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Conference report

Pathways to safe medicines: protecting patients through unified global action

Wednesday 26 – Friday 28 June 2013 | WP1185

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Pathways to safe medicines: protecting patients through unified global action

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Access to safe, genuine medicines is a fundamental characteristic of equitable and well- governed health systems; highlighting the link between public health, social and economic development and international trade. In both the developed and developing world, substandard, spurious, falsely-labelled, falsified or counterfeit (SSFFC) medical products likely contribute to thousands of avoidable deaths each year and thwart efforts to fight diseases like malaria, some cancers, TB and HIV/AIDS. The estimated international trade in SSFFC medicines amounts to over £45 billion and continues to escalate due to a lack of global enforcement and deterrents.

This Wilton Park conference brought together senior-level policymakers, academics, representatives from pharmaceutical manufacturers and civil society health advocates to examine the critical public health/socio-economic development/trade nexus that impacts global access to safe medicines. The meeting enabled participants from mature, growth- leading and emerging markets to examine converging and interoperable solutions that strengthen international cooperation in combating the production and distribution of SSFFC drugs.

Participants evaluated how universal access to genuine medical products can be achieved through better governance and oversight, capacity building in the areas of greatest need, enhanced powers of enforcement and most fundamentally, cross-cutting global collaboration between policymakers, regulators, industry and civil society.

Key points

- The issue of SSFFC drugs affects the availability of safe medicines everywhere. A global solution needs to be applied to what is currently perceived as a national problem. No single nation, region or company can tackle this problem by itself because of the interdependency of the manufacturing and distribution networks.
- An effective response requires firm action by individual countries, complemented by a collective international approach involving regulators, law enforcement, pharmaceutical companies, NGOs and academics. The first step must be to build political support and this will require a demonstration of the economic impact of the issue. Although the G8 Camp David Declaration included references to global health, the challenge now is to find ways to keep access to safe medicines sufficiently high up the agenda so that definite progress can be made. . Controlling online sales requires a specific strategy.

- The World Trade Organisation's (WTO) free trade laws have opened up markets, but there is an imbalance because corresponding and adequate public health protections have not been developed. A Treaty would attract international attention and resources. The European Directive on Falsified Medicines[i] and the Council of Europe Medicrime Convention[ii] are potential starting points. Should there be a legal duty to report SSFFC drugs, and if so who should the duty apply to and who should receive the reports? Should the countries which suffer the most from SSFFC drugs take the lead on developing a Treaty? The UN Guidelines for Consumer Protection could be used as a model for new Guidelines for Patient Rights. A McKinsey report[iii] highlighted the cost savings and patient safety benefits of adopting a single global standard. However new law would not be a panacea as the countries most at risk from SSFFC drugs probably also lack the technical capacity necessary to fully implement legislation. The US also has a track record of not signing Treaties but taking its own alternative forms of action.
- The breadth of the SSFFC blended definition may be one of the causes of the current inertia. There is consensus around the term 'counterfeit', both in terms of what counterfeit means and that counterfeits are a problem which must be tackled. However 'substandard' is more controversial. Substandard describes medicines that have less Active Pharmaceutical Ingredient (API) than required, and medicines that have been manufactured correctly but which are subsequently compromised. It is possible for substandard medicines to be acceptable and effective in some contexts but not in others. Many manufacturers of generic medicines are based in India which has its own definitions.
- Progress was made through a 2012 World Health Assembly resolution[iv] about a State Mechanism for the World Health Organisation (WHO), but overall the WHO has proved to be a difficult venue for arriving at consensus on how to tackle the SSFFC medicines issue. International regulation of the pharmaceutical industry remains primitive because the WHO works on a consensus basis, which can be slow and difficult to achieve. It is difficult to understand why IMPACT was discontinued, or why the WHO has successfully delivered a Framework Convention on Tobacco Control but has failed to deliver a similar framework Convention on SSFFC medicines.

Context

1. The problem of SSFFC drugs reflects the challenges posed by globalisation. Safe and effective high-quality medicines and the regulatory systems that ensure them reside at the nexus of public health, global trade and economic development. The human cost can be high including drug resistance, increased suffering and fatalities. The true extent of the problem is unknown and the extent of the SSFFC drugs problem in relation to noncommunicable diseases is particularly opaque, eg the extent of SSFFC diabetes drugs. The amount of funding and attention that the issue receives is estimated to be very small in relation to the true size of the problem.

