World Health Organization

SURVEY OF THE QUALITY OF MEDICINES IDENTIFIED BY THE UNITED NATIONS COMMISSION ON LIFE SAVING COMMODITIES FOR WOMEN AND CHILDREN






2015

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

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Glossary of terms and abbreviations

Sample	for the purposes of this project means a product in given presentation (identified by the name, content of APIs, dosage form, strength, batch number and manufacturer) collected at the specific collection site. That means that the same product characterized by the same name, content of APIs, the same dosage form, strength, batch, and from the same manufacturer collected in two different sites represents two samples.

Country codes and medicines abbreviations used for the purposes of coding samples are shown in the Survey protocol (Appendix 1) on page 78.

API	Active pharmaceutical ingredient
BP	British Pharmacopoeia
CHX	Chlorhexidine
CMS	Central medical store
CWG	Chlorhexidine Working Group
CPh	Chinese Pharmacopoeia
EWEC	Every Woman Every Child
FL	Fiducial limit
GMP	Good Manufacturing Practice
HPLC	High performance liquid chromatography
INN	International Nonproprietary Names for pharmaceutical substances
IP	Indian Pharmacopoeia
MoH	Ministry of Health
NGO	Non-governmental organization
NLT	Not less than
NMRA	National Medicines Regulatory Authority
NMT	Not more than
ORS	Oral Rehydration Salts
PATH	Program for Appropriate Technology in Health
Ph. Eur.	European Pharmacopoeia
Ph. Int.	The International Pharmacopoeia
UNCoLSC	United Nations Commission on Life-Saving Commodities for Women and Children
USP	United States Pharmacopeia
VP	Vietnamese Pharmacopoeia
WHO	World Health Organization
WHO PQT	WHO Prequalification Team

Executive summary

The survey focused on selected medicines from the list of 13 life-saving commodities as identified by the UN Commission on Life-Saving Commodities for Women and Children (UNCoLSC). As a primary objective, it aimed to identify products of good quality already available in selected EWEC countries. This information should help responsible authorities in the surveyed countries as well as other EWEC countries to meet the requirements of the Commission's recommendation No. 4, i.e. that by 2015 quality-certified and affordable products from at least three manufacturers per commodity are marketed in each of the 49 EWEC countries. The secondary objective was to evaluate the quality of target medicines collected at the first level of the distribution chain. This approach was chosen so that the results would reflect as closely as possible the quality of products as released from manufacturing sites, with minimal influence of potentially inappropriate conditions during storage or transportation in countries.

The survey was organized by the WHO Prequalification Team (WHO PQT) in cooperation with the National Medicines Regulatory Authorities / Ministries of Health of Burkina Faso, Kenya, Madagascar, Nepal, Nigeria, Tajikistan, Tanzania, Uganda, Viet Nam and Zimbabwe. A total of 204 samples of the following medicines were collected and tested:

- oxytocin injection,
- magnesium sulfate injection,
- gentamicin injection,
- procaine benzylpenicillin injection,
- ampicillin injection,
- ceftriaxone injection,
- dexamethasone phosphate injection,
- amoxicillin dispersible tablets,
- zinc sulfate dispersible tablets/syrup,
- levonorgestrel tablets, and
- mifepristone tablets.

In total, medicines produced by 106 manufacturers from 22 countries were collected in the survey. Products of some manufacturers were available in several countries, some manufacturers produced several of the target medicines. Testing was performed in three WHO-prequalified laboratories according to the monographs of the International Pharmacopoeia, British Pharmacopoeia, US Pharmacopeia, or a laboratory validated method.

The survey provided a snapshot picture of the quality of the sampled products and generated information about the availability of the target medicines in selected countries. The results were discussed with regulatory authorities of the participating countries. The authorities adopted necessary regulatory actions and participated in the formulation of recommendations.

Of 204 samples tested, 157 (77%) complied with the specifications set for this survey. These samples represented 109 different products and were produced by 91 manufacturers from 21 countries. No failures were found for samples of procaine benzylpenicillin injection, amoxicillin dispersible tablets, zinc tablets, zinc syrup and mifepristone tablets. On the other hand, there were 47 (23%) samples (representing 40 products) which failed one or more tests. The highest proportion of non-compliant samples was found for oxytocin injection (64%), and relatively high failure rates were also recorded for gentamicin injection (41%), ampicillin injection (35%) and dexamethasone phosphate injection

(32%). A substantially lower proportion of samples failing one or more tests was found for levonorgestrel tablets (14%), magnesium sulfate injection (11%) and ceftriaxone injection (7%).

The high overall rate of non-compliance can be partially explained by the relatively strict testing criteria and the fact that all samples were tested against pharmacopoeial specifications rather than the manufacturers' specifications approved in the countries of collection.

Similarly as in quality surveys organized previously by WHO PQT, an attempt has been made to identify those deviations from specifications which most likely impact the therapeutic effect due to the low content of active principle or its limited release from the dosage form. The proportion of samples with such extreme deviations was much lower than the overall failure rate, i.e. 2% (5 of 204 samples). Extreme failures were found in one sample of levonorgestrel tablets, one sample of dexamethasone phosphate injection and three samples of oxytocin injection. The quality of these medicines therefore deserves further attention. For samples of ceftriaxone injection, gentamicin injection, magnesium sulfate injection and ampicillin injection only moderate deviations from the specifications set for this survey were found. However, it has to be kept in mind that even if some deviations from specifications are considered moderate they are still failures. They most likely indicate that the manufacturers have problems to operate in compliance with Good Manufacturing Practice (GMP) and with adherence to international quality standards or with product formulation, and that, as a result, the quality of the products may not be assured.

Even if the number of collected samples varied in individual countries and in general was quite low, differences were observed in the proportions of quality-compromised products found in participating countries (7% in Zimbabwe; 14–20% in Tanzania, Tajikistan, Uganda and Nepal, and 29 – 35% in Viet Nam, Burkina Faso, Kenya, Madagascar and Nigeria). These findings may reflect market complexity as well as differences in the level of regulatory scrutiny and standards applied.

The samples tested in this survey included both locally manufactured (19%) and imported products (81%). Locally manufactured products were sampled for nine of 11 tested medicines, and no major quality issues were identified. All samples of locally produced amoxicillin dispersible tablets (in Nepal and Uganda), and zinc-containing products (in Kenya, Nepal, Nigeria, Tanzania, Viet Nam and Zimbabwe) complied with testing specifications. All other samples of locally manufactured products were collected in Viet Nam. There were some deviations found for these samples, however, they were never extreme and, according to information received from Vietnamese regulators, some of the samples would comply with the specifications registered in Viet Nam.

