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

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WHO Prequalification Team
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PREQUALIFICATION OF MEDICINES PROGRAMME
A UNITED NATIONS PROGRAMME MANAGED BY WHO

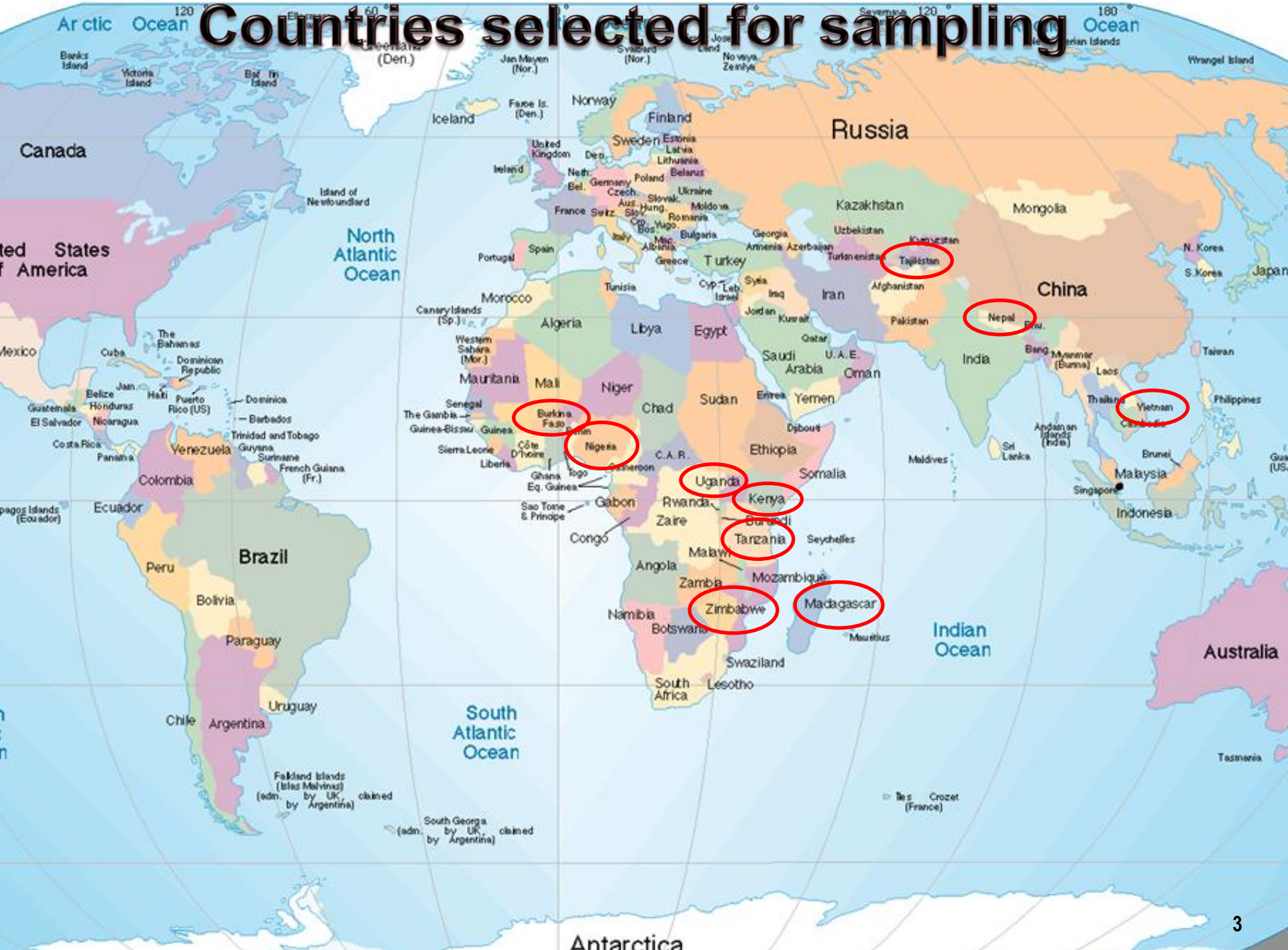
World Health Organization

QUALITY MEDICINES FOR EVERYONE

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

