

The road to quality products

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- What do we mean by quality?
- What are the implications of poor quality products?
- What are we doing about it?

What do we mean by quality?

Quality assurance (QA). A wide-ranging concept covering all matters that individually or collectively influence the quality of a product. It is the totality of the arrangements made with the object of ensuring that pharmaceutical products are of the quality required for their intended use.

Good Manufacturing Practices (GMP). The part of QA which ensures that pharmaceutical products are consistently produced and controlled to the quality standards appropriate to their intended use and as required by the marketing authorization. GMP is an important part of a comprehensive system of QA. They also represent the technical standard upon which the medicinal products registration and the WHO Prequalification Programme are based.

What do we mean by quality?

Principles of quality assurance maximize the probability that the finished product consistently and predictably meets all quality and design specifications.

- Quality, safety and efficacy must be designed and built into the product, including API.
- Quality cannot be inspected or tested into the finished product.
- Each critical step of the manufacturing process must be validated and all steps be under control.

What are the implications of poor quality products?

Poor quality product can:

- Contain extraneous impurities or increased levels of known degradation products from the API, improper manufacture or inappropriate storage
 - can lead to increase in known side-effects; other adverse events; and in extreme circumstances, serious adverse events, such as anaphylactic shock or death.
- Have poor content uniformity
 - leading to overdosing or failure of treatment.

What are the implications of poor quality products?

In the past year or so poor quality product has lead to:

- Cases of anaphylaxis and death of a woman from anaphylactic shock after injection of a generic DMPA.
- Withdrawal of batches of misoprostol from several countries. Degradation could have lead to ineffective treatment of post-partum haemorrhage, which in itself could lead to death.
- Packs of oral contraceptives with mixed active and placebo pills.

What are the implications of poor quality products?

Designing and assuring quality products may lead to higher production costs but lower overall costs! Problems lead to:

- Additional testing and rejection of batches
- Loss of time
- Waste of product and money
- Legal fees
- Stock outs

So what is the situation today?

Many generic manufacturers have not:

- used APIs that have supportive documentation, such as drug master file and in the case of injectables, validated the sterilization step;
- met CGMP;
- been able to compile appropriate dossiers or have inadequate data to do so;
- have not been willing or able to undertake bioequivalence studies or have not done them as required

What are the issues?

Hormonal contraceptives

- contain highly potent drugs
- require separate manufacturing facility with appropriate containment, own HVAC, water, etc
- require worker protection
- oral contraceptives contain tiny amounts of API (the estrogen can be 1/10,000th of the tablet)
- content uniformity can be a problem for both tablets and injectables
- injectables must be sterile
- the need for bioequivalence for interchangeability

Drug regulation

- Most countries have national drug regulatory agencies (NRAs) – their GMP texts are regulations and are enforced by the NRA. However, many countries' GMP regulations are lacking to some extent.
- Most developed countries have well-resourced NRAs (stringent drug regulatory agencies, SRAs) which can evaluate all aspects of the quality, safety and efficacy of medicines.
- NRAs are responsible for implementing the criteria and processes to ensure the quality of the products that they approve for distribution in the country. However, there are many challenges facing NRAs - raised in a report by Moran (2010) focussing on Africa

What are we doing about it?

Purchasing a product that has been approved by a stringent drug regulatory agency (SRA) or prequalified by the WHO PQ programme means that all aspects of quality and safety and efficacy of the product have been assessed.

This can never be a 100% guarantee but these actions help minimize risk and allows procurers greater confidence in their risk management strategies to purchase quality products.

RHSC Quality of RH Medicines programme

Output 1 – Increasing number of quality assured RH medicines

Focus on manufacturers – providing support to apply to WHO-PQP to increase number of PQd products

Output 2 – Harmonizing procurement policies and approaches

Focus on procurers – harmonization of quality policies and practices by international procurers

Output 3 – Addressing markets and QA policies and practices in selected countries

Focus on countries – situation analysis in four pilot countries

Output 4 - Raising awareness of QuRHM and related quality issues.

