




Accessing Quality Assured Supplies

RHSC Membership Meeting, London,
2009



“The main priority is to get sufficient quantities of product to the people who need them, quickly and at the lowest possible cost.

An absence of contraceptives in the market is a more serious public health concern than overkill on quality issues!”

Background

- As patents for hormonal contraceptive methods expired, an increasing number of new manufacturers began to make identical (bio-equivalent/bio-similar) products
- These “new” manufacturers are described as “generic” manufacturers and are located in both developed and developing countries
- Initial marketing efforts are focused on home markets and large public tenders, NGO and other social sector contracts, by offering lower prices
- In 2004, quality assurance of products from developing country generic manufacturers was unclear and a cause for concern

Who is affected?

- At a time when financial and other resources for RH commodity security are decreasing, and demand is growing
 - International public procurement agencies
 - Social Marketing Organizations
 - National procurers – Governments, NGOs
 - Service providers
 - National Regulatory Agencies
 - **CLIENTS**

Background

- The international RH community recognized changing landscape and challenges as early as 2004
 - Presentation and discussion at Washington meeting of RHSC – unpublished, total market concept paper, 2004
 - Unpublished Jerry Chambers/USAID report on manufacturers attitudes to commodity security, 2005
 - Assessment of India's locally manufactured contraceptive product supply (Kim Beer/Francoise Armand, PSP-one, March 2006)
 - Improving hormonal contraceptive supply, the potential contribution of manufacturers of generic and biosimilar drugs (F.Armand, Abt/PSP-one, January 2006)
 - MDA generic manufacturing sub-group, 2005/6 >>>>>>
 - A study of the capability of manufacturers of generic hormonal contraceptives in lower & middle-income countries (Contraception Journal, Peter E. Hall et al, Concept, UNFPA, IPPF, PPD, November 2006)
 - WHO prequalification programme for hormonal contraception begins with publication of first EOI, October 2006


Background

The Coalition reached consensus at its [Bonn membership meeting](#) in October 2006 on the principle to procure only products that have either been prequalified by WHO or approved by a stringent regulatory drug agency

RHSC question - generic hormonal contraceptives -2006

- Can generic pharmaceutical manufacturers in lower and middle income countries make quality products available to donor agencies, governments and social marketing organizations at a affordable price, while meeting the requirements of stringent regulatory agencies?
- **Yes**, if the active pharmaceutical ingredients (APIs) and production facilities conform to internationally accepted cGMP standards; and data is available to comply with regulatory requirements
- Based on the study, up to **ten** companies could comply in 2007 with additional technical or procedural inputs (except for the completion of BE studies) and a further **three to four** could potentially do so with more substantive investment and technical assistance

Challenges - 2006

- Few companies manufacture products according to cGMP requirements (some outdated cGMP, others, outside GMP completely)
 - Most are not in a position to supply products into international markets, not having considered regulatory approval for their products outside their home markets
 - Overcapacity in production
 - Cost of API
 - Absence of bioequivalence testing
 - How to avoid the long-term effect of creating monopolists
-  *Should the RH community assist to improve quality assurance with technical assistance subsidies, or will “good” manufacturers make the necessary investments themselves to reach cGMP and overcome regulatory challenges?*

So why hasn't this happened?

1. *Mentality* – lack of support by senior management/owners. Why make investment when orders not guaranteed, or if we have reasonable local market?
2. *Lack of attention* - understanding the root causes of quality and processing them out
3. *Understanding* - what is required for the PQ process – being addressed by WHO but needs support from RHSC members
4. *Meeting cGMP* (WHO, PICS, USFDA) – realizing that this is likely to be different from national GMP requirements – time, cost and changes
5. *Cost APIs* - supported by a DMF
6. *Bioequivalence* – undertaking studies and meeting WHO requirements

