UNICEF’s Quality Assurance system for procurement of medicines

Peter Svarrer Jakobsen – Sep 2012
Quality Assurance Centre

SUPPLY DIVISION
For every child
Health, Education, Equality, Protection
ADVANCE HUMANITY
Today’s presentation addresses 3 questions:

1. How do UNICEF manage quality assurance of essential medicines?
2. What does UNICEF check before it enters into a contract with a supplier?
3. What does UNICEF check after it enters into a contract with a supplier?
UNICEF’s quality system is based on:

- Division and Centre Procedures
- Principles of WHO Model QA system for Procurement Agencies TRS 937 Annex 6 is implemented
- Principles of Quality System for GMP inspections in accordance with PIC-S Quality System requirements for GMP inspectorates is followed
Today’s presentation addresses 3 questions:

Conclusion (1)

UNICEF has a well established Quality Assurance System in place

What does UNICEF check before we contract a supplier
Pre-qualification - Pharmaceuticals

- Suppliers
  - Review of submitted documentation and/or
  - Good Manufacturing Practice (GMP) inspections to ensure compliance with WHO GMP guidelines

- Products
  - Product Questionnaire as in Model QA System WHO TRS 937
Pre-qualification of suppliers – How?

- Technical questionnaire
  - Manufacturing site
  - Dosage forms / products of interest
  - Export experience

- License to manufacture pharmaceuticals

- Is a GMP inspection needed?
GMP inspections

- Decision based on the regulatory environment in country of origin and prior experience of UNICEF

- GMP inspection by UNICEF or a representative selected by UNICEF

- Contract Manufacture only accepted if subcontractor also is approved by UNICEF
GMP inspections by UNICEF

• To check compliance with WHO GMP Guidelines
• Primarily done by UNICEF staff
• 100 GMP inspections carried out in 2007-2012. 19 companies failed (19%)
• Detailed GMP inspection report forwarded to company with request to respond within 1 month
GMP inspections – collaborations

- Local authority invited to participate
- Joint inspections with WHO, ICRC, MSF
- UNICEF is a Partner to the Pharmaceutical Inspection Cooperation Scheme (PIC-S)
- UNICEF use available information to waive UNICEF inspections
Pre-qualification of products

- Done in connection with Invitation to Bid
- Product Questionnaire as in Model QA System WHO TRS 937 and forward supporting documentation such as analytical procedures, stability report, information on sources of active ingredients.
Pre-qualification of suppliers of Vaccines, HIV/AIDS, malaria and TB products

• Products must be pre-qualified by WHO and listed on the WHO website

• Supplier has confirmed to UNICEF that products are identical to those assessed by WHO/UNICEF

• UNICEF’s purchase is “traced” in WHO/UNICEF GMP inspections.
Today’s presentation addresses 3 questions:

Conclusion (1): UNICEF has a well established Quality Assurance System in place

Conclusion (2): UNICEF focuses on ensuring quality of the supplier and the product before we sign the first contract

What does UNICEF check after it enters into a contract with a supplier
QAC is performing the following activities after we contract a supplier:

- Supply Division licensed by the Danish Medicines Agency (DMA)
  - to wholesale pharmaceutical products
  - to handle narcotic or psychotropic substances

- Compliance with European Union guidelines on Good Distribution Practice (GDP)
GDP ensures

- Quality system implemented
- Organisation defined
- Training of personnel in GDP
- Adequate facilities
- Written procedures
- Records of purchase and sale
- Self-inspections performed
- Recalls can be carried out
Products received in the warehouse are always quality inspected

- Visual inspection
  Product
  Dosage form and strength
  Quantity

- Certificate of analysis
  Satisfactory remaining shelf-life?
  Was it manufactured by the approved site? (manufacturing site needs to be mentioned on certificate)
Problems observed at receipt

- No packing list
- Missing Certificate of Analysis at time of receipt
- Pallets too high, not fumigated etc
- Problems with barcodes
- Space in batch numbers
Problems observed at receipt

- Quality of shipper carton too low
- Too little remaining shelf life
- “Loose” labels on primary packs
- No leaflets or leaflet not packed together with primary pack
Problems observed at receipt

- There should be no UNICEF logo or reference to UNICEF on products
- Storage conditions should be with temperatures and not: “Store in a cool dry place”
Quality control testing

• Analysis performed on a random basis according to an annual plan

• Analysis performed by Therapeutic Goods Administration, Australia, TUV, Singapore, NIDQC, Vietnam and USP, USA

• Few problems observed in 2007 – 2012 (low assay)
Quality control of direct shipments

- Pre-delivery inspections
  - Third party
  - Country Office
- Review of packing list and Certificate of Analysis
- Random quality control testing in accordance with prior experience
Temperature control during shipment

• GDP requirement that needs to be implemented

• All manufacturers/suppliers will in future be requested to document correct shipment conditions at supply to Supply Division

• Temperatures during direct shipments will also need to be monitored
GMP inspections

• All manufacturers are GMP inspected at regular intervals – normally every 2 – 5 years
GMP deficiencies from UNICEF GMP inspections

• This presentation summarize some of the major / critical deficiencies from WHO GMP Guidelines observed during UNICEF inspections

• Presentation focus mainly on issues found at current suppliers of medicines to UNICEF
Organisation and personnel

• Training in product release is poorly documented

• Training in aseptic fill (poor clean room procedures) / certification of staff

• Production clothes should not be worn in uncontrolled areas
Quality management

- Change control procedure established but system not implemented in practice
- Handling of deviation procedure established but system not implemented in practice
Facilities

- Poor separation between controlled and non-controlled areas.
- Poor construction materials / surfaces, which result in poor maintenance.
- Change rooms not well designed so flow secures staff wash their hands prior to entry into production.
- Toilet in production area.
Facilities

• Equipment wash areas has no separation between dirty and clean equipment; lack of ventilation
• Equipment cleaning in tap water
• Poor separation in packaging areas
• Risk of cross-contamination e.g. with penicillin's and/or cephalosporins
• Double standard facilities for local marked / export generally not acceptable
Equipment

• HVAC not designed to ensure a good airflow in the area. Airflow patterns not known.
• Re-circulation of air in non-sterile dusty areas without HEPA filtration – both in general ventilation and in specific equipment e.g. Fluid Bed Dryers
• Risk of cross-contamination due to wrong airflow direction
Documentação

- Procedimentos não atualizados regularmente.
- Especificações e procedimentos analíticos de materiais não elaborados.
- Nenhum registro de lote-mestre para cada tamanho de lote.
Production

- No summary sheets in validation master plans
- IQ and OQ not documented for old facilities/equipment
- Manufacturing processes not validated for all products supplied to UNICEF
- In-sufficient media fills e.g. frequency / worst case simulation
Quality Control

- Different API source, than the one approved by UNICEF
- Handling of analytical working standards
- Inadequate facilities for long term conditions in stability studies
- No formal stability report for each product
- Zone IV B products most relevant for UNICEF
- Annual Product Review not carried out
**Conclusion (1):**
UNICEF has a well established Quality Assurance System in place.

**Conclusion (2):**
UNICEF focuses on ensuring quality of the supplier and the product before we sign the first contract.

**Conclusion (3):**
UNICEF continuously monitors the performance of our suppliers.