Focus on RHSC stakeholders – advocacy/communication around the case for quality.

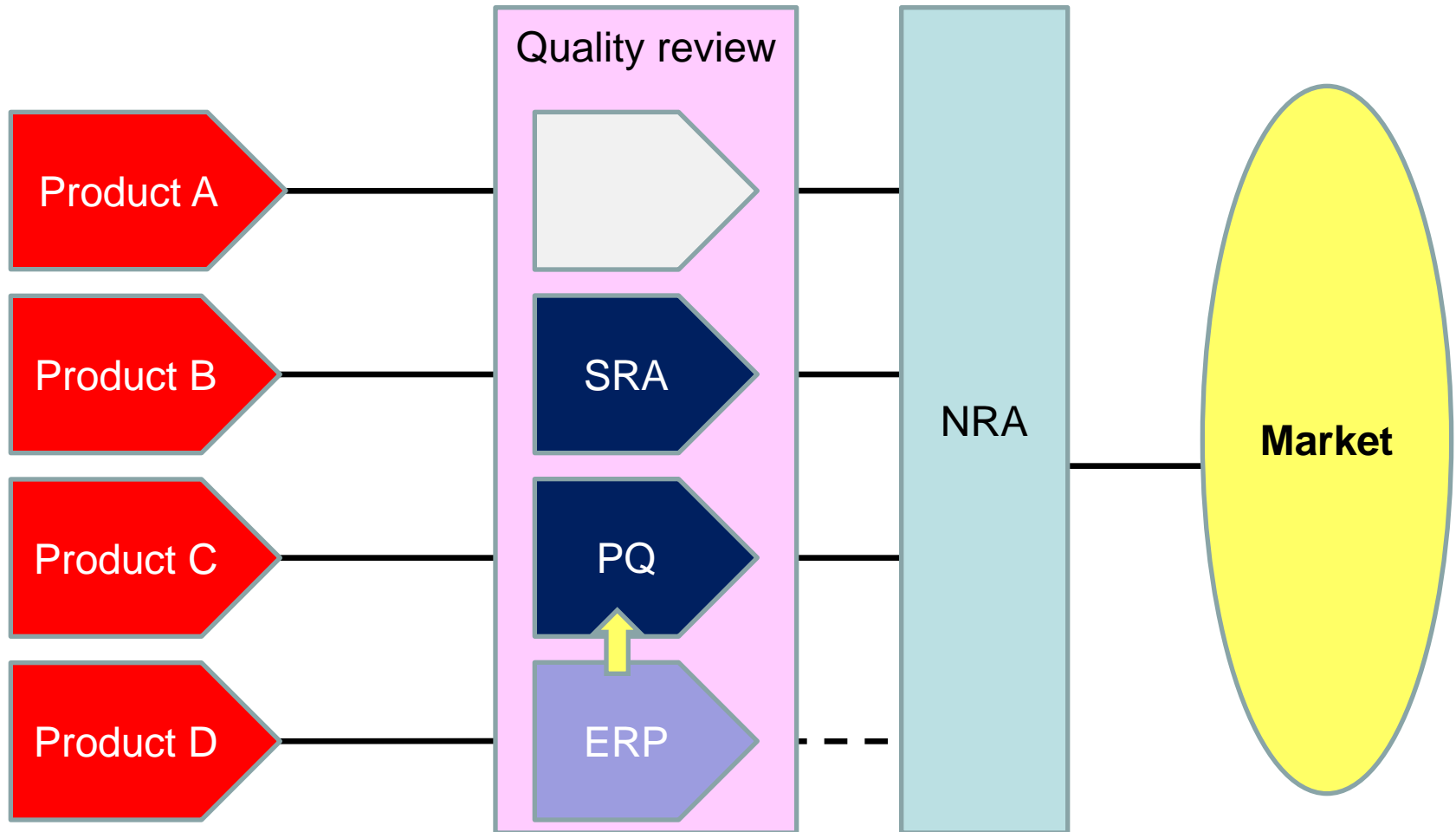
What has QuRHM done?