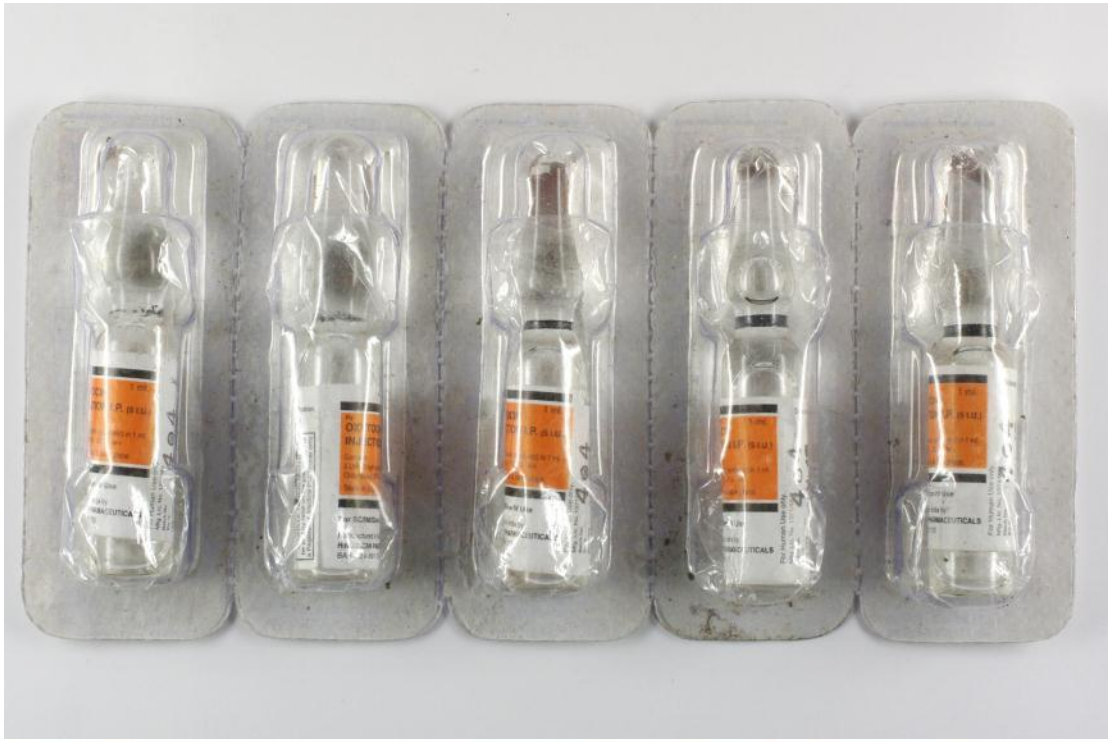
- Testing has been completed and 95% of results are available and evaluated
  - 3 laboratories used NQCL Kenya, InphA Germany, SGS Belgium
- Performed as per a protocol for the survey that was prepared and finalized after discussion with focal persons from 10 countries
  - Meeting with focal persons 12-13 Aug 2014 in Tanzania
- 205 samples collected and sent to testing laboratories in the period Sep – Nov 2013

