Quality assurance of antimalarial medicines

WORKSHOP ON MALARIA CASE MANAGEMENT AND IMPLEMENTATION CHALLENGES,

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Global Malaria Programme

World Health Organization
Quality Assurance of medicines

- Quality Assurance (QA) is the totality of the arrangements made to ensure that pharmaceutical products are of the quality, safety and efficacy required for their intended use.

- Quality Control (QC) is concerned with the sampling, specifications and testing, the documentation and acceptance/rejection procedures which ensures that the relevant tests are carried out, and that the starting materials, intermediates and finished products are not accepted for use, sale or supply until their quality has been judged to be satisfactory.

  QC is a component of QA

- QA cannot absolutely guarantee the production of quality products, unfortunately, but makes this more likely. Quality cannot be tested into a product, it needs to be built into the product.
Different international QA systems

- WHO/UNICEF/UN Project
- Pre-qualification of Medicines
  - WHO/UNICEF Procurement list
  - GFATM QA policy
  - Compliance list
Why QA harmonization for ACTs

- The built-in chemical instability of artemisinin and its derivatives, necessary for their biological action, causes pharmaceutical problems both in the manufacturing process and in the co-formulation with other compounds. The problems of instability are accelerated under tropical conditions.

- The requirement for observing stringent quality manufacturing standards is particularly important for this class of compounds, for which both manufacturers and national drug regulatory authorities have limited experience.

- Differences in quality selection criteria create opportunities for substandard artemisinin-based antimalarial medicines to access funds for procurement, and discourage manufacturers to comply with more stringent quality standards.

- Substandard antimalarials (subpotent or not bioavailable) lead to treatment failures and to sub-therapeutic levels which promote drug resistance.
The UNICEF/WHO procurement list and the Global Fund QA compliance list

- Majority of international funds allocated so far for procurement of artemisinin-based antimalarial medicines for use in the public sector of endemic countries have been based on two above lists.
- Both lists combined include 20 pharmaceutical products (manufactured by 10 companies), but only 9 products (manufactured by 5 companies) are present in both.
- Three possible options were considered:
  1. Adoption of the UNICEF/WHO procurement criteria.
  2. Adoption of the GFATM QA criteria for single- and limited-source pharmaceutical products.
  3. Adoption of a new system based on the clinical and quality review of medicines and harmonization of existing systems.
Inter-agency harmonized criteria for the selection of artemisinin-based antimalarials

UNICEF/WHO tender criteria

- Restricted annual joint tender
- Evaluation of:
  - registration information,
  - regulatory (licensing) situation,
  - finished product specifications and compliance with International Pharmacopoeia standards,
  - stability data (in Zone IV),
  - labeling information,
  - API characteristics and certification.

GFATM QAP criteria

- Inclusion only in National Treatment Guidelines
- Dossier submission only to SNRA

1. WHO Treatment Guidelines
2. PQ approved or SNRA-registered
3. Dossier submission to WHO PQ
4. GMP compliance after inspection by WHO PQ or SNRA

Review of efficacy and safety
Harmonization of selection criteria for antimalarials

**ONE of the two following clinical selection criteria**

- Inclusion in the WHO Treatment Guidelines and in the national treatment guidelines, or

- Inclusion in the national treatment guidelines, but not in WHO Treatment Guidelines, after technical review committee approval

**PLUS the following quality selection criteria**

- Product prequalified by WHO or registered by Stringent Drug Regulatory Authority (SDRA) to be selected in priority

- If there are less than two WHO prequalified or SDRA-registered products, or, if the products which meet these standard are unavailable, then products complying with partial quality criteria can be selected
Recommended quality assurance standards

1. WHO Prequalified products or products registered by a Stringent Drug Regulatory Authority (SDRA) to be selected in priority.

2. In case there are less than three (or two) WHO prequalified or SDRA registered products, or if the products that meet these standards are unavailable, then the product needs to comply with all the following:
   - GMP compliance certified after inspection by WHO or by a SDRA for the dosage form concerned;
   - Submission of the “Product Dossier” to the WHO PQ Programme and acceptance by WHO PQ Programme to review the dossier;
   
   Acceptance of the product after technical review of the documentation submitted by the supplier by an “ad hoc” technical review committee convened by WHO on the following:
   - registration information,
   - regulatory (licensing) situation of finished pharmaceutical product and manufacturing facility,
   - finished product specifications and compliance with international pharmacopoeia standards, if available.
   - stability testing data (both accelerated and real time studies in Zone IV) as per ICH and/or WHO guidelines,
   - labeling information,
   - active pharmaceutical ingredient (API) characteristics and certification,
   - safety and efficacy data.
# Quality Control of Pharmaceutical Products

<table>
<thead>
<tr>
<th>Quality Control Test</th>
<th>Multi Source</th>
<th>Single and limited source products complying with option A or B</th>
<th>Single and limited source products complying with option C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responsibility</td>
<td>PR or sub recipient</td>
<td></td>
<td>GF Secretariat</td>
</tr>
<tr>
<td>Condition (s)</td>
<td>In accordance with the Good Procurement Practice</td>
<td></td>
<td>Notification submission by PR to GF</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No Objection by GF</td>
</tr>
<tr>
<td>When</td>
<td>After receipt of drugs at country level</td>
<td></td>
<td>Before any shipment of drugs to the country</td>
</tr>
<tr>
<td>Frequency</td>
<td>At random, to be determined by the PR</td>
<td></td>
<td>Mandatory for all Purchase Order</td>
</tr>
<tr>
<td>Laboratory</td>
<td>To be selected by PR, laboratory recognized by NDRA, WHO prequalified lab when possible</td>
<td></td>
<td>SGS laboratory, contracted by GF</td>
</tr>
<tr>
<td>Procedures and Assays</td>
<td>To be defined by the PR and selected laboratory</td>
<td></td>
<td>Listed in SGS/GF Contract</td>
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</tbody>
</table>

All details in FAQ:
Harmonization effective by July 2009

WHO/UNICEF/UN Project

Pre-qualification of Medicines

WHO/UNICEF

QA Policy &

Procurement List

GFATM

QA policy &

Compliance List