Attitudes to prequalification

There are companies who aspire to achieve PQ

1. Realistic potential
2. Unrealistic prospects (time and investment)

There are companies who may/may not have potential to achieve PQ

1. Not interested, or unwilling to make the investment or required effort because:
 - a) The local market/s in which they are registered represents sufficient business potential
 - b) Are supplying the RH community anyway, regardless of lack of PQ
 - c) Recognize that for them PQ is unattainable

Target groups to be identified

Category	Status
1	Applied for PQ – realistic potential cGMP Require TA
2	Aspire to PQ – realistic potential cGMP Require TA
3	Lack interest in PQ – good potential cGMP Require engagement + TA
4	PQ – unnecessary – supplying anyway Require engagement +/-
5	PQ/cGMP unattainable

Meeting WHO PQ requirements

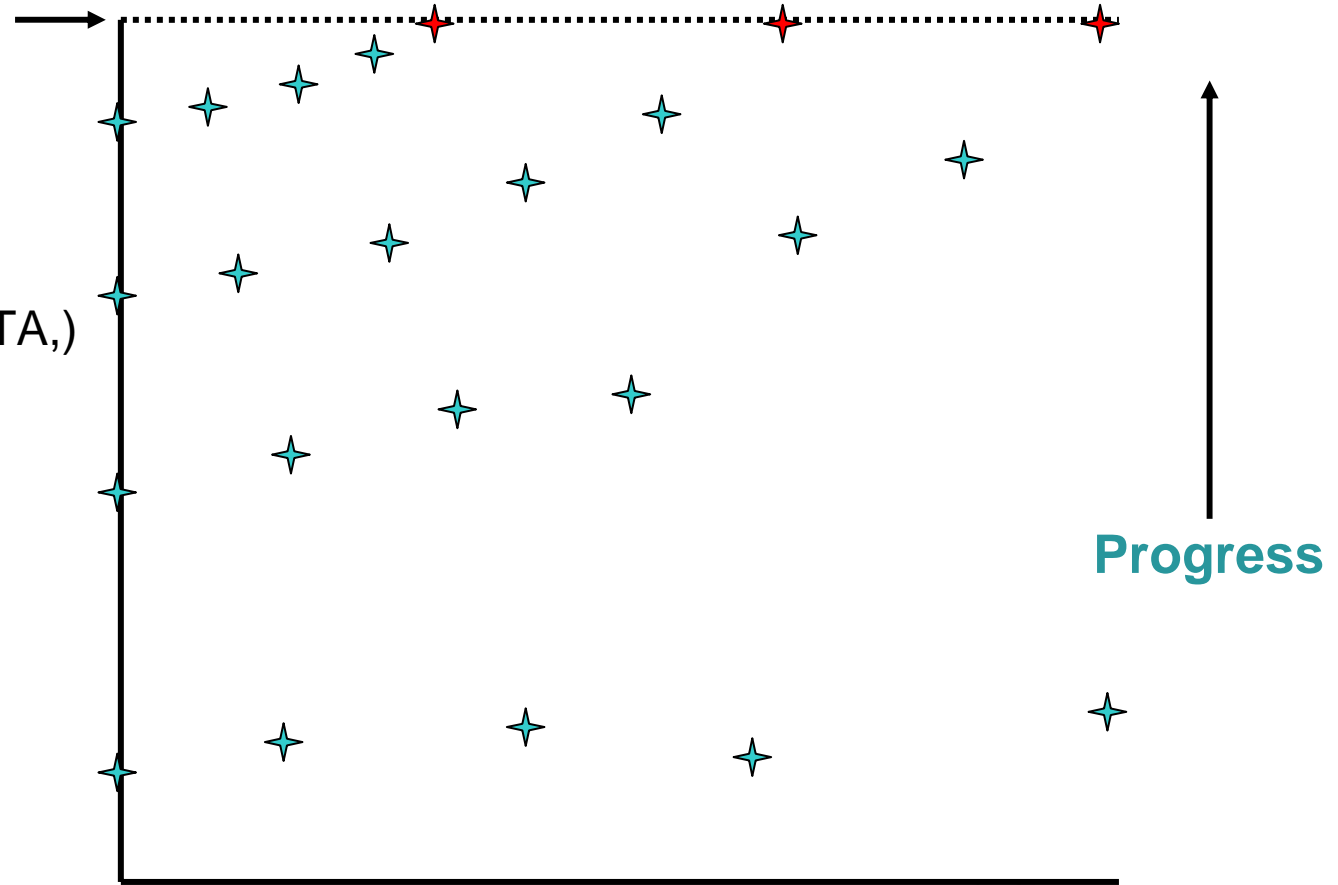
WHO cGMP + safety/efficacy requirements met