Preliminary outcomes

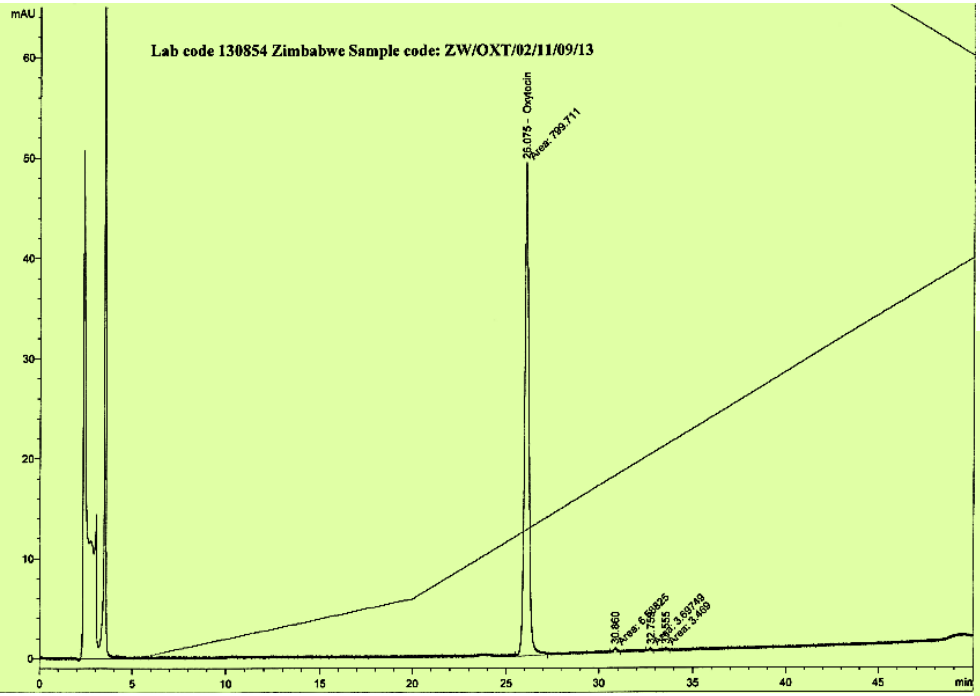
- **Oxytocin injection**
  - 22 samples from 15 manufacturers from 6 countries
    - India, China, Germany, Hungary, Italy, Russia
  - Samples collected in all 10 countries
    - In Burkina Faso, Nepal, Tajikistan, Tanzania, Vietnam only 5IU (10IU not available)
  - Some problems with the content (8 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 2-8ºC
    - 1x 2-15ºC
    - 7x below 20/25/30ºC
    - 1x above 0ºC
    - 3x not available

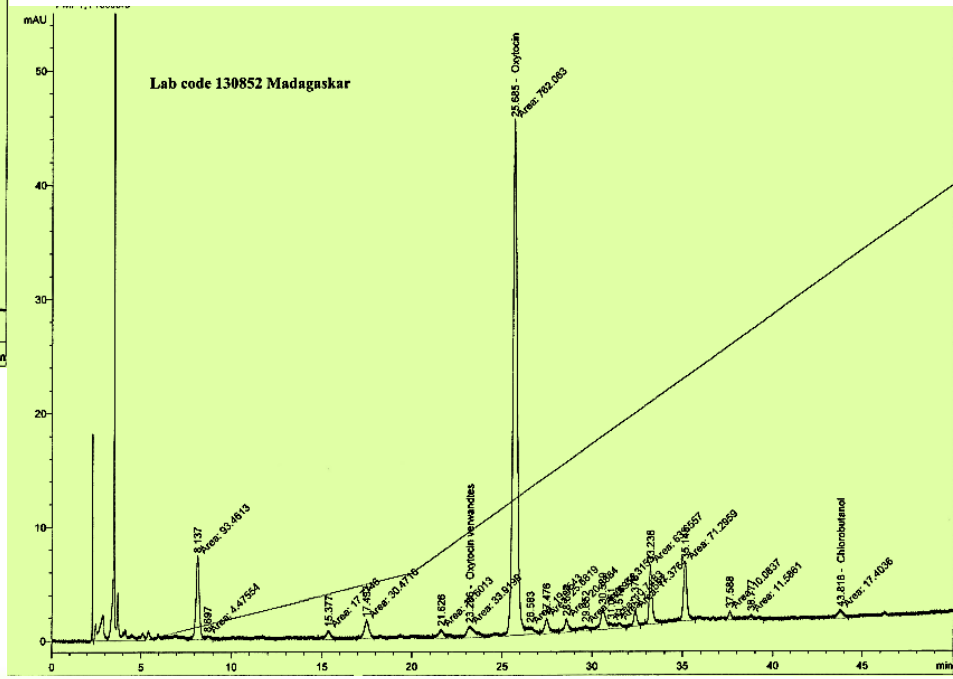


Preliminary outcomes
Oxytocin - differences in impurity profiles



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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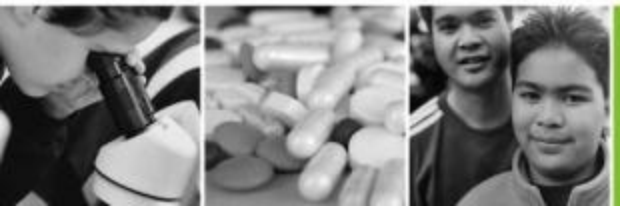

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