- Provided technical assistance to manufacturers of APIs and FPPs to allow submission of dossiers to PQP.
- Worked with procurers to promote adoption of procurement policies that support quality products by WHO prequalification or SRA approval.
- Established Expert Review Panel for Reproductive Health Medicines to undertake risk analysis on products entering or in PQ to allow time-limited purchase.

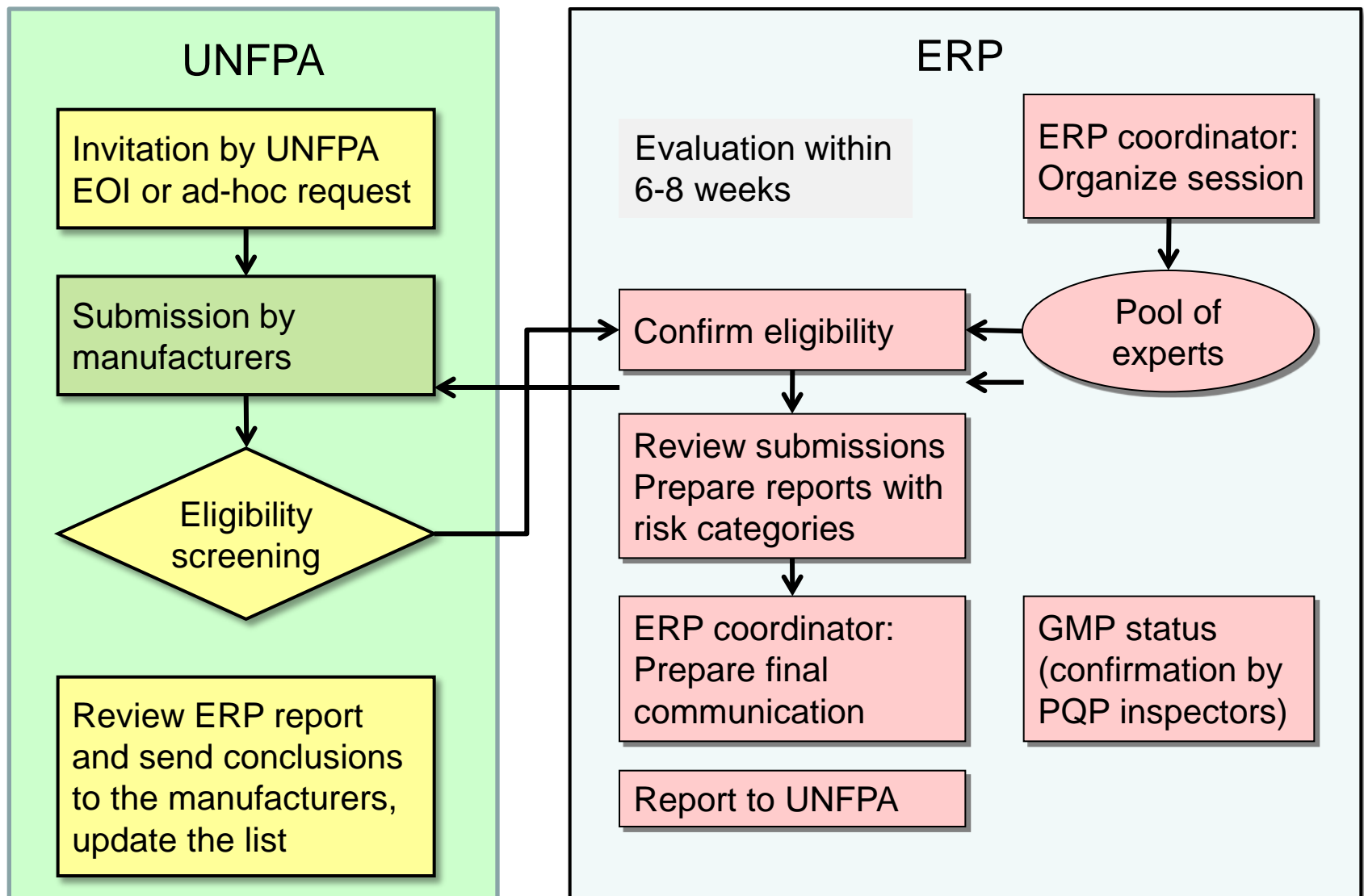
Status of FPPs

Company	COC LNG/EE	POP LNG	ECP LNG	DMPA	MPA/ EC	Miso	Mife	Oxytocin	CF Priority
1	PQ		ERP 1-13 ERP 1-13			ERP 1-13		ERP 2-13	1
2	PQ ERP	ERP	ERP ERP 1-13	ERP 2-13		ERP 2-13			1
3			ERP FU						1
4				ERP FU					1
5	ERP 2-13		ERP 2-13			ERP 1-13	ERP 1-13		1
6									1
7				ERP FU					1
8						ERP 2-13			1
9						ERP FU			1
10								ERP 1-13	1
11				ERP 2-13		ERP FU			1
12									1
13				ERP 1-13					1
14	ERP	ERP	ERP						1
15									2
16	In PQ								2
17									2
18									2
19	ERP FU			ERP FU					2
20									2
21									3
22								In PQ	3
23	ERP FU								3
24									3/4
25	In PQ								4
26									4
27									4

