Survey of the quality of medicines identified by the United Nations Commission on Life-Saving Commodities for Women and Children

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Objectives of the medicines quality survey

• Primary
  – To identify products which are of good quality (or the quality of which can be improved in short period of time)

• Secondary
  – To evaluate the quality of products currently available in selected countries at the first level of distribution chain (e.g. central medical stores, NGO central stores, warehouses of importers or major distributors)
    • To avoid any influence of inappropriate storage conditions
  – Results should also assist responsible authorities in the countries in meeting the Commission target
Countries selected for sampling
10 countries selected for sampling

• Burkina Faso, Kenya, Madagascar, Nepal, Nigeria, Tajikistan, Tanzania, Uganda, Vietnam, Zimbabwe

• Criteria
  – Majority of selected medicines in country registers
  – Several products from various manufacturers per medicine
  – Longer experience in medicines regulation
  – Representation of countries from various geographic regions
  – Willingness of NMRAs to cooperate

• Advice requested from regional and country offices
Selection of medicines for sampling & testing

- To optimize use of resources the assessment of benefits brought by testing and risks posed by individual medicines was performed
  - Medicines the quality of which is assured not included
    - Contraceptive implants, Ulipristal tablets – only innovator products
    - Misoprostol tablets, Chlorhexidine digluconate gel/solution already in focus of partners (Concept, Path)
  - Low-risk ORS not included
Medicines included in the survey

- Oxytocin injection 10IU in 1ml (if not available, 5UI/ml)
- Magnesium sulfate injection 500mg/ml in 2ml, 5ml or 10ml ampoule (if not available, lower strength)
- Gentamycin injection
  - 40mg/ml in 1ml or 2ml ampoule (80mg/2ml) or
  - 20mg/ml in 1ml ampoule or
  - 10mg/ml in 2ml ampoule
- Procaine benzylpenicillin injection 1g (= 1 000 000 IU) in a vial (synonyms: Procaine penicillin, Procaine penicillin G)
- Ampicillin injection 250mg, 500mg or 1g in a vial
- Ceftriaxone injection 250mg, 500mg or 1g in a vial
- Betamethasone injection
  - Suspension 5.7mg/ml (3mg/ml as betamethasone sodium phosphate + 2.7mg/ml as betamethasone acetate) in 1ml ampoule (aqueous injection) or
  - Solution 4mg/ml in 1ml ampoule or 8mg in 2ml ampoule (as betamethasone phosphate disodium salt)
- Dexamethasone injection 4mg/ml in 1ml ampoules (as dexamethasone phosphate disodium salt)
- Amoxicillin 250mg or 500mg dispersible tablet
- Zinc sulfate 10mg or 20mg dispersible tablet or 10mg/5ml syrup
- Levonorgestrel 1.5 mg or 0.75mg tablet
- Mifepristone 10mg, 25mg tablet
Current Achievements

• Testing has been completed and 95% of results are available and evaluated
  – 3 laboratories used NQCL Kenya, InphA Germany, SGS Belgium

• Performed as per a protocol for the survey that was prepared and finalized after discussion with focal persons from 10 countries
  – Meeting with focal persons 12-13 Aug 2014 in Tanzania

• 205 samples collected and sent to testing laboratories in the period Sep – Nov 2013
Preliminary outcomes

• Oxytocin injection
  – 22 samples from 15 manufacturers from 6 countries
    • India, China, Germany, Hungary, Italy, Russia
  – Samples collected in all 10 countries
    • In Burkina Faso, Nepal, Tajikistan, Tanzania, Vietnam only 5IU (10IU not available)
  – Some problems with the content (8 samples<90.0%), impurities (test in PhInt only) and visible particles (3 samples)
Preliminary outcomes

- Manufacturers' storage conditions for Oxytocin inj
  - Samples from 15 manufacturers
    - 3x 2-8°C
    - 1x 2-15°C
    - 7x below 20/25/30°C
    - 1x above 0°C
    - 3x not available
Preliminary outcomes
Oxytocin - differences in impurity profiles

Ph.Int. limits:
• 1 impurity >2%
• No impurity >5%
Preliminary outcomes

- **Magnesium sulfate injection**
  - 19 samples from 14 manufacturers from 9 countries
    - India, France, Russia, China, Germany, Saudi Arabia, UK, Ukraine, Vietnam
  - Samples collected in 9 countries
    - No sample collected in Madagascar
    - In Tajikistan collected only 250mg/ml and in Vietnam only 150mg/ml (500mg/ml not available)
  - All samples complied with specifications
Preliminary outcomes