Category 1/2 (once committed, needs minimal TA)

Category 3 (needs engagement + some TA,)

Category 4 (needs TA & orientation/learning)

Category 5 (little understanding or commitment)



(★ milestone)




Time

Progress

UNFPA Consultative Meeting, March 2009 - conclusions

- The majority of the recommendations made at the end of 2006 to RHSC members have not been implemented
- The quality options has further deteriorated and reduced since end 2006
- There was a specific problem around API sourcing and quality
- There was a presumption that the advent of the WHO prequalification programme would solve the crisis in 2007
- Problems remain with generic vendor's utilized by procurement agencies, Governments and SMOs
- Without a some form of intervention there was a high probability that the situation would further deteriorate

Recommendations to RHSC - 2006

-  1. Ensure that companies invited to respond to national or international procurement tenders/contracts demonstrate full cGMP compliant manufacturing practices with product approved by a stringent regulatory authority and/or prequalified WHO's prequalification programme
-  2. Donor and procurement agencies that are members of the Reproductive Health Supplies Coalition should state unequivocally that they will only purchase generic products that have been prequalified by WHO
-  3. Establish a mechanism for technical assistance to prospective "good" manufacturers by which certified factory inspectors undertake a full review of processes, standard operating procedures and documentation and make recommendations of what companies need to do to meet international requirements

Recommendations to RHSC - 2006

4. Undertake a similar mapping/assessment with API manufacturers



5. Provide assistance on developing registration dossiers that meet stringent regulatory requirements



6. Explore an independent quality monitoring programme in collaboration with WHO, which should be mandatory for any supplier prequalified by WHO and optional for other companies



7. Develop an advocacy strategy and materials for governments, national NGOs and international partners explaining the WHO prequalification programme and the need to use suppliers prequalified by WHO for the procurement of hormonal contraception



8. As an incentive to manufacturers that would allow them to offer cost advantages to international purchasers and to exploit the full low-cost potential of generic supplies, to develop a continuous purchase and supply platform to replace the current uncoordinated, *ad hoc* and discontinuous tender mechanism



UNFPA Consultative Meeting – action plan

- Develop an intervention approach to speed up maturity of hormonal contraceptive manufacturing, under the auspices of an MDA Sub-Group, and in collaboration with WHO
 - To establish a competitive manufacturing base comprising a minimum 5 quality assured reliable manufacturers for each product
 - Could be a 3 year undertaking and required a phased approach, building upon existing work and knowledge
 - Needed to be complementary, rather than duplicative of WHO efforts
 - Should seek to achieve lasting impact and change of attitudes
- Incentivize manufacturers – technical investment, volumes, LTAs
- Advocacy – manufacturers – benefits of participation
- Advocacy – RHSC – awareness raising among broader Coalition
- Crosscutting - could be linked to Access RH project - SSWG
- Develop proposal and identify funding for Phase 1