"Safe and effective high-quality medicines and the regulatory systems that ensure them reside at the nexus of public health, global trade and economic development"

2. The level of attention and resources that have been applied to counterfeit passports and currency needs to be applied to SSFFC drugs. The strategy must be one of prevent, detect, and respond. Counterfeiters are sophisticated and consumers are confused. There is a dilemma because increasing costs through regulation risks driving up the price of legitimate medicines, which in turn can hamper consumer access and create markets for counterfeiters. However, the price of medicines isn't the only reason for counterfeits, as demonstrated by the counterfeiting of Chlorquine, which is a relatively cheap drug.
3. The developed world's main challenge is how to make sure that legitimate drugs are taken as prescribed in order to prevent the spread of super bugs. There are also problems around misuse of drugs, eg Temazepam being used to supplement heroine

or methadone. SSFFC drugs are much more likely to be detected through appearance and taste in the developed world. The UK's Medicines and Healthcare Regulatory Agency (MHRA) has detected 10 incidents in 10 years.

4. There is a distinction between lifestyle drugs, such as Viagra, and life-saving drugs, such as those for malaria or HIV. SSFFC drugs in the developed world tend to be lifestyle drugs obtained online, whereas in the developing world the issue applies to lifestyle and life-saving drugs.

"Counterfeiters are sophisticated and consumers are confused "

5. Vulnerabilities apply to all parts of the process, starting with manufacturing and extending to all links in the supply chain, including packagers and repackagers, pharmacists, medical practitioners and retailers. Medical products may be sold and resold many times before they reach the patient who may or may not purchase their own medicines. Pharmaceutical companies lose direct control of their products in this process, which is why some companies are considering undertaking quality assurance tests on the ground in the countries they export to. The mark ups required by distributors and wholesalers can be as much as 200%, and this should be matched with their input into dealing with the problem, eg through good stock and supply chain control. Pharmaceutical companies need to track and trace, with associated training so that pharmacists and consumers know what to if they detect an SSFFC drug.

6. Counterfeiting can be small scale, eg a single pharmacist with a printer. Counterfeiters can also work through complex transnational criminal conspiracies including colluding with medical practitioners. Some counterfeiters invest a great deal in their enterprises and therefore they are highly motivated. They know that to succeed they must have a long term strategy which accepts losses, including the risk of their low level people being imprisoned. For law enforcement or regulators to be successful they must start to think like the bad guys.

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7. As SSFFC drugs are often identified through their packaging counterfeiters focus on making their packaging look as genuine as possible. Criminals have been known to pay for empty packets of legitimate drugs which they can then fill with SSFFC drugs. In China there have been cases of nurses replacing genuine drugs with SSFFC drugs using the genuine packaging. Pharmaceutical companies should be concerned if their packaging is misused as this is a public relations threat to their branding. Counterfeiters don't always take the same care when copying tablets, eg indentations may not be copied or may be poorly copied. Certain drug compositions can help ensure that SSFFC drugs look different from genuine drugs- disintegration can be helpful.

"There should an attitude of health before money"

8. IP and competition are the elephants in the room but they need to be put aside, even though there is much more IP legislation than legislation concerning SSFFC drugs. Enforcement of trademarks should be separated from enforcement of health standards and patient care. There should be an attitude of health before money. Access to safe medicines needs to be incorporated into the core business plans of the pharmaceutical companies and incentivises need to be built around health outcomes. Behind the SSFFC drugs issue is the problem that some people don't have access to any medicines. Medicines may not be affordable, or stocks may quickly run out.

Regulation and policy

9. The approach taken by individual countries to the quality and licensing of pharmaceutical companies is very important. Which countries are granting the appearance of legitimacy to manufacturers of SSFFC drugs by licensing them? Is corruption part of the problem? No global strategy, or international law or standards will work unless this problem is addressed. When a Ministry of Health in a South East Asian country went to close a distributor the military were already present and they had been tasked with preventing the closure.