Collectors evaluated registration status of collected samples, i.e. if sampled products were authorised by the competent National Medicines Regulatory Authority (NMRA) for marketing and distribution in the country of collection. In the case that they found a sample of unregistered product they investigated the basis on which those products were supplied and placed on the market. Unregistered products were sampled in Burkina Faso, Nepal, Tajikistan, Uganda and Zimbabwe. They accounted for 9% of products sampled, all were imported and all were placed on the market legally using various specific mechanisms in line with national regulations (e.g. they were supplied centrally based on a global tender, as donations or on a special import permit). This finding shows that alternative mechanisms that bypass the national registration processes are used to supply needed medicines. In general, the samples of these unregistered products supplied in line with national regulations were of good quality, with a lower failure rate than was found among samples of registered products. This indicates that the donors' quality assurance mechanisms as well as the regulatory control of these alternative pathways in countries were effective.

Although few WHO-prequalified medicines were sampled (11 samples of 4 products), the survey confirmed their consistently good quality. The zero failure rates of WHO-prequalified products suggest that WHO prequalification reliably assures uniform quality standards.

When interpreting the survey results, limitations of the methodology should be taken into account. First, relatively small numbers of samples were collected as the availability of products was rather limited. Second, neither the selection of sampling sites nor selection of samples from each site could have been done according to a randomized sampling procedure. Hence, it cannot be claimed that the samples collected and tested were representative of all target medicines used in the selected countries at the time of the survey. Additional medicines could be channelled via other first level distribution sites or via the same sites at different time periods. Nevertheless, the findings provided an understanding of the quality of the target medicines at the first level of distribution chain.

The availability of the target medicines may be underestimated in this survey due to the sampling methodology used. Several medicines were relatively well available in all countries (ceftriaxone injection, gentamicin injection, ampicillin injection, oxytocin injection), others only in several countries (zinc-containing products, dexamethasone phosphate injection, magnesium sulfate injection, levonorgestrel tablets) and some were frequently not available at all (procaine benzylpenicillin injection, amoxicillin dispersible tablets, mifepristone tablets). In each country at least one of the medicines recommended by UNCoLSC could not be identified for collection. For betamethasone injection, no samples were available in any country. In some countries the innovator product was available but the collectors respected the instructions in the protocol to exclude innovator products.

The survey confirmed that comprehensive approaches are necessary to improve the availability and quality of UNCoLSC target medicines. It is obvious that the lack of availability of certain medicines in individual countries is driven by a low demand among local physicians, and updates of therapeutic treatment guidelines and training of physicians are therefore recommended. Some medicines were available in different strengths than those recommended by UNCoLSC (e.g. oxytocin injection, magnesium sulfate injection) or in different dosage forms (e.g. amoxicillin products). This illustrates the differences in current therapeutic use. Some medicines (such as amoxicillin dispersible tablets) were not available even in countries with the potential of domestic production.

To improve availability, UNCoLSC should clearly specify the needed medicines by their dosage form and strength (indicating to which API form the strength relates), and include possible alternatives in the list of commodities. This would help countries and manufacturers to understand the needs and act accordingly. For certain categories of medicines that are relatively easy to produce and control (e.g. zinc products), availability can be improved by local production and pragmatic regulatory requirements. More intensive cooperation and exchange of information among regulators would help to eliminate poor quality medicines. This can be achieved through exchange of assessment and inspection reports, cooperation in sample testing and/or consultations before regulatory action is taken against substandard medicines. Regulatory cooperation, harmonization of regulatory requirements and procedures can also help to improve regulatory efficiency and incentivize manufacturers to register more UNCoLSC-relevant medicines in the respective countries.

The survey met its primary and secondary objectives. It generated information which led to a better understanding of the availability and quality of UNCoLSC target medicines in selected EWEC countries. It provided a broad picture of the manufacturers whose products were available in the selected countries. It also contributed towards evidence-based regulatory actions in some countries.

The results of the survey serve WHO to focus on selected manufacturers and to confirm to which extent good quality confirmed by testing is also supported by compliance with GMP and proper regulatory documentation.

1. Introduction

1.1 Background

The United Nations Commission on Life-Saving Commodities for Women and Children (UNCoLSC) was established in March 2012 in response to the call in the UN Secretary-General's Global Strategy for Women's and Children's Health for increasing access to and appropriate use of medicines, medical devices and health supplies that effectively address leading avoidable causes of death during pregnancy, childbirth and childhood.

With a strong focus on the reproductive, maternal, newborn and child health the Commission, in its report published in September 2012 **[1]**, identified 13 essential but overlooked life-saving commodities that, if more widely accessed and properly used, could save the lives of more than 6 million women and children. The Commission also identified key, interrelated barriers that prevent access to and use of the 13 commodities. These barriers include: severely under-resourced regulatory agencies in low-income countries, leading to delayed registration of commodities; lack of oversight of product quality and general inefficiencies; market failures, where return on investment is too low to encourage manufacturers to enter the market or produce sufficient quantities; and user supply and demand challenges such as limited demand for the product by end-users, local delivery problems and incorrect prescription and use. **Table 1** lists the target commodities identified by the Commission, their proposed usage, and examples of key barriers to their availability and appropriate use.

Table 1 Target commodities

	Commodity	Usage	Examples of key barriers
Maternal health	Oxytocin	Post-partum haemorrhage	Often poor quality
	Misoprostol	Post-partum haemorrhage	Not included in national essential medicine lists
	Magnesium sulfate	Eclampsia and severe pre-eclampsia/ toxaemia of pregnancy	Lack of demand by health workers
Newborn health	Injectable antibiotics (gentamicin, procaine-benzylpenicillin, ampicillin, ceftriaxone)	Newborn sepsis	Poor compliance by health workers
	Antenatal corticosteroid (betamethasone, dexamethasone)	Respiratory distress syndrome for preterm babies	Low awareness of product and impact
	Chlorhexidine	Newborn cord care	Limited awareness and demand
	Resuscitation equipment	Newborn asphyxia	Requires trained health workers
Child health	Amoxicillin	Pneumonia	Limited availability of child-friendly product
	Oral rehydration salts	Diarrhoea	Poor understanding of products by mothers/ caregivers
	Zinc	Diarrhoea	Poor understanding of products by mothers/ caregivers
Reproductive health	Female condoms	Family planning/ contraception	Low awareness among women and health workers
	Implants (levonorgestrel, etonogestrel)	Family planning/ contraception	High cost
	Emergency contraception (levonorgestrel, ulipristal, misoprostol)	Family planning/ contraception	Low awareness among women

The Commission focuses on 49 of the world's poorest countries identified under the "Every Woman Every Child" (EWEC) movement (see **Box 1**).

Box 1. EWEC countries

Afghanistan	DR of Congo	Kyrgyz Republic	Niger	Tajikistan
Bangladesh	Eritrea	Lao PDR	Nigeria	Tanzania
Benin	Ethiopia	Liberia	Pakistan	Togo
Burkina Faso	The Gambia	Madagascar	Papua New Guinea	Uganda
Burundi	Ghana	Malawi	Rwanda	Uzbekistan
Cambodia	Guinea	Mali	Sao Tome and Principe	Viet Nam
Central African Republic	Guinea-Bissau	Mauritania	Senegal	Yemen
Chad	Haiti	Mozambique	Sierra Leone	Zambia
Comoros	Kenya	Myanmar	Solomon Islands	Zimbabwe
Côte d'Ivoire	DPR of Korea	Nepal	Somalia	

To address these challenges and deliver on the promise of saving the lives of millions of women and children, the Commission recommended 10 time-bound actions (see **Box 2**). These actions focus on the need for improved global and local markets for life-saving commodities, innovative financing, quality strengthening, regulatory efficiency, improved national delivery of commodities, and better integration of private sector and consumer needs.

