Session 5: Increase in Use of the WHO Prequalification Programme
Perceived Need for Prequalification

In an ideal world:

- Regulated pharmacies and service providers would supply medicines to clients
- Regulatory agencies would authorize, monitor and enforce standards for safe, effective, quality products

In the real world, life threatening epidemics emerge, and life saving products need to be sourced in countries with unknown regulatory capacity, to be delivered in countries with unknown regulatory capacity, and procured by procurement agencies with unknown capacities.
Perceived Need for Prequalification

Increased use of WHO Prequalification Programme driven by recognition of:

• Need to rapidly scale up life-saving programmes with quality products
• Need to expand supplier base to increase product supply and promote competition
• Varying capacities in National Regulatory Authorities (NRAs) and procurement agencies to enforce local quality assurance (QA) standards
Prequalification Programme Timeline

1989

- WHO publishes vaccine prequalification procedure

2000

- UNFPA begins inspecting factories
- WHO releases first EOI for HIV/AIDS

2001

- WHO releases first EOI for tuberculosis

2002

- UNFPA begins prequalification for Condoms and IUDs

2003

- WHO releases first EOI for malaria

2004

- WHO/UNFPA publish condom specifications and guidelines for procurement

2005

- UNFPA begins prequalification for Condoms and IUDs

2006

- WHO releases first EOI for contraceptives

2007

- WHO and UNFPA harmonize process for condoms and IUDs

Note the trend toward using prequalification as a system for mitigating product quality risks
Donors and Programs Endorsing the WHO Prequalification Programme

- UN Agencies and World Bank
- Global Fund
- Roll Back Malaria Partnership
- Stop TB Partnership
- Clinton Foundation
Other Systems Implementing Harmonized Standards

• Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (PIC/S)
  - GMP standards

• International Conference on Harmonization (ICH)
  - Harmonizes requirements of the most industrialized countries on development, registration, and safety monitoring
  - WHO has observer status
Growth in WHO Prequalification Programmes

- Disease programmes and other partners continue to request WHO to add products to existing prequalification programmes.

- The basis for adding new product categories is determined by:
  - Need: Does the product appear on the essential medicines list?
  - Resources: Is funding available to support the additional effort?
Core List of RH Medicines for Priority WHO Prequalification

Priorities:

- DMPA [injectable]
- Ethinylestradiol + levonorgestrel tablet
- Levonorgestrel tablet [various doses/pkg]
- Oxytocin
- Magnesium sulfate injection
- Misoprostol
- Clotrimazole

Already in WHO’s Prequalification Programme:

- cefixime
- ceftriaxone
- ciprofloxacin
- clindamycin
Day 2: Session 5

Handout:
Timeline for Development of the WHO Prequalification Programme

- WHO publishes vaccine prequalification procedure
- WHO releases first EOI for HIV/AIDS
- UNFPA begins inspecting factories
- WHO releases first EOI for tuberculosis
- UNFPA begins prequalification for condoms and IUDs
- WHO releases first EOI for contraceptives
- WHO and UNFPA harmonize process for condoms and IUDs
- WHO/UNFPA publish condom specifications and guidelines for procurement

The WHO Prequalification Programme for Essential Reproductive Health Medicines: A Workshop on Using the Programme in Procurement Practices
Donors and Programs Endorsing the WHO Prequalification Programme

Global Fund

The Global Fund to Fight AIDS, Tuberculosis, and Malaria was created to dramatically increase resources to fight three of the world's most devastating diseases—HIV/AIDS, tuberculosis (TB), and malaria—and to direct those resources to areas of greatest need. The Global Fund is a partnership between governments, civil society, the private sector, and affected communities.

The Global Fund’s original procurement policy allowed for three options in procuring single- or limited-source pharmaceutical products (products for which there are no public monographs for finished dosage form in the International, British, or US pharmacopoeia). These options were the two identified here:

- WHO prequalified product
- Product authorized by a stringent regulatory authority. A stringent regulatory authority is defined as a national regulatory authority participating in the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) or the Pharmaceutical Inspection Co-operation Scheme (PIC/S).

A third option to procure products approved by the NRA of the recipient country expired in 2005 and is no longer available.

The Global Fund policy on quality assurance (QA) standards for procurement will be discussed in more detail in a later session.