10. If countries don't make certain medicines available this also creates a market for SSFFC drugs, eg the HPV vaccine isn't available in China and this increases the risks

of counterfeiting.

11. The WHO has estimated that 30% of regulatory authorities don't have the capacity to regulate their countries' drugs supply.[v] More pressure needs to be put on governments to set up and resource regulatory agencies and once they are established, there should be a programme of technical assistance provided by other countries, such as the WHO prequalification program. The successes of the Malaria Programmes must not be undermined by SSFFC drugs. There is growing emphasis on measuring impact, so if impact is reduced because of SSFFC malaria drugs the programme's funding may be reduced.[vi] There is a debate to be had as to whether or not one regulator per country is optimum, or whether large countries should have multiple state regulators like India.

12. Every country seems to want a pharmaceuticals industry and therefore all countries need to get on the same path in terms of regulation, even if it is inevitable that some countries will be weaker. Incremental improvements are a realistic objective for weaker countries. In developed countries regulators don't necessarily need to be widely known by the public in order for them to be effective, but that may differ in developing countries. Regulators should come together to share their experiences and there are a number of Forums which could be used for this; Health Canada International Regulatory Forum, CDER Forum for International Drug Regulatory Authorities of the USFDA and the African Vaccine Regulatory Forum. The UK's MHRA has twinned with Ghana, and the WHO's rapid alert system also links regulatory authorities together.

13. As a result of international pressure medicines that leave China are now checked and this is a practice that other exporting countries should also consider regardless of their tax position. In 2004 China invested $70 million in mobile laboratories. 2 million batches were screened and 4% were identified as SSFFC drugs and therefore withdrawn from the market, including some traditional Chinese medicines. Noninvasive methods of surveillance can be helpful, eg x-rays. Infrared technology can detect adulteration, although detection is more difficult if the API isn't known.

Law enforcement

14. Any failures in the chain of custody of legitimate medicine can be used by counterfeiters as opportunities to introduce SSFFC drugs into the system. For this reason law enforcers and regulators must be able to intervene and take action at all stages. The nature of these interventions will vary between countries because they face different risks, ie some countries suffer from a large volume of imported SSFFC drugs, perhaps as a result of porous borders, whereas in other countries SSFFC drugs are produced locally for local consumption as well as for export. Much of the supply to the developing world is from local national generic companies and therefore the problem isn't always international. The British Medical Journal recently ran an article about 120 deaths in Pakistan as a result of drugs produced locally[vii]. It is probably not a coincidence that the Pakistani Health Ministry was closed the year before.

15. Seizures of SSFFC drugs may not be the best ambition for law enforcers and regulators. More effective approaches may include disrupting supply chains, or prosecuting senior figures in the criminal enterprises and seizing their personal assets. In other words, a more intelligence driven approach may be better than a reactive approach. A difficulty encountered in any enforcement action is how to encourage people to act as witnesses.

16. Enforcement successes must be publicised, eg the reduction in SSFFC drugs in Cambodia as a result of action taken against five major exporters to the region. It is contradictory to say this issue needs energy and focus but then keep information secret. Pharmaceutical companies need to know which of their medicines have been counterfeited in order to take action, but at the same time they may be reluctant to agree to publicity if it could affect sales. Members of the Pharmaceutical Security Institute are provided with more information than is usually available. Publicity should

focus on patient harms rather than just recite statistics, eg go beyond seizure statistics.

17. SSFFC medicines should always be a priority for Customs even where medicines aren't taxed. In order to be effective customs officials need powers granted under national legislation. Customs officials need to make very quick decisions about whether to open containers but fortunately the use of customs holding areas no longer poses jurisdictional problems. The World Customs Organisation recognises the need for better training and better use of technology.

18. Over time Chinese retailers have developed the tactics of shutting their shops or hiding medical products when mobile laboratories are in their area. It may be possible to get around this with mystery shopping and disguising mobile units. Despite these practical challenges, the levels detected in 2004 have remained roughly static for the last seven years, including in rural areas of China.