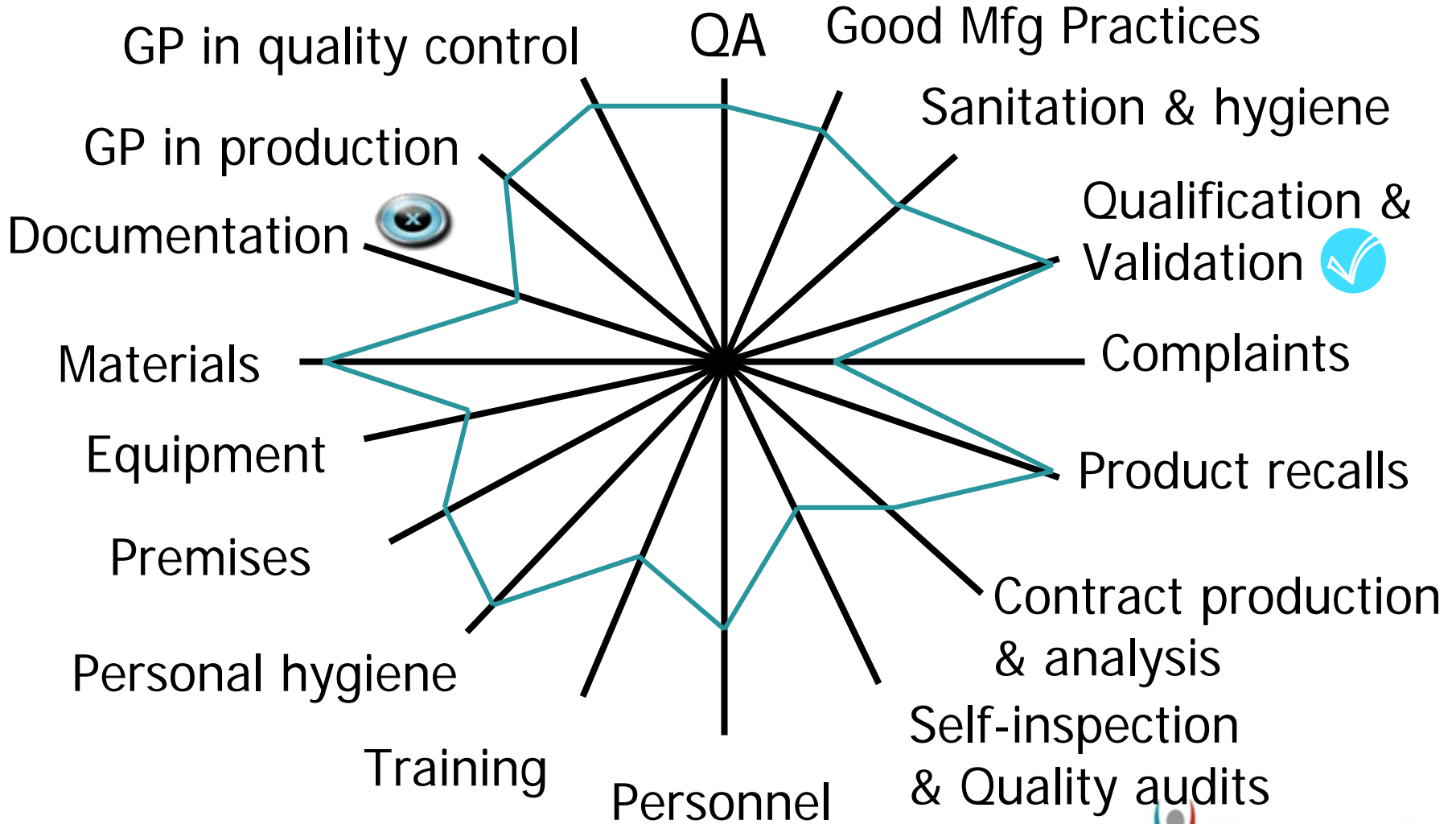
Approach

- To identify manufacturers who represent the best prospects of achieving full cGMP compliance and WHO prequalification in the shortest timeframe, their current manufacturing/quality deficits, and the level of investment required to bring them into compliance
- Provide technical support to manufacturing partners willing to implement the upgrades required and, work to toward continuous quality through the adoption of long-term change management strategies
- Encourage manufacturers to apply for WHO prequalification at the appropriate time

