Working Group report:
The Regulatory Environment

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The Regulatory Environment

Regulation of medicines and devices is a valuable and necessary investment of society to ensure the efficacy, safety and quality of medicines and devices in the market, to protect the health of women and children and to support the domestic pharmaceutical industry

Regulatory assessment and market control are ***not*** **an unnecessary bureaucratic evil** that needs to be evaded, reduced or removed.

Strengthening regulatory functions in low- and middle income countries is a **long-term development goal**

Overview of the problems

- There are real **quality problems** with several life-saving commodities
- **Insufficient market volume** does not justify manufacturer investments in product quality
- **Slow regulatory functions** can impede the use of safe medicines by lower-level health workers; and prevent universal access

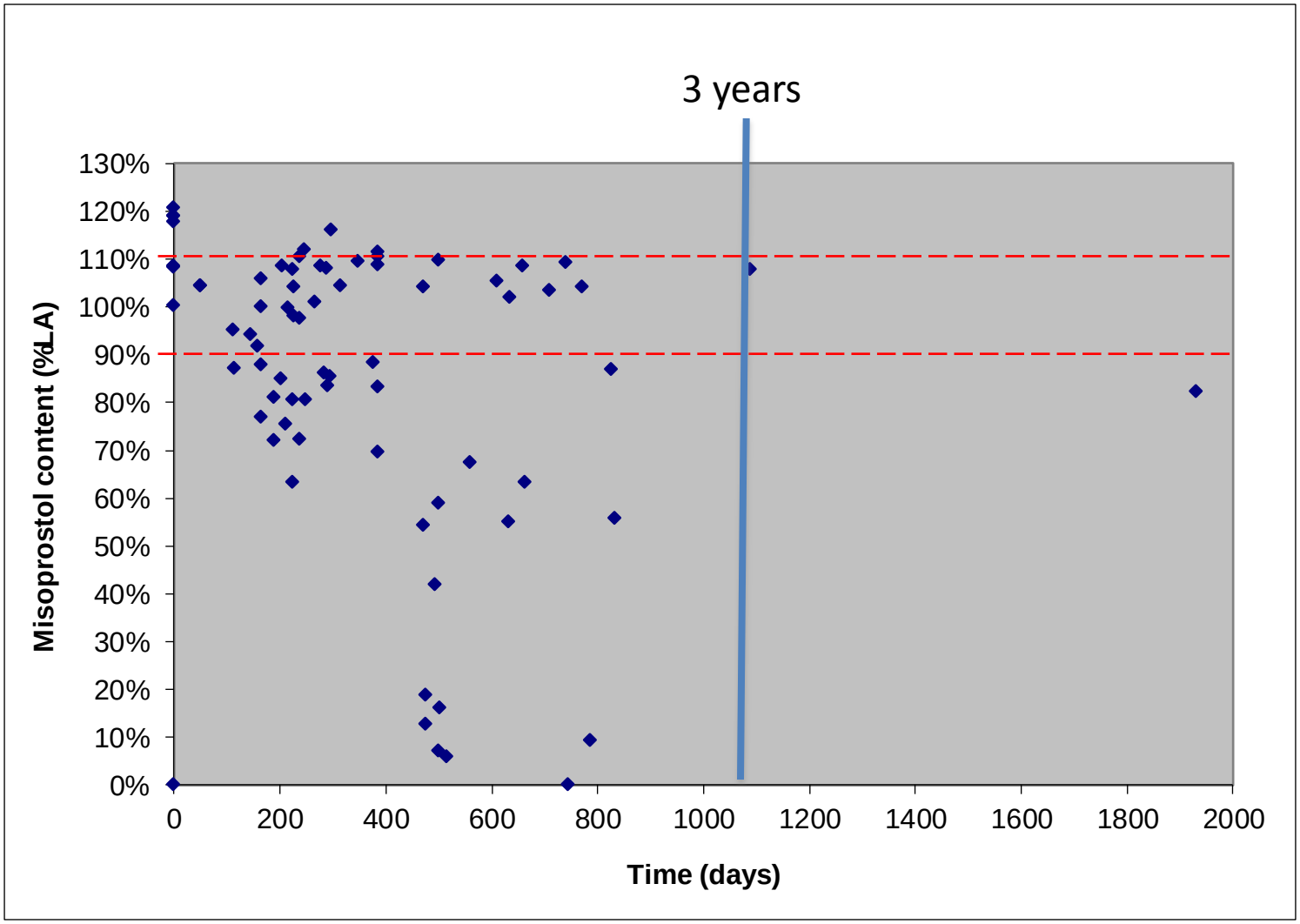
The problem (1)

There are real quality problems with several life-saving commodities

- Globally: more than 30 of 55 manufacturers of generic oral contraceptives from low- and middle income countries cannot fully guarantee the quality of their products
- 28/46 samples of oxytocin injection (routine use after delivery to prevent maternal bleeding) taken from pharmacies and drugstores in Ghana were not registered; all 28 were outside specifications; 18/46 had registration pending and of these 6/18 failed. In total, 34/46 (74%) of all samples failed
- 34/76 of misoprostol tablets (treatment of fatal maternal bleeding after delivery) sampled from 12 countries are of bad quality (see graph)

Example of bad quality tablet:

Misoprostol, content of active ingredient by age



The problem (2)

Insufficient market volume does not justify manufacturer investments in product quality

- None of six generic injectable long-term contraceptives had documented proof that it has the same biological effect as the originator product. Such proof is an essential regulatory requirement for a generic product. Performing the necessary "bioequivalence" study costs US$0.3-1 million
- The generic manufacturers hesitate to make such an investment as they are not sure about future sales

They can sell their low-quality product anyway because procurement agencies (and donors!) buy the cheapest products and most regulators are not checking – so why bother?