Stakeholder collaboration

19. More information sharing is needed on an international scale. Information is the blood of health systems but it isn't flowing well. There needs to be a move towards an international adverse event reporting system for regulators, law enforcement and the pharmaceutical companies. There also needs to be information sharing between companies, which will require mutual trust, new norms around not competing on security and a culture of companies protecting each other's customers. Information sharing is one of the objectives of RX-360. The Lancet could also be used.

"The blood of health systems is information but it isn't flowing well"

20. The role of NGOs is pivotal and they would benefit from more engagement with each other. NGOs were successful in mobilising against tobacco use, and they could apply this experience to SSFFC drugs. There needs to be more activism to create bottom up demand for change. The Partnership for Safe Medicines in India decided to accept funding from the pharmaceutical industry even though this was controversial. NGOs are constantly seeking pro bono legal services to help file court cases concerning intellectual property (IP). Unfortunately NGOs have been barred from the WHO state mechanism because of the concerns of the Indian government, even though this ban breaches a binding decision of the World Health Assembly.[viii]

21. Generics companies are suspicious that the blended SSFFC definition is designed to threaten their businesses and protect the pharmaceutical brands. In relation to this the interception of legitimate generics from India when they were in transit to the Netherlands was unfortunate. Generics companies view themselves as servicing a genuine need for affordable medicines that the pharmaceutical companies aren't satisfying. The price and quality of APIs is critical to the generics issue.

22. Greater recognition that genuine errors occur would help bring generics companies into the discussion. Criminal offences should not be strict liability; criminal intent should always be required for conviction. However, there is an argument that there must be criminal intent when unlicensed drugs are sold. This leaves the issue of how to deal with acts of negligence or incompetence which also put the public's health at risk.

23. Traditional practitioners should also be brought into the debate to help with the problem of defining what a medicine is. The trend in the use of traditional or alternative practitioners varies between countries. In India the use of alternative medicines is falling but in Ghana and Uganda its use is growing, with as many as 50% of the population using alternative medicines. China licences a significant number of herbal medicines. There are positive reports that herbal medicines can work even though it can be difficult to identify their API.

''There needs to be more activism to create bottom up demand for change"

Communicating and sharing information

24. Raising the awareness of consumers is key because without their cooperation there will always be a market for SSFFC drugs. Consumers must be encouraged to ask questions, but to do so they need simple information which deals with the counterfeit and substandard issues in a way that isn't clouded in jargon. Lessons should be learned from the public awareness and education campaign associated with the HIV epidemic.

25. The risks of SSFFC drugs must be covered in the training of medical practitioners, including community health workers. Attention also needs to be paid to retailers who sell medicines without the involvement of medical professionals. Many AIDS/HIV patients live in rural areas and rely upon retailers. Part of the solution may be to find a way to stop relying on a small number of retailers who cover large areas.

    International organisations should exercise influence through their procurement processes. The usual international competitive bidding practices may not be appropriate; lowest price isn't always an appropriate consideration and quality needs to be given more emphasis. The Global Fund and Médecins San Frontières have both mistakenly purchased SSFFC drugs or devices.

Technology applications

26. Innovative technology is being used by enforcers and regulators, particularly hand held devices. The US Food & Drug Administration's Counterfeit Detection Device #3 can detect counterfeit drugs and also picks up tampered packaging. 'True Scan' is popular in Nigeria. Screening can cost between 1-1.5 pence per pack.

27. Hand held technology is also becoming available to consumers. Self assessment has a role because security features on packaging aren't the whole answer, especially as it is not uncommon for medicines to be sold in single doses without packaging. However, as consumers' use of these types of technologies can be challenging, their availability must not stall other efforts to prevent SSFFC drugs. Donors must not start to think of technology as a quick fix to what is a very a complicated issue.

28. In the developing world levels of literacy (including ability to read English as a foreign language) are often low. Even if companies pay for text messaging consumers still need to have access to cell phones and the internet. Having said that, 80% of Nigerians have a cell phone and use text messaging, and 9 million people in India have a cell phone. Malaysia provides a positive case study of the value of new technologies. Seizures immediately increased when Meditag was introduced in mid 2005, and went up 300% between 2004 (the last full no Meditag year) and 2006 (the first full Meditag year).