Methodology

- The programme would be undertaken in 3 phases
 - *Phase 1* – The quality mapping and status of prospective manufacturers, based upon the findings at the end of 2006, taking into consideration any candidates which have emerged since then and current status of PQ programme
 - *Phase 2* – Technical support and guidance to identified manufacturers - cGMP 17 point star & designed to ensure lasting impact through change management strategies
 - *Phase 3* – Ongoing quality surveillance activities reducing over time to maintenance levels
- Undertake Phase 2, based upon the findings and feasibility of Phase 1

A cGMP map addressing WHO TRS 908, 2003 – Annex 4



Change management

- A tool borrowed from Quality By Design concepts, as contained within ICH Guidelines (primarily Q8)
- To institutionalize quality within the culture of the company, through encouraging a proactive approach by key decision-makers which can trickle-down throughout the organization
- To establish areas of quality deficiency and rectify, through identifying the cause of a deficit and processing out the chance of repetition
- Moving from uncertainty to certainty, resulting in increased incidence of continuous quality

5 phases of quality systems (P. Crosby, Quality Without Tears 1979)

1. **Uncertainty**

→ *We don't know why we have quality problems*

2. **Awakening**

→ *Is it necessary to always have quality problems?*

3. **Enlightenment**

→ *As a team we identify the root causes and take corrective and preventive action*

4. **Wisdom**

→ *Continuous defect prevention is routine in our operation*

5. **Certainty –**

→ *We know why we don't have quality problems*

Phase 1 - goals

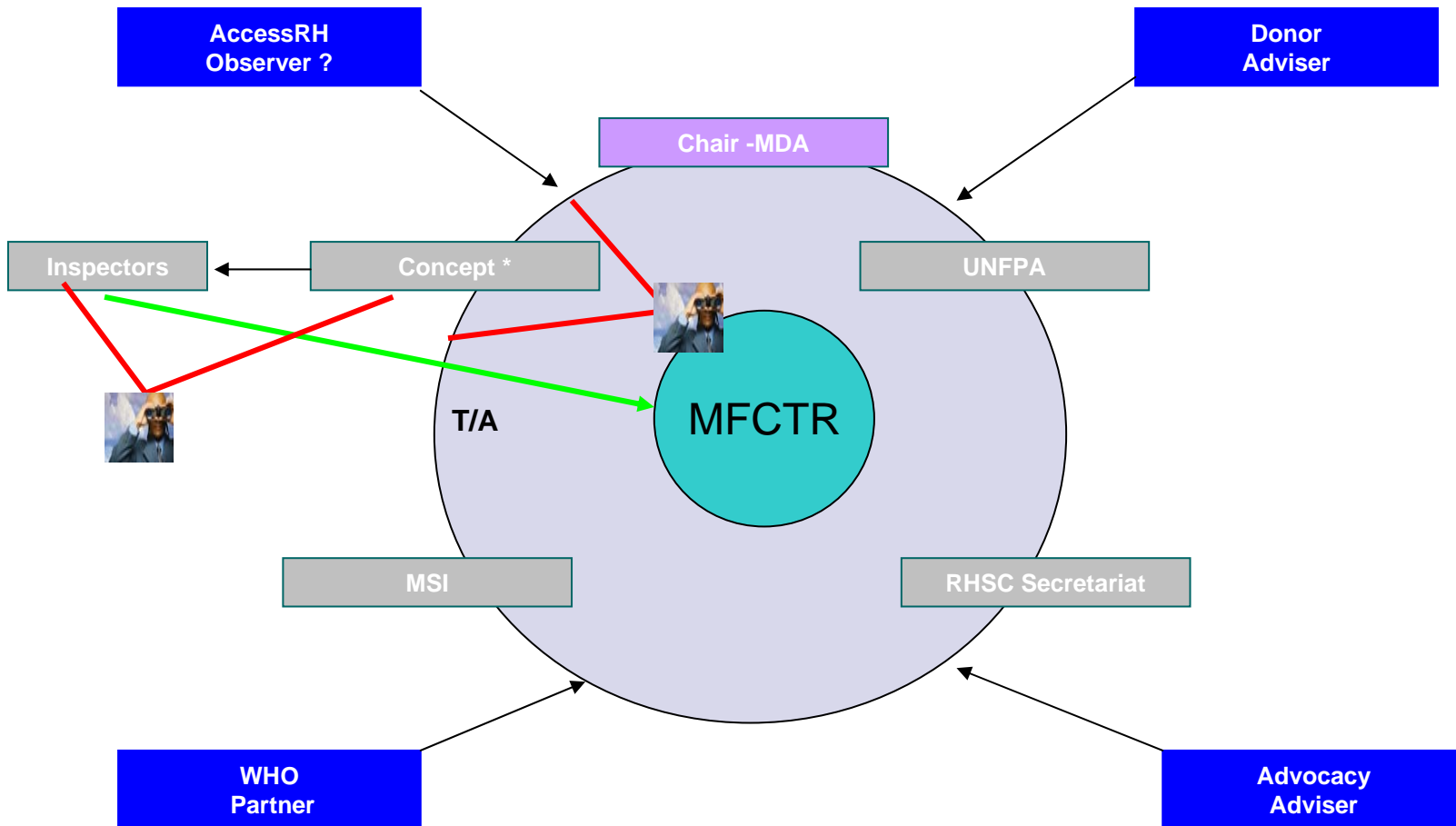
- **Overall Goal** - To establish a competitive, quality assured, cGMP compliant roster of hormonal contraceptive manufacturers in lower and middle income countries, able to provide a stable and continuous supply of quality assured products at an affordable price for public programmes, including social marketing.
- **Phase 1 Goal** - To identify a group of hormonal contraceptive manufactures with the potential to provide low-cost, cGMP compliant products of assured quality, who are capable and willing to adopt a change management strategies in partnership with the RH supplies sector