The Commission's recommendation No. 4, for which WHO is responsible, relates to quality strengthening and proposes to identify manufacturers of quality-certified and affordable products. The target is to ensure that, by 2015, quality-certified and affordable products from at least three manufacturers per commodity are marketed in each of 49 countries.

As one of the activities to implement this recommendation WHO has proposed a review of the quality of the most commonly used life-saving commodities to make a rapid analysis of global market quality, determine the most common safety and quality risks and identify the most promising manufacturers. The manufacturers identified may then be supported in developing and marketing a product of assured quality with a focus on good manufacturing practices, quality production, bioequivalence, stability and competitive pricing such that low- and middle-income countries can afford these commodities.

One of the first activities under this recommendation was to perform an initial quality survey of the target life-saving medicines available on the markets of selected EWEC countries. The survey and its findings are described in this report.

Box 2. The Commission's 10 recommendations [1]

Improved markets for life-saving commodities

1. **Shaping global markets:** By 2013, effective global mechanisms such as pooled procurement and aggregated demand are in place to increase the availability of quality, life-saving commodities at an optimal price and volume.
2. **Shaping local delivery markets:** By 2014, local health providers and private sector actors in all EWEC countries are incentivized to increase production, distribution and appropriate promotion of the 13 commodities.
3. **Innovative financing:** By the end of 2013, innovative, results-based financing is in place to rapidly increase access to the 13 commodities by those most in need and foster innovations.
4. **Quality strengthening:** By 2015, at least three manufacturers per commodity are manufacturing and marketing quality-certified and affordable products.
5. **Regulatory efficiency:** By 2015, all EWEC countries have standardized and streamlined their registration requirements and assessment processes for the 13 live-saving commodities with support from stringent regulatory authorities, the World Health Organization and regional collaboration.

Improved national delivery of life-saving commodities

6. **Supply and awareness:** By 2015, all EWEC countries have improved the supply of life-saving commodities and build on information and communication technology (ICT) best practices for making these improvements.
7. **Demand and utilization:** By 2014, all EWEC countries in conjunction with the private sector and civil society have developed plans to implement at scale appropriate interventions to increase demand for and utilization of health services and products, particularly among under-served populations.
8. **Reaching women and children:** By 2014, all EWEC countries are addressing financial barriers to ensure the poorest members of society have access to the life-saving commodities.
9. **Performance and accountability:** By end 2013, all EWEC countries have proven mechanisms such as checklists in place to ensure that health-care providers are knowledgeable about the latest national guidelines.

Improved integration of private sector and consumer needs

10. **Product innovation:** By 2014, research and development for improved life-saving commodities has been prioritized, funded and commenced.

1.2 Objectives of the survey

This quality survey focused on medicines defined as target commodities in the UNCoLSC project. The survey primarily aimed to identify products which were of good quality, or the quality of which could be improved in a short period of time. Following this survey, the quality of identified products was intended to be further verified through the evaluation of the respective level of compliance of identified manufacturers with GMP and assessment of product dossiers. Technical assistance may be provided to promising manufacturers.

The secondary objective of the survey was to evaluate the quality of products at the first level of distribution chain (e.g. central medical stores, non-governmental organizations (NGO) central stores, warehouses of importers or major distributors) in order to understand which products were available

and whether they could be recommended for use in additional countries. The first level of the distribution chain was selected to minimize the influence of potentially inappropriate storage and/or transport conditions in countries on the survey results, and to find out the quality of products as manufactured.

The results of this survey will also assist responsible authorities in the surveyed countries in implementing the Commission's recommendation No. 4, and they may be informative for the authorities of other EWEC countries.

Limitations of the survey

Due to time and resource constraints and the need to focus on the objectives of the UNCoLSC project, this survey did not evaluate the quality of the target medicines throughout the distribution chain to assess the effect of storage and transportation conditions and evaluate the risk of patients' exposure to substandard medicines.

The survey findings are relevant only to the samples tested and can be extrapolated to other produced batches (or even within a tested batch) only to a limited extent. Therefore any conclusion on the quality of products should be made after taking into account additional information such as the outcomes of evaluations of manufacturers' GMP compliance and assessment of products' dossiers.

2. Methodology

The survey was conducted according to a common protocol (Appendix 1) developed in cooperation with participating countries.

2.1 Survey period

A preparatory meeting with the focal persons nominated by each participating country was held in Dar es Salaam, Tanzania on 12-13 August 2013 to discuss availability and quality of selected medicines in the participating countries, finalize the survey protocol and provide detailed instructions for collection and transportation of samples to testing laboratories.

Following this meeting the samples of selected medicines were collected in the three-month period from September to November 2013. Collected samples were sent to three preselected testing laboratories, and testing was performed between December 2013 and April 2014. Testing results were summarized and provided to the participating countries in May 2014. In July 2014, WHO PQT met with the representatives of the participating countries in Harare, Zimbabwe and analysed the survey outcomes.

2.2 Selection of medicines for sampling and testing

Target medicines

This survey focused only on medicines included among target commodities of the UNCoLSC project, not on medical devices.

To collect samples, the appropriate dosage forms and strengths of target medicines corresponding to usage defined by UNCoLSC were identified as follows:

Maternal health commodities

- Oxytocin injection 10IU in 1mL ampoules
- Misoprostol 200µg tablets
- Magnesium sulfate injection 500mg/mL in 2mL, 5mL and 10mL ampoules (recommended to be co-packed with Calcium gluconate injection 100mg/mL in 10mL ampoules for treatment of magnesium toxicity)

Newborn health commodities

- Injectable antibiotics
  - Gentamicin injection 40mg/mL or 20mg/mL or 10mg/mL in 1mL or 2mL ampoules
  - Procaine benzylpenicillin injection 1g (1 000 000 IU = 1 MIU) in a vial
  - Ampicillin injection 250mg, 500mg or 1g in a vial
  - Ceftriaxone injection 250mg, 500mg or 1g in a vial
- Antenatal corticosteroids
  - Betamethasone injection 5.7mg/mL (3mg/mL as betamethasone sodium phosphate + 2.7mg/mL as betamethasone acetate) in 1mL ampoules
  - Betamethasone injection 4mg/mL (as betamethasone phosphate disodium salt) in 1mL or 2 mL ampoules
  - Dexamethasone phosphate injection 4mg/mL (as dexamethasone sodium phosphate) in 1mL ampoules