29. Consumers in the developing world may travel long distances in order to buy medicines for themselves or their relatives or others they care for and this aggravates the problem of what happens if a consumer finds they have a SSFFC drug which they have already purchased—who will provide them with a replacement? Any system of consumer reimbursement or replacement must be robust so that it does not become subject to fraud. The system provided by Orange in Kenya involves texting a number on a leaflet, and if there is a mismatch in terms of the batch number or expiry date the drug can be returned to wherever it was purchased from. Scratch codes don't necessarily have to be on packets; pharmacists can give codes to consumers separately.

30. The development of effective technology requires a clear vision about what needs to be achieved, early alignment and agreement amongst stakeholders, and constant effort over a sustained period of time, including extensive pilots. There are challenges around the correct amount of information to link with the technologies, and what information should be made available to whoever is using the technology—should information about original source and/or information about the whole supply chain be linked and

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made available? It has been possible to make consumers aware of the source of organic food, so the same must be possible for medicines. Legal or regulatory restrictions on direct manufacturer to consumer communications must be taken into consideration. The risks of counterfeiters setting up fake help lines and SMS services must also be managed.

31. The ultimate aim for telecommunication projects is that they scale up as this will push the price down. Expansion raises the possibility of integration with social networking. There are questions around whether the best way forward is for companies to aim towards integrating their systems, or whether companies should continue to go it alone. A lot of companies use differing but similar serialisation and holograms on their packaging, and the same pattern may emerge in relation to the new technologies.

Conclusions

- There are multiple stakeholders in the compliance cloud and all of their views need to be taken into account.
- SSFFC drugs should form part of the post-Millennium Development Goals agenda.
- A new Medicines Transparency Index could assist efforts to advocate for change, but it would need a strong institutional home. The development of an index would take time because it would need to start with consistent collation of the right raw data.
- A central repository for case studies of events could also be helpful provided the studies are presented from a human interest angle and provide complete stories from start to finish.
- A new Global Commission on Medicine Quality could be established, possibly linking with the Global Fund (who are keen to do more), the WHO, the International Organisation on Standardization and the Human Rights Commission. A new Commission could operate on a majority vote basis rather than on a consensus basis.

Liz Richards
Wilton Park | 1 August 2013

Our partners

GSK – Enhancing access to safe medicines

GSK is a science-led global healthcare company, making a range of products that help people do more, feel better and live longer.

We manufacture and distribute more than four billion packs of products to over 150 countries around the world. With a focus on patients, we strive to make our products as widely accessible as possible.

In Western markets, we have developed new reimbursement approaches for our medicines, where we agree risk-sharing arrangements with payers. We have adopted more flexible pricing approaches to reflect countries' wealth and ability to pay. This has resulted in significant increases in demand for our products in emerging economies.

To increase access to our products in the world's least-developed countries, we have capped the price of our patented medicines in this region at no more than 25% of our developed world prices and we reinvest a fifth of the profits we make from sales in these territories back into local healthcare infrastructure projects.

Patient safety is our priority through all stages of research and after a new product goes on sale. We are open about how we work and we disclose the results of clinical research. Our high ethical and quality standards apply to all our research and development, wherever it takes place.

We continue to work with regulatory and enforcement agencies to address the problem of counterfeit medicines and we have developed innovative initiatives such as a verification text messaging service in Nigeria, Kenya and Tanzania for patients to ensure the authenticity of purchased products.

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[i] The Falsified Medicines Directive 2011/62/EU.
[ii] Council of Europe Convention on the counterfeiting of medical products and similar crimes involving threats to public health.
[iii] Strength in unite: The promise of global standards in healthcare
[iv] Annex to Resolution WHA65.19, May 2012.
[v] World Health Organisation: What encourages counterfeiting of medicines?
[vi] Hyperparasitaemia and low dosing are an important source of anti-malarial drug resistance. White et al. Malarial Journal (2009) 8:253.
Poor quality vital anti- malarials in Africa- an urgent neglected public health priority. Newton et al. Malarial Journal (2011) 10:352.
[vii] Contaminated drugs are held responsible for 120 deaths in Pakistan. Arie S. BMJ 2012; 344:e951.
[viii] Principles Governing Relations Between the WHO and NGOs (Resolution WHA40.25).