UNICEF
Quality Assurance in the procurement of medicines

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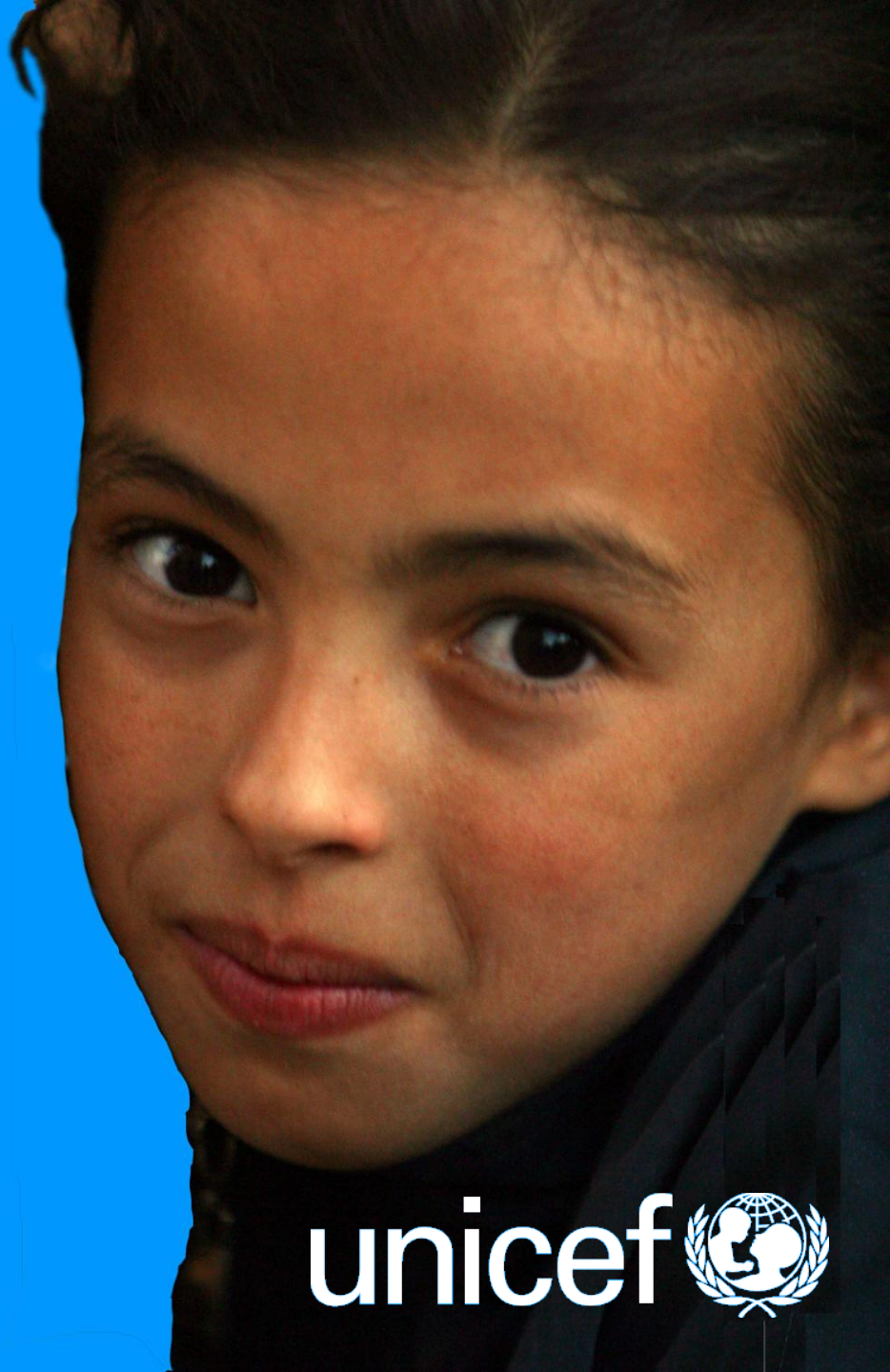
Quality Assurance Centre

SUPPLY DIVISION

For every child
Health, Education, Equality, Protection
ADVANCE HUMANITY



Today's presentation addresses 3 questions:

How do UNICEF manage quality assurance of essential medicines

What does UNICEF check before it enters into a contract with a supplier

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 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 sub-contractor also is approved by UNICEF

GMP inspections by UNICEF

- To check compliance with WHO GMP Guidelines
- Primarily done by UNICEF staff
- 89 GMP inspections carried out in 2006-2009. 27 companies failed (30%)
- 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)

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.
- Supply Agreement with “best offer”
- 1 - 2 back-up suppliers

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):

Quality Assurance has a team of professionals and a well documented quality system

Conclusion (2):

Quality Assurance 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

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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 not fumigated
- EURO pallets not used
- Pallets too high
- Mixed batches on pallets
- Problems with barcodes

Problems observed at receipt

- Quality of shipper carton too low
- Too little remaining shelf life
- “Loose” labels
- “End of run” packs with no labels or missing batch number / expiry

Problems observed at receipt

- There should be no UNICEF logo or reference to UNICEF on products (except ORS)
- 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 and USP, USA
- No major problems observed in 2007 - 2009

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

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GMP inspections

- All manufacturers are GMP inspected at regular intervals – normally every 2 – 5 years

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Highlights from UNICEF GMP inspections

- This presentation summarize some of the main deficiencies from WHO GMP Guidelines observed during UNICEF inspections
- Observations are not classified in this presentation and the presentation focus mainly on issues found at current suppliers to UNICEF

Organisation and personnel

- Organisation chart should be part of the documentation system
- Job descriptions are not authorized
- Training in product release is poorly documented
- Training in aseptic fill / certification of staff
- Production clothes should not be worn in uncontrolled areas

Quality management

- Quality Manual not elaborated
- Change control procedure established but system not implemented in practice
- Handling of deviation procedure established but system not implemented in practice
- Quality Assurance not covered in self-inspection

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

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
- 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

Documentation

- Procedures not updated at regular intervals.
- Uncontrolled copies sometimes a problem
- In-house specifications and analytical procedures for starting materials not elaborated.
- No master batch record for each batch size
- Latest edition of pharmacopoeias not used

Production

- All materials not labeled and traceable e.g. cleaning agents, PVC bags.
- 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

- Deviations not adequately handled as part of batch review
- 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

Contract manufacture

- Technical agreements missing or not sufficient detailed. All responsibilities has to be defined
- GMP guidelines must be defined
- Products covered must be specified

PLEASE NOTE THAT USE OF NEW CONTRACT MANUFACTURING SITE REQUIRES PRIOR APPROVAL.

UNICEF ensure our customers quality products from premium suppliers

Conclusion (1):

Quality Assurance has a team of professionals and a well documented quality system

Conclusion (2):

Quality Assurance are spending many resources on securing supplier and product quality before we sign the first contract

Conclusion (3):

Quality Assurance continuously monitors the performance of our suppliers

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