- Chlorhexidine digluconate gel or solution containing 4% chlorhexidine (i.e. 7.1% chlorhexidine digluconate)

Child health commodities

- Amoxicillin 250mg or 500mg dispersible tablets
- Oral rehydration salts (ORS) of the composition recommended by WHO and UNICEF **[2]**
- Zinc sulfate
  - 10mg or 20mg dispersible tablets
  - 10mg/5mL syrup

Reproductive health commodities

- Contraceptive implants
  - Levonorgestrel 75mg/rod implants, 2 rods
  - Etonogestrel 68mg /rod implants, 1 rod
- Emergency contraception
  - Levonorgestrel 1.5mg or 0.75mg tablets
  - Ulipristal acetate 30mg tablets
  - Mifepristone 10mg or 25mg tablets

Target medicines available in countries

Medicines registers of 13 EWEC countries were searched for availability of target medicines. In the case of Kenya, Madagascar and Uganda the registers were downloaded from the NMRA websites, for Viet Nam the MIMS Drug Information System **[3]** was searched, and registers from Burkina Faso, Democratic Republic of Congo, Kyrgyzstan, Nigeria, Senegal, Tajikistan, Tanzania, Uzbekistan and Zimbabwe were obtained from the respective NMRAs/Ministries of Health (MoH) with the assistance of WHO regional and country offices.

Medicines excluded from the survey

To optimize the use of resources available for this survey a benefit-risk analysis was performed with the aim to exclude from testing the following categories of medicines:

- Medicines deemed to be of assured quality as they are produced under the supervision of a Stringent Regulatory Authority (SRA),[1]
- Medicines the quality of which is already in the focus of international NGOs or other organizations, and
- Medicines posing a low risk (see the risk assessment table in Annex 1 to Appendix 1).

Based on the information gathered, the medicines mentioned below were not included in quality testing for the following reasons:

[1] Stringent regulatory authority (SRA): a regulatory authority which is: (a) a member of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) (as specified on www.ich.org); or (b) an ICH observer, being the European Free Trade Association (EFTA), as represented by Swissmedic and Health Canada (as may be updated from time to time); or (c) a regulatory authority associated with an ICH member through a legally-binding, mutual recognition agreement including Australia, Iceland, Liechtenstein and Norway (as may be updated from time to time); http://www.who.int/prequal/info_applicants/Guidelines/2014/ANNEX-6_SRA-Guide_DRAFT.pdf.

- **Ulipristal acetate 30mg tablets** and **etonogestrel 68mg/rod implants** – Only innovator products were available, and the respective innovator companies (HRA Pharma, France and N.V. Organon, Netherlands) were under stringent regulatory supervision.
- **Levonorgestrel 75mg/rod implants** – The available products were either from the innovator company (Bayer Schering, Finland) or from Shanghai Dahua Pharmaceutical Co. Ltd China, the development of which was supported by the organization fhi360. The first product is well under control and the second one is currently under WHO PQT review.
- **Misoprostol 200µg tablets** – Production of misoprostol tablets of good quality has been a long term focus of the Concept Foundation. In 2011 the Concept Foundation performed a quality survey of misoprostol products and identified potential causes of substandard quality. The Foundation has been working with several manufacturers on improving their production of misoprostol tablets. None of these manufacturers had placed an improved product on the market at the time when this survey was planned.
- **Calcium gluconate injection 100mg/mL** – This medicine is recommended to be used for treatment of magnesium toxicity when magnesium sulfate injection is used for treatment of eclampsia. The two medicines are recommended to be co-packaged. Once a manufacturer of good quality magnesium sulfate injection will be identified, negotiations will be initiated on possible production of the product co-packed with calcium gluconate injection. Calcium gluconate injection was therefore not included in quality testing in this phase of the project.

Further, a risk assessment was performed on the other medicines from the list of UNCoLSC target commodities based on:

- Estimated probability of occurrence of a quality problem (taking into account the complexity of manufacture, stability of the medicine and suitability of specifications to control potential problems),
- Exposure of patients to the medicine (way of dispensing and size of exposed population), and
- Seriousness of potential harm (vulnerability of target population; risks related to the medicine′s dosage form and route of administration and to therapeutic properties such as safety margins and risk of side effects; risk of therapeutic failure; acute versus chronic use; risk of development of resistance).

The outcomes of this risk assessment are provided in Annex 1 to the survey protocol (Appendix 1).

Based on the risk assessment outcomes and additional market information, chlorhexidine digluconate gel/solution and oral rehydration salts (medicines with the lowest risk score) were excluded from the sampling and testing in this phase of the project. In case the need emerges in the future, samples of these medicines can be targeted later.

- **Chlorhexidine** digluconate gel or solution containing 4% chlorhexidine (i.e. 7.1% chlorhexidine digluconate) is a new formulation which was submitted in November 2012 by PATH on behalf of the Chlorhexidine Working Group (CWG) to the WHO Expert Committee on the Selection and Use of Essential Medicines for inclusion in the WHO Model List of Essential Medicines. In 2013 it was included in the 18th WHO Model List of Essential Medicines **[4]**. According to the PATH submission **[5]** the product is available from Lomus Pharmaceuticals in Nepal. In 2012 UNICEF Supply Division procured chlorhexidine digluconate 7.1% solution from Galentic Pharma Pvt. Ltd., India. In addition Purna Pharma, Belgium and Sirmaxo Pharma, India are also suppliers of 5% chlorhexidine through UNICEF

Supply Division and have indicated their willingness to start producing 7.1% chlorhexidine digluconate when the demand for this commodity increases. The CWG is also encouraging local manufacture of chlorhexidine for umbilical cord care in low and middle income countries to increase product availability. Therefore, it was considered that potential suppliers of this product had already been identified and the CWG was adequately following the availability of this product.

- For **oral rehydration salts (ORS)**, most of the products in the registers of screened countries were products with slightly different compositions from that recommended in 2006 by WHO and UNICEF **[2]** (i.e. 2.6g/l sodium chloride + 13.5g/l glucose anhydrous + 1.5g/l potassium chloride + 2.9g/l trisodium citrate dehydrate; total osmolarity 245mOsmol/l). The companies identified in registers as producing ORS of the recommended low osmolarity composition (Cosmos Kenya, Medipharm Industries Ltd Uganda, Shelys Tanzania and CHI Pharmaceuticals Nigeria) cooperate already with WHO PQT and may be inspected in connection with other products of interest within UNCoLSC. Thus the verification of quality by laboratory testing was not considered necessary during this phase of the project.