Phase 1 - objectives

1. Assess current status and capability of selected manufacturers to provide cGMP compliant products of assured quality for public and social marketing programmes in less developed countries
2. To identify the outstanding process and manufacturing challenges/deficits of each company in relation to cGMP, and document/cost the remedial action required
3. To effect a strategic shift in the mindset of key decision-makers in the target companies toward the benefits of adopting attitudinal change management strategies and work in partnership with members of the RHSC

A proactive instead of reactive approach to quality!

RHSC –MDA Sub-Group Initiative - Oversight



* Project Lead

Next steps - process

<u>Objective</u>	<u>Monitoring</u>	<u>Decision-making</u>	<u>Resource</u>
Short list of Potential "good" Manufacturers established		<ol style="list-style-type: none">1. Extended list of prospective candidates agreed2. Review and approval – questionnaire/evaluation criteria3. Short-list of companies for technical inspection	AC AC AC
	Outcome Review Objective 1		CF > Sub-group

Next Steps – preliminary timeline

Objectives/ Activities	Milestone	Completion Date(s)
Objective 1: Activity 1 Activity 2 Activity 3 Activity 4	Short list of potential “good” manufacturers established 1. Long-list of companies is agreed and ITP issued 2. Questionnaire and evaluation criteria is completed/issued 3. Review and evaluation completed 4. Identity of companies selected for on-site validation and inspection known	<u>1 September 09</u> 16 June 16 July 31 August 31 August

Recommendations

1. To proactively implement this initiative to ensure an adequate supply of quality assured products are available in less-developed countries
2. To establish time-bound transition guidelines to assist procurers in order to reduce risk in current procurement practices
3. Increase advocacy efforts at the country level around appropriate quality assurance awareness



Thank - you