusions and Recommendations

Both fake and substandard medicines represent a public health concern, and MSF experience considers putting the focus on quality to be paramount. Doing so means improving the regulatory function of NMRAs at country level.

The following policy measures should be pursued:

- National medicine regulatory agencies must be strengthened and have the political support they need to be autonomous and functioning. This should be a national priority, with the support of donors and WHO, and through regional and international initiatives.
- Exporting countries (both developed and developing countries) need to ensure that medicinal products produced in and exported from their territory meet WHO quality standards.
- WHO's normative work in the field of pharmaceuticals is essential. This role should therefore be reinforced and adequately resourced.
- Donors should set a clear quality assurance policy in accordance with WHO standards to ensure that their health programmes in countries with weak medicine regulatory capacity support quality medicines.
- Procurement agencies, distributors and purchasers, as the main actors purchasing medicines on behalf of developing countries, should be 'pre-qualified' by a centralised neutral body, potentially hosted by WHO, on the basis of existing WHO standards.
- MSF strongly supports WHO's proposal to change the term from 'counterfeit' to 'falsified' medicines (A/SSFFC/WG/3, point 28) and calls on countries to support this change and adapt an appropriate definition that excludes patents and civil trademark infringements. A new term and clear definition is needed to ensure activities address the public health need.
- WHO should distance itself from IMPACT, strengthen its own programme on falsified medicines and collaborate with other government agencies as appropriate.