Medicines included in the survey

Taking into account the above considerations, the following medicines were selected for sampling and testing within this survey, focusing only on specified dosage forms and strengths:

- Oxytocin injection 10IU (if not available then a lower strength) in 1mL ampoules;
- Magnesium sulfate injection 500mg/mL (if not available then a lower strength) in 2mL, 5mL or 10mL ampoules;
- Gentamicin injection 40mg/mL or 20mg/mL or 10mg/mL in 1mL or 2mL ampoules;
- Procaine benzylpenicillin injection 1 MIU (= 1g) in a vial (if not available then a higher strength); *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 5.7mg/mL (3mg/mL as betamethasone sodium phosphate + 2.7mg/mL as betamethasone acetate) in 1 mL ampoules, or 4mg/mL (as betamethasone sodium phosphate) in 1mL or 2 mL ampoules;
- Dexamethasone phosphate injection 4mg/mL (as dexamethasone sodium phosphate) in 1mL ampoules;
- Amoxicillin 250mg or 500mg dispersible tablets (if not available then a lower strength);
- Zinc sulfate 10mg or 20mg dispersible tablets or 10mg/5mL syrup;
- Levonorgestrel 1.5 mg or 0.75mg tablets; and
- Mifepristone 10mg or 25mg tablets.

2.3 Participating countries

Countries for collection of samples were selected from 49 EWEC countries using the following criteria:

- Countries should have on the market a majority of the selected medicines; several registered products from various manufacturers should be available to make sampling feasible.
- Countries with relatively long experience in medicines regulation should be selected, as they may have on their markets good quality products which can be recommended for use and registration in other countries.
- Countries from various geographic regions should be represented.
- Countries should be selected where the NMRA/MoH is willing to cooperate in collection of samples for the project.

Based on the information gathered and considering advice from other WHO units, regional and country offices, the following countries were selected for collection of samples:

- Burkina Faso
- Kenya
- Madagascar
- Nepal
- Nigeria
- Tajikistan
- Tanzania
- Uganda
- Viet Nam
- Zimbabwe

The NMRA/MoH in each of the selected countries agreed to cooperate and nominated a focal person for this survey to coordinate activities in the country. The responsibilities of the focal persons were as follows:

- Identify appropriate sampling sites and prepare a list of products corresponding to the target medicines available in the country,
- Prepare a national sampling plan,
- Organize sampling in the country and transportation of samples to the pre-specified testing laboratories,
- Participate in the analysis of outcomes of quality monitoring of products and in making recommendations for corrective actions in the country, if necessary.

Appropriate arrangements for cooperation and reimbursement of activities performed within the project were made with the NMRA/MoH in each of the selected countries.

2.4 Selection of sample collection sites

To obtain information about the quality of products as supplied by manufacturers and to limit any influence of inappropriate storage or transport conditions in countries, samples were collected at the first level of distribution chain, e.g. in central medical stores, NGO central stores, warehouses of

importers or major distributors or other facilities supplied directly within various programmes. As the distribution chains differed in individual countries, samples were collected in the public and/or private sector, wherever the target medicines could be found. Where samples were not readily available for collection at this level, sampling at manufacturers' stores was an option.

The approach to selection of sampling sites was discussed and agreed with the country focal persons during the preparatory meeting in Dar es Salaam, Tanzania, and national sampling plans were developed by each focal person in line with the survey protocol (Appendix 1).

2.5 Sample collection and transportation

For the purposes of this survey, a sample was defined as a product in a given presentation (identified by the name, API content, dosage form, strength, batch number and manufacturer) collected at the specific collection site. This means that the same product characterized by the same name, API content, dosage form, strength, batch, and produced by the same manufacturer collected in two different sites represented two samples.

Samples were collected by the staff of the NMRA/MoH in each participating country. Detailed national sampling plans were used (see the template in Annex 2 of Appendix 1), identifying the collection sites, medicines, number of batches and number of units per sample to be collected. The target number of samples to be collected in each country was set at 36 (three samples for each of 12 medicines). Bearing in mind the objective of the survey, i.e. to identify products of good quality, or of a quality which can be improved in a short period of time, the collectors were asked to collect samples of products from various manufacturers. If there were products available from more than three manufacturers per medicine, they were instructed to select those which were in their opinion of better quality. To make the best possible use of the resources available for this survey the collectors were asked not to collect medicines produced by manufacturers under the supervision of a Stringent Regulatory Authority (SRA)[*] (e.g. innovator products), which are deemed to be of assured quality. Detailed instructions for collecting samples, storage and dispatch to testing laboratories were prepared (see Annex 2 of Appendix 1), and the focal persons arranged for training of collectors with regard to the national sampling plan and the instructions.

Collectors were required to be mindful of the stock of sampled products in collection sites in order not to jeopardize the availability of medicines to patients. If there was a risk of product shortage after sampling, they were instructed to either arrange for replacement of the sampled amount or to refrain from collection of that particular product in that facility.

For each sample, collectors assigned a unique code number and completed a standardized sample collection form (Annex 3 of Appendix 1). The following details were recorded at the time of collection: product name, name of the API, dosage form, strength per unit dose, package size, type and material of primary container, batch number, date of manufacture, expiry date, name and address of manufacturer, quantity collected, registration status, site and date of sample collection, storage conditions at the site, and any observations made during collection. These details were considered essential not only to identify each sample and ensure its traceability but also for final data analysis.

The collected samples were required to be taken to NMRAs as quickly as possible and then to be stored under conditions specified on the label. For oxytocin injection samples it was recommended to use a cold box for transportation from the sampling sites to NMRA premises and to store the samples at 2°C to 8°C even if labelled storage conditions were different. Detailed instructions for transportation of samples to testing laboratories were provided in the survey protocol (section 4.5 of Appendix 1).

2.6 Testing laboratories

Three WHO-prequalified quality control laboratories were selected for testing of samples collected in this survey: InphA GmbH – Institute for Pharmaceutical and Applied Analytics, Official Medicines Control Laboratory (OMCL), Bremen, Germany; National Quality Control Laboratory (NQCL), Nairobi, Kenya; and SGS Lab Simon S.A., Wavre, Belgium. **Table** 2 shows the division of samples for testing by individual laboratories.

Table 2 Laboratories performing quality testing

Testing laboratory	Medicines tested
InphA GmbH Institute for Pharmaceutical and Applied Analytics, Official Medicines Control Laboratory (OMCL), Bremen, Germany	Oxytocin injection Procaine benzylpenicillin injection Ampicillin injection Ceftriaxone injection Betamethasone injection Levonorgestrel tablets Mifepristone tablets
National Quality Control Laboratory (NQCL), Nairobi, Kenya	Magnesium sulfate injection Dexamethasone phosphate injection Amoxicillin dispersible tablets Zinc sulfate dispersible tablets or syrup
SGS Lab Simon S.A., Wavre, Belgium	Gentamicin injection

WHO PQT covered all testing costs.

2.7 Quality tests conducted and test methods and specifications used

Samples were tested for the following as appropriate for each formulation and available specifications:

- Appearance;
- Identification;
- Assay;
- Related substances;
- For tablets – uniformity of mass (weight variation) / content uniformity, disintegration/ dissolution, fineness of dispersion;
- For syrups – pH, specific gravity (relative density);
- For injections – pH, extractable volume;
- For powders for injection – uniformity of mass, water content, pH after reconstitution.