Roll Back Malaria Partnership

The Roll Back Malaria (RBM) Partnership was established in 1998 by the WHO, the United Nations Children’s Fund (UNICEF), the United Nations Development Program (UNDP), and the World Bank to provide a coordinated global approach to fight malaria. Since then, the RBM Partnership has expanded to include a wider range of partners—including malaria-endemic countries, bilateral and multilateral development partners, the private sector, nongovernmental and community-based organizations, and foundations.

Partners are working together to scale up malaria-control efforts at the country level, to coordinate their activities to avoid duplication and fragmentation, and to ensure optimal use of resources.

A key role of the RBM Partnership is to lead continuing advocacy campaigns to raise awareness of malaria at the global, regional, national, and community levels.

The RBM does not procure malaria commodities. UNICEF provides procurement services in support of RBM and is the world’s largest buyer of mosquito nets. All mosquito nets procured by UNICEF must comply with the WHO pesticide evaluation scheme and all antimalarial medicines must be WHO-prequalified.
Stop TB Partnership

The Stop TB Partnership was established in 2000 to realize the goal of eliminating TB as a public health problem. It comprises a network of more than 500 international organizations, countries, donors from the public and private sectors, and nongovernmental and governmental organizations that have expressed an interest in working together to achieve this goal. WHO is a partner in the Stop TB Partnership, as is the Global Drug Facility (GDF).

The GDF is a mechanism to expand access to, and availability of, high-quality anti-TB medicines and diagnostics to support the Stop TB Strategy. The GDF both supplies donated medicines and procures medicines to support national TB programs. GDF offers a standardized WHO-approved catalog of anti-TB medicines and formulations designed to promote the products prioritized by the WHO Stop TB department.

All medicines supplied by the GDF must be WHO-prequalified or reviewed and approved by a committee of independent experts pending WHO prequalification.

Clinton Foundation

The mission of the Clinton Foundation is to strengthen the capacity of people throughout the world to meet the challenges of global interdependence. To advance this mission, the Clinton Foundation has developed programs and partnerships in the following areas:

- Health security
- Economic empowerment
- Leadership development and citizen service
- Racial, ethnic, and religious reconciliation

In 2003, the Clinton Foundation HIV/AIDS Initiative announced an agreement with five suppliers of generic antiretroviral (ARV) medications to dramatically cut the price of the most commonly used triple medicine therapy combinations for HIV/AIDS.

The Clinton Foundation’s quality standard mirrors the global fund requirements. The Foundation “is committed to the sustainable supply of high-quality ARVs, consistent with the specifications of dossiers approved by the World Health Organization or a stringent regulatory authority such as the USFDA” (Source: www.clintonfoundation.org).

75 percent of the medicines in the Clinton Foundation agreement are individual formulations and two- and three-medicine fixed-dose combinations that have been prequalified or have been submitted for prequalification to WHO.

World Bank

While the World Bank (WB) does not limit its funded projects to procuring only WHO prequalified products, it strongly supports the WHO Prequalification Programme as evidenced by statements and requirements in its published documents.

WB recognizes that not all countries have the capacity to conduct a valid product prequalification process. In its publication “HIV/AIDS: A Decision Maker’s Guide to Procurement of Medicines and Related Supplies,” the WB strongly recommends that in those circumstances, WHO prequalified HIV/AIDS medicines be procured.
In the World Bank’s recent announcement of its partnership with the Global Fund, Clinton Foundation, and UNICEF, the Bank announced that its quality standard for ARVs purchased under this partnership would be the same as the Clinton Foundation (i.e., prequalified by WHO or a stringent regulatory authority).

The World Bank also depends on WHO standards for malaria diagnostic test kits and bed nets approved by the WHO pesticide evaluation scheme.
Interagency Pharmaceutical Product Questionnaire

N.B. Please note that the information in this questionnaire can be shared confidentially among Agency 1 and Agency 2 for procurement purposes. If you have any objection, please indicate to the relevant agency that you are dealing with.

PLEASE COMPLETE SECTION I – IV, VI, VIII, IX and XII

I. Product identification

Active Pharmaceutical Ingredient(s) (use INN if any): …………………………………………………………….

Generic name of the product: …………………………………………………………………………

Dosage form: □ Capsules □ Tablets (please indicate if scored, dissolvable, dispersible) …………………………….

□ Ampoules □ Vial

□ Oral Liquid □ Suspension

□ Other: Describe: ………………………………………………………………………………………

Strength per dosage unit: …………………………………………………………………………………

Route of administration: □ Oral □ I.M. □ I.V. □ S.C.