- **Gentamycin injection**
  - 29 samples from 23 manufacturers from 8 countries
    - China, India, Germany, Slovenia, Vietnam, Bangladesh, Italy, Tunisia
  - Samples collected in all 10 countries
    - Majority 80mg/2ml
  - Main problems: content and composition of gentamicin: 3 samples were outside of 90.0%-110% and other samples presented minor deviations from the limits for composition
Preliminary outcomes

- **Procaine benzylpenicillin injection**
  - 6 samples from 3 manufacturers from 2 countries
    - China, France
  - Samples collected in 5 countries only
    - In Madagascar PBP 1 MIU
    - In Zimbabwe PBP 3 MIU
    - In Burkina Faso, Tanzania and Uganda only Fortified PBP (procaine benzylpenicillin 3 MIU + benzylpenicillin sodium 1 MIU)
  - All samples complied with specifications
Preliminary outcomes

• **Ampicillin injection**
  – 26 samples from 17 manufacturers from 5 countries
    • China, India, Vietnam, Germany, UK
  – Samples collected in all 10 countries
  – Some problems with the content (3 samples < 95.0% but > 90.0%), mass uniformity (1 sample) and impurities (test in BP only)

• **Ceftriaxone injection**
  – 30 samples from 24 manufacturers from 8 countries
    • India, China, Vietnam, Bangladesh, Korea, Poland, Russia, Ukraine
  – Samples collected in all 10 countries
  – Some problems with the content (2 samples < 95.0% but > 90.0%)
Preliminary outcomes

• **Betamethasone suspension** 5.7mg/ml (3 mg/ml as betamethasone sodium phosphate + 2.7 mg/ml as betamethasone acetate) or injection 4 mg/ml (as betamethasone phosphate disodium salt)
  – No sample collected in any of 10 countries

• **Dexamethasone injection**
  – 19 samples from 15 manufacturers from 5 countries
    • India, China, Vietnam, Russia, Ukraine
  – Samples collected in 9 countries
    • No sample collected in Burkina Faso
  – Problems found with content (4 samples <90.0%) and impurities (3 samples slightly higher free dexamethasone)
Preliminary outcomes

• Amoxicillin dispersible tablets
  – 10 samples from 8 manufacturers from 4 countries
    • India, Nepal, Russia, Uganda
  – Samples collected in 3 countries only
    • No sample collected in Burkina Faso, Kenya, Madagascar, Nigeria, Tanzania, Vietnam, Zimbabwe
  – Results of testing awaited
Preliminary outcomes

• Zinc sulfate dispersible tablets / syrup
  – 17 samples of dispersible tablets from 13 manufacturers from 8 countries
    • Nepal, India, Kenya, Nigeria, Bangladesh, France, Tanzania, Zimbabwe
  – 4 samples of syrup from 2 manufacturers from 2 countries
    • Tanzania, Vietnam
  – Samples collected in 8 countries
    • No sample collected in Burkina Faso and Madagascar
    • In Nepal 1 sample of zinc gluconate dispersible tablets collected apart from 2 samples of zinc sulfate dispersible tablets
    • In Vietnam only 2 samples of syrup collected
  – All samples complied with specifications
Preliminary outcomes

• **Levonorgestrel tablets**
  – 14 samples from 9 manufacturers from 4 countries
    • India, Vietnam, Bangladesh, Hungary
  – Samples collected in 8 countries
    • No sample collected in Burkina Faso and Nigeria
    • 13 samples 0.75 mg, 1 sample 1.5mg
  – Problems with dissolution (2 samples but method used could be the cause) and content uniformity (1 sample)

• **Mifepristone tablets**
  – 8 samples (all 10mg) from 5 Vietnamese manufacturers
  – Samples collected in Vietnam only
  – All samples complied with specifications
Planned activities

• Testing results will be provided to all participating NMRAs

• Outcomes will be discussed with NMRAs in the closing meeting (3rd quarter 2014)
  – Corrective measures, if necessary, will be recommended
  – Responsibility to take any relevant measures in the countries lies with the respective NMRAs

• Outcomes and report from the survey will be published by WHO

• Survey outcomes serve as a source for selection of manufacturers for discussion and potential technical assistance
Thank you!

Questions, comments?

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