

# Interview

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### **Explain the difference between the definitions of substandard and falsified medicines; how important is it to make clear this distinction?**

There remains debate about both terms and definitions. There is a growing trend in using the term ‘falsified’ rather than counterfeit in case the latter is used to invoke intellectual property considerations. The term used is relatively unimportant but the underlying definition is crucial. We have used the definitions that WHO has utilised as the basis for defining counterfeit (=falsified) and substandard medicines. Falsified medicines are produced fraudulently and often, but not always, lack any of the stated active pharmaceutical ingredients. In contrast, substandard medicines are produced by authorised manufacturers that do

not meet national pharmacopeial standards because of errors in the quality or quantity of raw materials or in manufacturing.

The distinction is important as the origins and solutions for the two types of poor quality medicines differ considerably. Falsified medicines are deliberate criminal attempts to deceive health workers and patients, requiring primarily police/ Medicines Regulatory Authority (MRA) legal action. In contrast, substandard medicines result from poor quality control and manufacturing processes, potentially remedied by MRA intervention and support for improvement of factory processes.

### **A legal debate on the correct definitions and terminology has thwarted progress in combating counterfeit and substandard medicine. What will standardised terminology resolve? And how damaging has this drawn-out wrangling been?**

The lack of consensus and the extraordinarily long delays have impeded progress in improving medicine quality. Consensus on appropriate standardised terminology will help reporting and understanding of medicine quality epidemiology and discussion of appropriate interventions. Those deciding this issue should remember the human cost of poor quality medicines and come to a rapid conclusion. If a new pathogen, such as a new ‘flu variant with ‘visible’ mortality had arisen, it would not have taken the international community nearly

2 years to debate definitions.

WHO and member states should be strongly encouraged to invest more resources in the regulation and protection of the global medicine supply. Whether the new WHO Member State mechanism will be able to improve the current situation remains to be seen. It will need to take rapid action if the public health of vulnerable patients is to be protected.

### **What is the size of the problem now and what are the consequences in term of death and induction of drug resistance in a series of microbial agents?**

There are no data that allow anything more than (badly) informed guesses as to the global extent of the problem. However, attempts to collect such statistically valid data have only started recently. Notably, there is still much debate, despite over 100 years of collecting data, as to how many people contract and die of malaria each year. However, that has not, and should not deter public health attempts to control the disease. Similarly, although we do not have good estimates of the proportion of the medicine supply that is poor quality, this should not deter attempts to improve medicine quality. Although there are many examples of poor quality medicines, the paucity of reliable data means that it is difficult to know whether the problem is getting better or worse, how the epidemiology of substandard and falsified medicines differ and

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whether interventions are effective.

Medicines that contain zero or insufficient active ingredient will not give patients the benefit they and their health workers rightly expect. Hence, such 'medicines' must logically increase mortality and morbidity, increase patient and health system health expenditure and result in loss of confidence in health systems and pharmaceuticals. Medicines with more than the stated amount of active ingredient or wrong active ingredients can result in confusing adverse events. The severe consequences of poor quality medicines are often invisible, hidden within health statistics by the difficulty of investigating morbidity, deaths and medicine content in the rural tropics.

Anti-infective medicines containing inadequate amounts of the stated active ingredient, usually substandards, will engender drug resistance. Pathogens will be exposed to subtherapeutic amounts of active ingredient, allowing the more resistant pathogens to multiply while the susceptible pathogens are eliminated. Hence, subsequent patients are more likely to be infected with pathogens selected to be resistant to the active ingredient in the poor quality medicine. For infections treated with combination therapy of multiple drugs, such as HIV, TB and malaria, if one active ingredient is at low concentrations the pathogens also risk becoming co-resistant to the partner drugs.

**You've reported previously that it is poor quality data that is contributing to the problem. What are the gaps in knowledge?**

Medicine quality research, including some of our group's earlier work, must be one of the last branches of medicine that

does not routinely use statistically valid sampling strategies.

Convenience sampling can be useful for yielding alerts about poor quality medicines but cannot be used to reliably estimate their prevalence, which would require random sampling. However, we know enough already to suggest, for example, that medicine regulatory authorities (MRAs) need urgent support.