Sterility testing was not included in this survey given that this testing can never provide 100% certainty about the sterility of all units within the batch and is resource-demanding. Moreover the quality of products with promising testing results was intended to be further confirmed by GMP inspections at manufacturing sites to assure that sterility is guaranteed by the manufacturing process.

The test for bacterial endotoxins was also not included in this survey for similar reasons, and because the small volume parenteral products selected for this survey have a relatively low risk.

Test methods and specifications were those of the respective monographs from the British Pharmacopoeia 2013 (BP), International Pharmacopoeia 4th edition (Ph. Int.) or United States Pharmacopeia 36 (USP) that were valid at the time of testing as detailed in **Table 3** and in the testing protocol (Annex 4 of Appendix 1). When a monograph for a particular medicine was available in more than one pharmacopoeia, the ability of the respective specifications and methods to reveal quality problems was considered and the monograph was selected accordingly. In some cases tests from another pharmacopoeia were added to provide a more comprehensive picture of the quality of a particular medicine. As there was no monograph for mifepristone tablets in the Ph. Int., BP or USP, the testing laboratory used the specifications and methods kindly provided by one of the manufacturers of the collected samples and re-validated the methods before use.

Table 3 Specifications and methods used for testing

Medicine	Specifications and methods
Oxytocin injection	Ph. Int. monograph
Magnesium sulfate injection	Ph. Int. monograph
Gentamicin injection	BP monograph
Procaine benzylpenicillin injection	BP (Veterinary) monograph with addition of tests for water and pH according to USP monograph for penicillin G procaine for injectable suspension
Ampicillin injection	BP monograph
Ceftriaxone injection	BP monograph
Betamethasone injection	USP monograph for betamethasone sodium phosphate and betamethasone acetate injectable suspension BP monograph for betamethasone injection
Dexamethasone phosphate injection	BP monograph for dexamethasone sodium phosphate injection
Amoxicillin dispersible tablets	USP monograph for amoxicillin tablets for oral suspension
Zinc sulfate dispersible tablets or syrup	USP monograph for zinc sulfate tablets with addition of test for fineness of dispersion according to Ph. Eur. USP monograph for zinc sulfate oral solution
Levonorgestrel tablets	BP monograph with addition of test for dissolution according to Ph. Int. monograph
Mifepristone tablets	Laboratory validated methods based on methods and specifications kindly provided by one of the manufacturers of collected samples

The following general specifications were used for evaluation of samples:

Appearance

- Tablets should be undamaged, smooth, and usually of uniform colour. Presence of excessive powder and/or pieces of tablets in the container, cracks, chipping in the tablet surfaces or coating, swelling, mottling, discoloration, fusion between tablets, appearance of crystals on the container walls or on the tablets are signs of physical instability and are not acceptable.
- Solutions for injection, solutions for infusion, and reconstituted solutions should be clear and free from visible particulate matter.

Uniformity of single-dose units

Zinc sulfate dispersible tablets and levonorgestrel tablets were tested for content uniformity and the results were evaluated in each case according to the requirements of the pharmacopoeia used for testing of the particular medicine (i.e. USP <905> for zinc sulfate dispersible tablets, and BP/Ph. Eur. 2.9.6. for levonorgestrel tablets).

The other medicines in tablet or powder for injection dosage forms were tested for uniformity of mass according to the requirements of BP/Ph. Eur. 2.9.5. or for weight variation according to USP <905>, again following the requirements of the pharmacopoeia used for testing of the particular medicine.

Disintegration

The disintegration test was performed in line with the harmonized pharmacopoeial monograph. For conventional uncoated tablets the limit of not more than 15 minutes was used, while a shorter time limit as specified in the respective monograph was applied for dispersible tablets (i.e. 3 minutes for amoxicillin dispersible tablets and 60 seconds for zinc sulfate dispersible tablets).

Dissolution

Dissolution was in principle tested in line with the harmonized pharmacopoeial monograph in three stages, with the following acceptance criteria:

Stage	Number of units tested	Acceptance criteria
S1	6 units	Each unit is not <Q*+5%
S2	Another 6 units	Average of 12 units (S1+S2) is ≥ Q, and no unit is <Q-15%
S3	Another 12 units	Average of 24 units (S1+S2+S3) is ≥Q, not more than 2 units are <Q-15%, and no unit is <Q-25%

**Q is the amount of dissolved active ingredient specified in the individual monograph, expressed as a percentage of the content stated on the label. The testing is continued through the three stages unless the results conform at either stage 1 or stage 2.*

Specifications applied in terms of Q values and testing time limits are shown in the testing protocol (Annex 4 to Appendix 1).

Fineness of dispersion

Fineness of dispersion was tested according to the requirements of Ph. Eur. monograph for dispersible tablets. Two tablets were placed in 100 mL of water and stirred until completely dispersed. A smooth dispersion produced should pass through a sieve screen with a nominal mesh aperture of 710 µm (USP No. 25).

2.8 Compliance of samples with standards

The samples were considered to be in compliance with standards if they met the specifications set for this survey and outlined in the section above and/or listed in the respective tables of results in Appendices 3-13.

All results which were found out-of-specification were investigated and tests were repeated as appropriate according to each laboratory standard operating procedure on handling out-of-specification results.

In this survey all samples containing the same active ingredient(s) in the same dosage form were tested according to the same specifications to enable comparison of samples from different manufacturers. It should be noted that individual manufacturers may use different specifications and different methods for testing of their products, and these specifications and methods may be approved by regulatory authorities in individual countries. Non-compliance with the specifications selected for this survey does not necessarily imply non-compliance with the specifications approved in the country.

3. Results

3.1 Overview of samples collected

3.1.1 Medicines collected

A total of 206 samples were collected which represented 151 products[2] in 157 different strengths (of individual products) from 106 pharmaceutical companies (manufacturers)[3]. The breakdown of numbers of samples and products collected for individual medicines is shown in **Table 4**.

Sample collectors adhered to the instructions and collected the requested products in the specified strengths and dosage forms. There was only one deviation – one sample of levonorgestrel tablets 0.03mg was collected. As this strength did not correspond to the intended use as defined by UNCoLSC, the sample was excluded from the survey and was not tested.

It was very difficult to collect samples of procaine benzylpenicillin injection so that samples were only found in Madagascar and Zimbabwe. To collect any sample of procaine benzylpenicillin injection, the collectors in three other countries (Burkina Faso, Tanzania and Uganda) had to deviate slightly from the instructions and collect samples of powder for injection containing procaine benzylpenicillin 3 MIU in combination with benzylpenicillin sodium 1 MIU (Fortified Procaine Penicillin). These samples were included in the testing phase.

For zinc-containing medicines, samples of zinc sulfate in various dosage forms (dispersible tablets, conventional tablets, effervescent tablets, syrup) and one sample of zinc gluconate dispersible tablets were collected. WHO guidelines **[6]** accept various water soluble zinc salts (zinc sulfate, zinc gluconate, zinc acetate) as equally effective in the management of diarrhoea; zinc sulfate is the most widely used because it is the cheapest. Therefore the sample of zinc gluconate dispersible tablets was included in the testing phase even if the instructions mentioned zinc sulfate only.