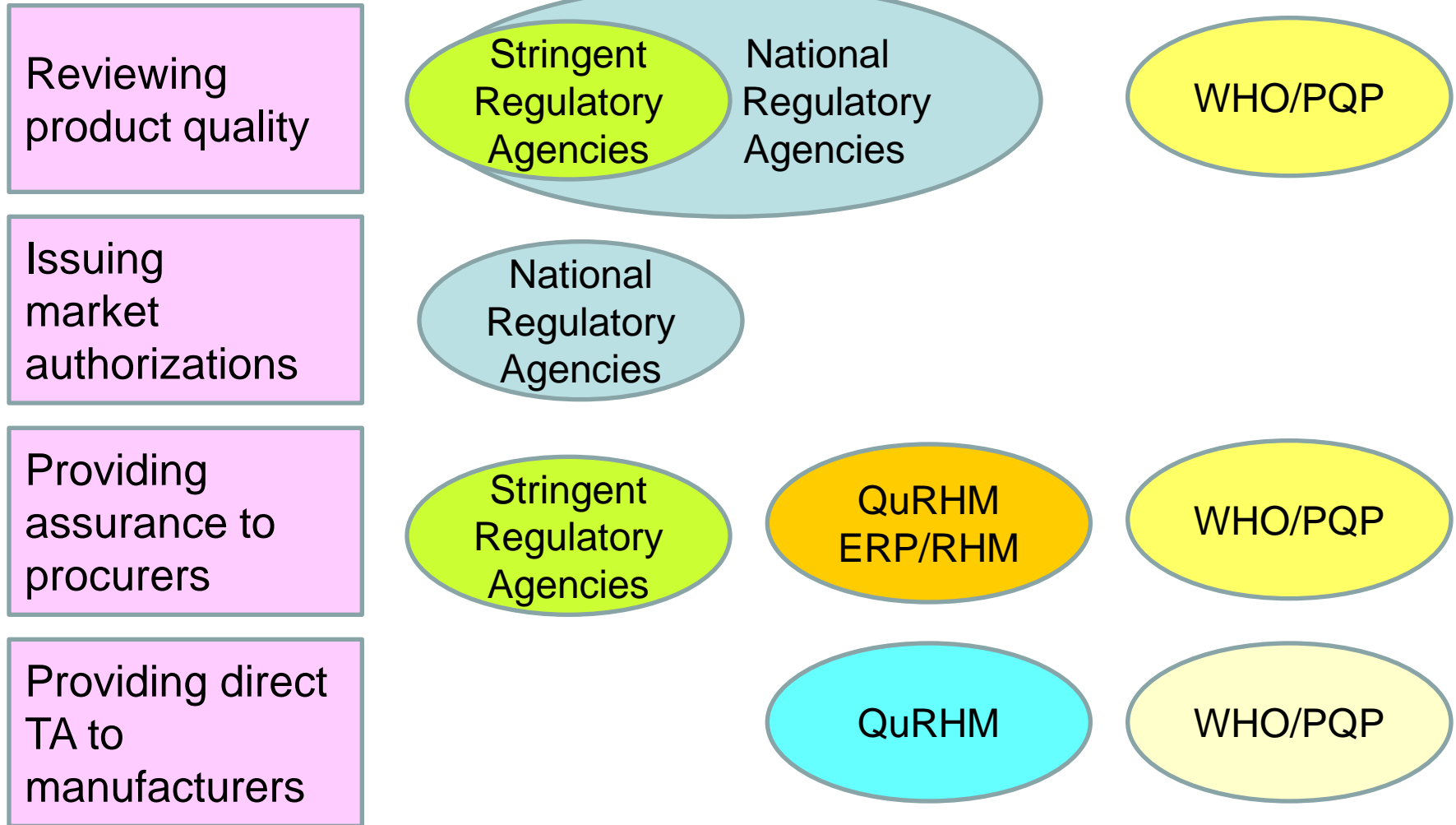
Product quality review



What is the ERP/RHM review process?



Who does what?

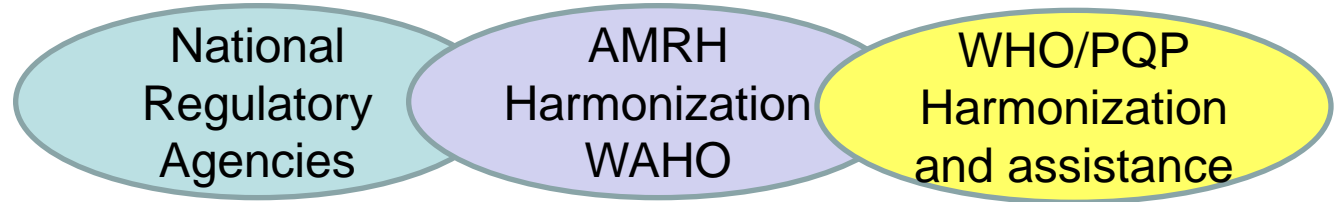


A road map to quality products

Reviewing product quality



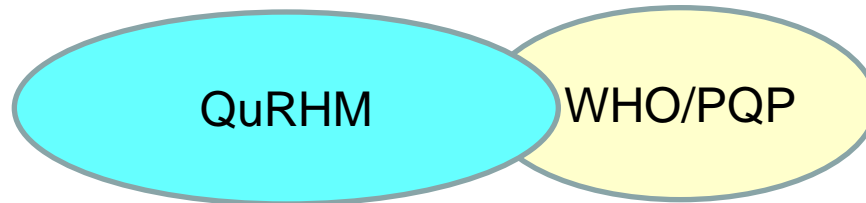
Issuing market authorizations



Providing assurance to procurers



Providing direct TA to manufacturers



Challenges – market shaping

- Engaging countries, expansion in scope of advocacy and communications activities beyond the pilot countries.
- Mapping current country product availability and product registrations.
- Forecasting global volume requirements by product type.
- Developing the business case for all stakeholders not only manufacturers.
- Linking scope of participating manufacturers against market needs and timelines.