The problem (3)

Inefficient and non-standardized registration procedures require different registration dossiers for different national and international processes

- Gentamycin injection is a life-saving antibiotic for newborn children. But the quantity is too small for the usual 2-ml syringe. Overdose is very toxic (permanent hearing loss). The solution is a pre-filled very small syringe, or a patch (plaster) with micro-needles. Such an innovative product would need to be reviewed and approved by all 50+ African regulatory agencies
- Dispersable amoycillin tablets (makes antibiotic syrup for simple treatment of childhood pneumonia) was approved in one country in clinical guidelines in September 2011; by May 2012 the medicine was still not yet approved and not legally available.

The problem (3)

Slow regulatory functions can impede the use of safe medicines by lower-level health workers; and prevent universal access

- Zinc tablets are effective treatment of acute diarrhoea; its safety is well-known and the medicine is approved for Over-The-Counter use in many developed countries. Yet many developing countries still have it registered as a medicine or even as a "prescription-only" medicine. The regulatory process to change its status is costly and time-consuming; in practice the product is freely sold anyway
- But: nurses cannot be trained in its use, as doing so would imply training them in illegal prescriptions

The same applies for amoxycillin dispersable tablets, which in most countries need a doctors prescription

Recommendation 4:

Quality strengthening

By 2015, WHO and partners have

(i) included all 13 essential commodities in the WHO/UN Expert Review Panel* (ERP) and Prequalification* processes, and

(ii) based on the risk-approach, have supported at least three committed manufacturers per each of the 13 commodities to develop, manufacture and market affordable products of assured quality in EWEC countries.

* ERP: Ad-hoc WHO/UN review of non-prequalified products for one-year procurement contract (not published)

** PQ: WHO/UN systematic review of prodcuts for UN procurement (list of selected products published by WHO for use by others)

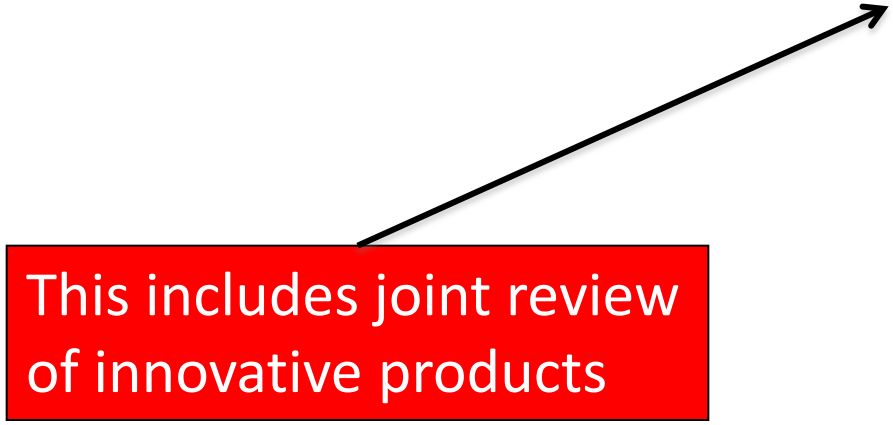
Recommendation 5:

Regulation efficiency

By 2015, all EWEC countries have:

(i) standardized their registration requirements following the format of the internationally agreed Common Technical Document, where possible with regional collaboration, and

(ii) streamlined their assessment procedures with support from stringent regulatory agencies and the WHO.



Recommendation 8:

Reaching women and children

By end 2013, all EWEC country governments are undertaking regular reviews of financial and regulatory barriers women and children face in accessing services and commodities in their country, and are actively proposing financial mechanisms (i.e. user fee waivers, cash transfers, insurance and voucher schemes) and adapted regulatory mechanisms to overcome these barriers in the next fiscal cycle..

This includes regulatory change of schedule to allow use by lower level health workers

Recommendation 10:

Product innovation

By 2014, a group of interested countries, donors, NGO partners, and UN agencies has been formed and has developed an incentive mechanism to support regular consumer marketing research and further research and development to optimize formulation, improve packaging, enhance delivery devices, and facilitate rapid regulatory approval of the 13 essential commodities in line with consumer and provider preferences, safety and ease of use.

This includes regulatory advice to PPPs in planning and development of regulatory dossier, prequalification review and joint (regional) assessment of new products

Next steps

- **Incorporate comments by the UN Commission**
- **Expand report with detailed practical recommendations for each of the 13 commodities**
- **Prepare detailed Plan of Action, Budget and Time Frame**
- **Complete full report and annexes by 23 June 2012**