For betamethasone injection no eligible samples according to the instructions in the survey protocol were available in any of the participating countries. Bethamethasone injection was only available as an innovator product produced by manufacturers under supervision of a SRA, and this product type was excluded from the survey. Thus no samples of this medicine were collected and tested.

The breakdown of numbers of collected samples and corresponding products for each medicine by country is displayed in **Table 5**. A total of 205 samples of 11 medicines were tested.

[2] A product was identified by the name of manufacturer, dosage form and content of API(s) in qualitative terms, i.e. various strengths were not differentiated.

[3] A manufacturer was identified by the name of company declared on labelling and was considered to be the same even if different addresses appeared on labelling of some products.

Table 4 Numbers of samples per medicine in total and in different strengths collected in the survey, and corresponding numbers of manufacturers

	No. of samples (not differentiating strengths)	*No. of manufacturers*[4]	No. of samples (differentiating strengths)	*No. of manufacturers*[4]
Oxytocin injection	22	*15*		
10IU/mL			10	*8*
5IU/mL			12	*9*
Magnesium sulfate injection	19	*14*		
500mg/mL			13	*9*
250mg/mL			3	*3*
150mg/mL			3	*2*
Gentamycin injection	29	*23*		
80mg/2mL			26	*20*
40mg/1mL			1	*1*
20mg/2mL			2	*2*
Procaine benzylpenicillin injection	3	*3*		
1MIU/vial			2	*2*
3MIU/vial			1	*1*
Procaine benzylpenicillin + benzylpenicillin sodium injection	3	*2*		
3MIU + 1MIU			3	*2*
Ampicillin injection	26	*17*		
1g/vial			12	*9*
500mg/vial			12	*9*
250mg/vial			2	*1*
Ceftriaxone injection	30	*24*		
1g/vial			26	*21*
500mg/vial			2	*2*
250mg/vial			2	*2*
Dexamethasone phosphate injection	19	*14*		
4mg/1mL			19	*14*
Amoxicillin dispersible tablets	10	*8*		
500mg			1	*1*
250mg			4	*4*
150mg			5	*3*
Zinc tablets	18	*14*		
20mg			15	*11*
10mg			3	*3*
Zinc syrup	4	*2*		
10mg/5mL			4	*2*
Levonorgestrel tablets	15	*10*		
1.5mg			1	*1*
0.75mg			13	*9*
0.03mg[5]			1	*1*
Mifepristone tablets	8	*5*		
10mg			8	*5*
Total	**206**		**206**	

[4] Some manufacturers produce several medicines and/or several strengths of a medicine.

[5] The strength deviated from the levonorgestrel tablet strengths specified in the protocol. The sample was therefore excluded from testing.

Table 5 Summary of numbers of samples and products collected in individual countries

Country	Burkina Faso	Kenya	Madagascar	Nepal	Nigeria	Tajikistan	Tanzania	Uganda	Viet Nam	Zimbabwe	**Total**
Product*	Number of samples (number of products, not differentiating strengths)										
Oxytocin injection	2 (2)	1 (1)	1 (1)	3 (3)	3 (3)	3 (3)	3 (2)	3 (2)	1 (1)	2 (2)	**22 (20)**
Magnesium sulfate injection	1 (1)	2 (2)	NC	3 (1)	3 (3)	3 (3)	2 (1)	1 (1)	3 (2)	1 (1)	**19 (15)**
Gentamicin injection	3 (2)	3 (3)	2 (2)	3 (3)	3 (3)	3 (3)	4 (3)	3 (3)	3 (3)	2 (2)	**29 (27)**
Procaine benzyl-penicillin (PBP) injection	0	NC	2 (2)	NC	NC	NC	0	0	NC	1 (1)	**3 (3)**
PBP+ benzyl-penicillin sodium injection	1 (1)		0				1 (1)	1 (1)		0	**3 (3)**
Ampicillin injection	3 (2)	2 (2)	3 (3)	3 (1)	1 (1)	3 (3)	2 (2)	3 (3)	3 (3)	3 (3)	**26 (23)**
Ceftriaxone injection	3 (2)	4 (4)	3 (3)	3 (3)	3 (3)	3 (3)	3 (3)	3 (3)	3 (3)	2 (2)	**30 (29)**
Dexamethasone injection	NC	1 (1)	2 (2)	3 (3)	2 (1)	3 (3)	2 (1)	2 (1)	3 (3)	1 (1)	**19 (16)**
Amoxicillin dispersible tablets	NC	NC	NC	2 (2)	NC	3 (3)	NC	5 (3)	NC	NC	**10 (8)**
Zinc sulfate/ gluconate dispersible tablets	NC	3 (3)	NC	3 (3)	2 (2)	3 (3)	2 (1)	3 (2)	0	2 (2)	**18 (16)**
Zinc sulfate syrup		0		0	0	0	2 (1)	0	2 (1)	0	**4 (2)**
Levonorgestrel tablets	NC	3 (3)	2 (2)	2 (2)	NC	1 (1)	1 (1)	2 (1)	2 (2)	1 (1)	**14 (13)**
Mifepristone tablets	NC	NC	NC	NC	NC	NC	NC	NC	8 (5)	NC	**8 (5)**
Total	**13 (10)**	**19 (19)**	**15 (15)**	**25 (21)**	**17 (16)**	**25 (25)**	**22 (16)**	**26 (20)**	**28 (23)**	**15 (15)**	**205 (180)**

NC Not collected

* See footnote 2 on page 26

3.1.2 Manufacturers and batches

The 205 samples tested in this survey represented 202 different batches and originated from a total of 106 manufacturers[6] based in a total of 22 different countries.

A list of manufacturers of collected samples with information on product strength, number of different batches collected, and countries of collection is provided in Appendix 2. The addresses of manufacturers included in the table were taken from the product labelling. It is believed that in the majority of cases they represent the addresses of manufacturing sites. However, some may be addresses of company's headquarters or even registration holders or suppliers. If needed, individual cases can be clarified with the respective manufacturer.

Manufacturers and countries of origin

The manufacturers were from the following countries:

- India (35);
- China (18);
- Viet Nam (12);
- Russian Federation (6);
- France, Germany (4 from each);
- Bangladesh, Nepal, Ukraine (3 from each);
- Kenya, Nigeria, Slovenia, Tanzania, United Kingdom (2 from each); and
- Hungary, Italy, Republic of Korea, Poland, Saudi Arabia, Tunisia, Uganda, Zimbabwe (1 from each).

Imported and locally manufactured products

In total, 166 of 205 (81%) samples were from products imported into the country of collection, 39 were from locally manufactured products and were collected in seven countries as listed in **Table 6**. In Burkina Faso, Madagascar and Tajikistan no samples of locally manufactured products were collected.