□ Other: ……………………………………………………………

Pack size: ……………………………………………………………………………………………

Description of Primary packaging materials: ………………………………………………………………………

Weight, Volume and Dimensions: ………………………………………………………………………

Description of Secondary packaging materials: ……………………………………………………………

Nr of units, Weight, Volume and Dimensions: ……………………………………………………………

Nr of secondary packs per standard pallet: ……………………………………………………………

II. Manufacturer of the product

Name, address and activities of the manufacturer(s) (or contract manufacturer(s)):

<table>
<thead>
<tr>
<th>Name of Manufacturer</th>
<th>Physical address</th>
<th>Telephone number, Fax number and e-mail contact details</th>
<th>Activity (e.g. packaging)</th>
</tr>
</thead>
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</table>

All sites listed above are licensed by the relevant Authority to perform the activity? □ Yes □ No

This product is pre-qualified by the World Health Organization? □ Yes □ No

The manufacturing site for THIS product is GMP compliant and approved by (If yes, please indicate all applicable organisation(s))

<table>
<thead>
<tr>
<th>PICS¹ member?</th>
<th>Agency 1</th>
<th>Agency 2</th>
</tr>
</thead>
<tbody>
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¹ (PICS): Pharmaceutical Inspection Cooperation Scheme member countries
The manufacturing method for each standard batch size has been validated?  

☐ Yes  ☐ No

List the standard batch size quantities: ...........................................

PLEASE ATTACH A COPY OF THE MANUFACTURING LICENSE FOR EACH MANUFACTURING SITE USED FOR THIS PRODUCT

III. Supplier identification (to be filled in if not identical to that indicated in question II)

Name: ...........................................................................................................................

Address: ..............................................................................................................................

Telephone number: ...........................................................................................................

Facsimile number: ............................................................................................................

E mail contact details: .........................................................................................................

Link with the product: ☐ Marketing license holder ☐ Distributor

☐ Manufacturer ☐ Other....................................................

IV. Regulatory situation (licensing status) specific

This product has full registration in the country of manufacture, and is marketed for use in the country? ☐ Yes ☐ No

license n° .................................................................

This product is registered for marketing in the country of manufacture, but currently NOT marketed? ☐ Yes ☐ No

license n° .................................................................

This product is registered for export only ☐ Yes ☐ No

license n° .................................................................

This product has full registration with a stringent regulatory authority, (ICH) and is marketed for use in the country? ☐ Yes ☐ No

List countries: ...................................................................................................................

This product has tentative registration with a stringent regulatory authority (FDA), for use in government funded projects e.g., PEPFAR ☐ Yes ☐ No

license n° .................................................................

This product not registered (please clarify): ....................................................................................

Please attach a Certificate of Pharmaceutical Product (CPP) according to the WHO Certification Scheme (WHO Technical Report Series No. 863. Earlier version is not acceptable).

If CPP cannot be obtained from the National Drug Regulatory (NDR), please state the reason:

.............................................................................................................................................

V. Regulatory situation (licensing status) general

List other countries where the product is registered and is currently marketed:

.............................................................................................................................................
VI. Finished product specifications


☐ Other ........................................................................................................................................

Please attach a copy of the finished product specification, if different from BP, USP or International Pharmacopoeia specification.

Limits in % for the assay in active ingredient(s):  ☐ 95-105%  ☐ 90-110%  ☐ Other ...................

Additional specifications to those in the pharmacopoeia (e.g. dissolution, syringeability):

........................................................................................................................................

Attach a copy of the model certificate of analysis for batch release.

Are you willing to provide necessary information (analytical method) for the tests to be replicated by another control laboratory?

☐ Yes  ☐ No

VII. Stability

Stability testing data available:  ☐ Yes  ☐ No

If yes, type and conditions of testing:

• Satisfactory accelerated testing:
  Type of container:
  Conditions (Temperature/Relative Humidity/Duration):
  Number of batches:
  Batch sizes:
  Date of the study:

• Satisfactory real time testing:
  Type of container:
  Conditions (Temperature/Relative Humidity/Duration):
  Number of batches:
  Batch sizes:
  Date of the study:

Can a stability report be forwarded within one week of being requested?  ☐ Yes  ☐ No

Was the stability testing done on a product of the same formula, manufactured on the same site and packed in the same packaging material as the product that will be supplied?  ☐ Yes  ☐ No

VIII. Label and insert information

Shelf-life:  ☐ 2 years  ☐ 3 years  ☐ 4 years  ☐ 5 years  ☐ other..................