There has been considerable confusion between substandard and falsified medicines in the lay and scientific press. Consensus on scientific public health orientated definitions is urgently required. This will help in reporting of surveys and enhance understanding of the relative global distribution of substandard and falsified medicines – this understanding is important as the causes and solutions of both types differ significantly. We need to know more about the comparative accuracy, cost-effectiveness and ease of use of the new rapid and portable analysis devices (*see below*).

There is very little quantitative information on the economic consequences of poor quality medicines or modelling of their consequences for drug resistance. There has also been very little research to understand what patients and health workers know about the problems of poor quality medicines. Without this information it is hard to design and evaluate effective educational interventions.

**What are the principle problems that countries' Medicine Regulatory Authorities face? Where is the roadblock to stop the trade of counterfeit medicines? How can international groups help? And how can they do more?**

Many MRAs face major problems in regulating the medicine supply. According to the WHO, '30% of countries have no

drug regulation or a capacity that hardly functions'. These countries are not explicitly stated but many are likely to be economically poor and malarious. There has been a woeful lack of investment in MRAs and it is likely that many of the current problems have arisen as a consequence as MRAs are the keystones for most of the interventions needed to improve a nation's medicine quality. Some governments have recently improved MRA capacity and organisations, such as the WHO and United States Pharmacopeia, have assisted. However, the task is enormous and international collaboration to ensure sustainable support (human, technical and financial) to build country-appropriate MRAs is urgently required. There are only three sub-Saharan African countries with WHO pre-qualified laboratories for the analysis of medicine quality. More support for regional centres would allow essential medicines to be analysed within Africa, rather than being sent to America and Europe. More investment is required to ensure that errors in pharmaceutical production are reduced to a minimum, through MRA inspection and industry capacity building, to reduce the prevalence of substandard medicines.

**How difficult is to track suppliers? Are they concentrated in particular world regions or do they operate in various parts of the world?**

Understanding trade routes of falsified medicines is an MRA and police function and hence, rightly, much of the information is not public. Criminals making and trading falsified medicines operate throughout the world, London, Beijing, Mumbai, Lagos, Texas .... The anecdotal evidence available in the public domain suggests that poor quality medicines are commonly

produced in countries with emerging economies, but insufficient regulation, in South and Eastern Asia. The major unwitting 'consumers' are the poor and vulnerable.

**Is technology making an impact? What advancements in Rapid Assessment tools have been made? How can IT technology help consumers find out that they are buying a counterfeit medicine?**

There have been three main groups of technological innovations. First, the use of SMS texting to allow patients to check the authenticity of a medicine through texting a unique code on the packet to a reference centre. Second, chemists and physicists have developed innovative portable, battery powered rapid assessment gun-like tools, based especially on Raman and Near Infrared spectroscopy. These have already 'caught' some falsified medicines in Nigeria. Although relatively expensive in capital outlay, they do not need consumables and may be able to empower drug inspectors to

screen the medicine supply in pharmacies in the 'field'. However, there has been no published research to examine the impact and effectiveness of either texting or portable tools. Thirdly, the World Wide Antimalarial Resistance Network (WWARN) has built an online system to map all reports of antimalarial quality, with the intention that this will help information sharing between MRAs and malaria control programmes. (*See the WWARN article in this issue.*)

**And WHO's Rapid Alert System? Has that made an impact?**

The Rapid Alert System has been pioneered by the Western Pacific Region of WHO and allows sharing of information about poor quality medicines amongst those with major interest and responsibilities, especially MRAs. If this could be expanded to give global linkages between MRAs and other relevant government departments and relevant partners it could have a global impact.

**In many parts of the world, it is only voluntary to report counterfeit medicines. What arguments are there for and against making it mandatory everywhere?**

As far as I am aware, there is still no country where it is mandated by law that pharmaceutical companies or distributors, pharmacists or other health workers have a legal duty to report suspect medicines. There should be such a legal duty to report to the country's MRA. It should not be left to companies or individuals, who may have a conflict of interest through concern that, by reporting a problem of poor quality medicines, their income or reputation will fall. Such decisions should be made by governmental bodies working primarily on behalf of public health and not on behalf of commercial interests. However, the risks and benefits of these decisions need to be carefully weighed, to avoid patients suffering from being scared of taking essential, life-saving medicines.