Storage conditions (e.g. «Do not store above 30°C - Protect from light»):
........................................................................................................................................

Label language (please attach a copy):
☐ Bilingual English/French  ☐ English  ☐ French  ☐ Other:..................

Package insert:  ☐ Yes (attach a copy)  ☐ No
IX. Samples
Can free non-returnable samples be obtained upon request within one week from being requested?
☐ Yes  ☐ No

X. Therapeutic equivalence

1) ☐ Demonstrated
   a) By in vivo bioequivalence studies
      Reference product: .................................................................
      Number of volunteers: .................. Country of study: .................................
      Performed year: .................. Bio batch size: ...........................................
      Bio batch API(s) source(s): ...........

   b) By another method claimed by the supplier/manufacturer (please describe briefly):

   c) By in vitro dissolution tests
      Reference product: .................................................................

2) ☐ Not demonstrated

3) ☐ Not relevant, please explain why:

4) ☐ Unknown

Can a copy of the report be obtained upon request within one week from being requested? ☐ Yes  ☐ No

The product used in the trial or test is essentially the same as the one that will be supplied (same materials from the same suppliers, same formula, and same manufacturing method). ☐ Yes  ☐ No

XI. Active Pharmaceutical Ingredients(s) (APIs)

(In case more than one active ingredient is used, please replicate this question)

Manufacturer (name, physical address + country):
........................................................................................................................................

GMP certified: ☐ Yes (attach a copy of the GMP certificate if any) ☐ No  ☐ Unknown ............
Certified by: ............................................................................................................................

Specifications and standard test methods exist for each API and excipient ☐ Yes  ☐ No

Each API used (in INN if any): .................................................................................................

☐ Has a Certificate of suitability to the European Pharmacopoeia (CEP)
Certificate: No: .................................................................

☐ The CEP is in our possession (including annex if any)
☐ The CEP is in possession of the finished product manufacturer (including annex if any)
   Technical File available: ☐ Yes  ☐ No

☐ Has a Drug Master File (DMF)
registered in: ........................................ (country) ..............................................................
registration in ..........................................................................................................................
The full or open part of the DMF is in our possession

The full or open part of the DMF is in possession of the finished product manufacturer

Technical File available: ☐Yes ☐No

Quality standard:

☐BP ☐USP ☐EP ☐International Pharmacopoeia

☐Other (e.g. “in-house”; specify:…………………………………)

☐No Pharmacopoeia monograph exists*

*If there is no monograph in a recognized Pharmacopoeia, then the following information should be provided and evaluated:

Chemical structure and physicochemical characteristics:

- If relevant, the isomeric nature of the active ingredient, including stereo chemical configuration (e.g. acemate, pure (S)-isomer, 50/50 mixture of (Z)- and (E)-isomers;
- The solubility of the active ingredient in water at 25 or 35C
- The solubility of the active ingredient in other solvents such as ether, ethanol, acetone, and buffers if different pH (if the active ingredient is acidic or basic),
- Other relevant physicochemical characteristics of the active ingredient such as partition coefficient (usually octanol/water) and the existence of polymorphs;
- Copies of infrared, nuclear magnetic resonance (proton and C-13), ultraviolet and mass spectra;
- Information on the chemical stability of the API, and on physicochemical stability if relevant (e.g. formation of a hydrate, change of polymorphic form).

XII. Commitment

I, the undersigned, ……………………………………………………………………………………………………………………………..,(position in the company, e.g. General Manager, Authorised Person, Responsible Pharmacist), acting as responsible for the company……………………………………………………………………………………………………………….(name of the company), certify that the information provided (above) is correct and true (if the product is marketed in the country of origin, tick the adequate following box)

☐and I certify that the product offered is identical in all aspects of manufacturing and quality to that marketed in …………………………………………………………………………………………………………………….(country of origin), including formulation, method and site of manufacture, sources of active and excipient starting materials, quality control of the product and starting material, packaging, shelf-life and product information.

☐and I certify that the product offered is identical to that marketed in ……………………………………………………………………………………………………………………………………………………………………..(name of country), except: …………………………………………………………………………………………………………………………………………………………………………………………………………………………………………(e.g. formulation, method and site of manufacture, sources of active and excipient starting materials, quality control of the finished product and starting material, packaging, shelf-life, indications, product information)

Date:…………………………… Signature……………………………………………….