Table 6 Samples of locally manufactured products

Country of collection	Proportion of locally manufactured samples	%	Number of products sampled
Viet Nam	24 of 28 samples	86%	19 products
Nepal	5 of 25 samples	20%	5 products
Tanzania	4 of 22 samples	18%	2 products
Nigeria	2 of 17 samples	12%	2 products
Kenya	2 of 19 samples	11%	2 products
Zimbabwe	1 of 15 samples	7%	1 product
Uganda	1 of 26 samples	4%	1 product

In Viet Nam, the samples of locally manufactured products included the following: mifepristone tablets (from five local manufacturers), ampicillin injection, ceftriaxone injection, dexamethasone phosphate injection, gentamicin injection and levonorgestrel tablets (from 2-3 local manufacturers

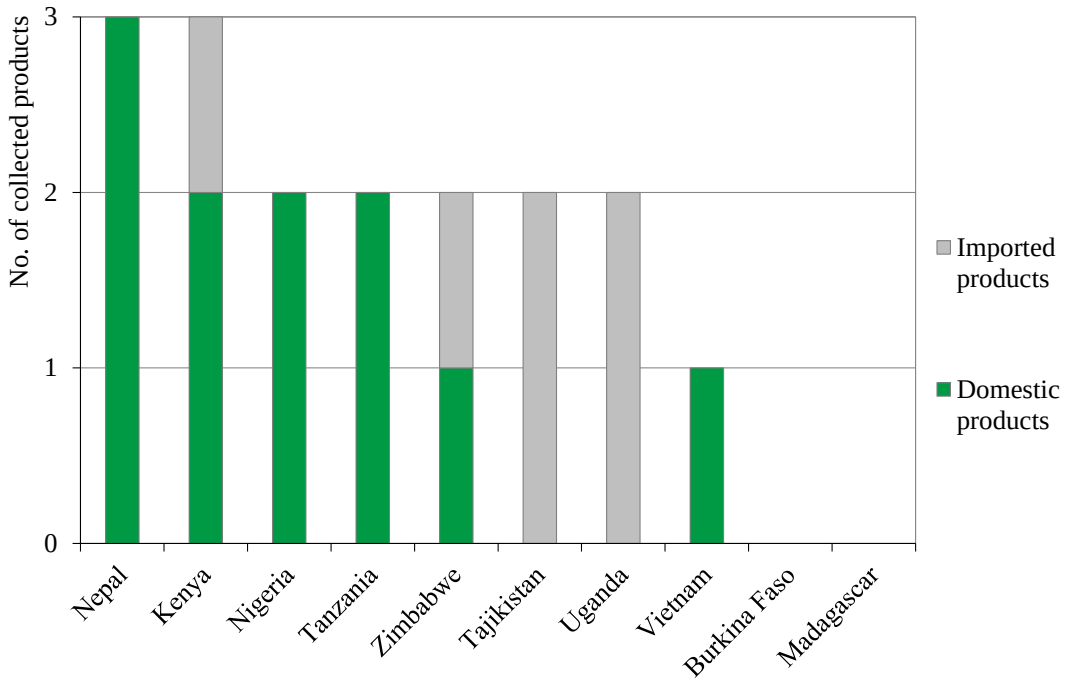
[6] See footnote 3 on page 25

each), and magnesium sulfate injection and zinc sulfate syrup (from one local manufacturer each). All oxytocin injection samples collected in Viet Nam were imported; procaine benzylpenicillin injection and amoxicillin dispersible tablets were not collected.

Samples of locally manufactured amoxicillin dispersible tablets were collected in Nepal and Uganda.

The most often found domestically produced medicine was zinc (both tablets and syrup), collected in Kenya, Nepal, Nigeria, Tanzania and Zimbabwe. The proportions of locally manufactured and imported zinc-containing products sampled in each country are shown in **Figure 1**.

Figure 1 Numbers of locally manufactured and imported zinc-containing products collected in countries



Manufacturers supplying multiple medicines and/or multiple countries

Of the 106 manufacturers 29 had samples of more than one medicine included in the survey (ranging from two to seven medicines), and for 20 manufacturers there were samples collected in more than one country, ranging from two to five countries (**Table 7**).

Table 7 Manufacturers with samples taken of multiple medicines and/or in multiple countries

Manufacturer	Collected medicines (by API)		Countries of collection	
North China Pharmaceutical Co Ltd (NCPC), China	**7**	ampicillin, ceftriaxone, dexamethasone phosphate, gentamicin, oxytocin, procaine benzylpenicillin, procaine benzylpenicillin+benzylpenicillin sodium	2	Burkina Faso, Madagascar
CSPC Zhongnuo Pharmaceutical (Shijazhuang) Co Ltd, China	**4**	ampicillin, ceftriaxone, procaine benzylpenicillin, procaine benzylpenicillin+ benzylpenicillin sodium	**5**	Kenya, Madagascar, Nigeria, Tanzania, Uganda
Shandong (Yanzhou) Xier Kangtai Pharmaceutical Co Ltd, China	**4**	ampicillin, ceftriaxone, dexamethasone phosphate, gentamicin	3	Kenya, Madagascar, Nigeria
CSPC OUYI (Shijiazhuang) Pharmaceuticals Co Ltd, China	**3**	ceftriaxone, dexamethasone phosphate, gentamicin	**4**	Kenya, Madagascar, Tajikistan, Uganda
Vital Healthcare Pvt Ltd, India	**3**	gentamicin, magnesium sulfate, oxytocin	**3**	Kenya, Tanzania, Uganda
Lincoln Pharmaceuticals Ltd, India	**3**	ampicillin, gentamicin, magnesium sulfate	2	Nigeria, Tanzania
Umedica Laboratories Pvt Ltd, India	**3**	ampicillin, ceftriaxone, oxytocin	2	Kenya, Zimbabwe
Fresenius Kabi Bidiphar JS Co, Viet Nam	**3**	dexamethasone phosphate, gentamicin, magnesium sulfate	1	Viet Nam
Hindustan Pharmaceuticals, India	**3**	dexamethasone phosphate, magnesium sulfate, oxytocin	1	Nepal
Rotexmedica GmbH Arzneimittelwork, Germany	2	gentamicin, oxytocin	**5**	Burkina Faso, Nigeria, Tanzania, Viet Nam, Zimbabwe
Gedeon Richter Plc, Hungary	2	levonorgestrel, oxytocin	2	Uganda, Tajikistan
Karnataka Antibiotics and Pharmaceuticals Ltd, India	2	ampicillin, ceftriaxone	2	Uganda, Zimbabwe
Shandong Reyoung Pharmaceutical Co Ltd, China	2	ampicillin, gentamicin	2	Burkina Faso, Viet Nam
Zhejiang Tianfeng Pharmaceutical Factory, China	2	gentamicin, oxytocin	2	Nigeria, Uganda
Aristo Pharmaceuticals Pvt Ltd, India	2	ampicillin, ceftriaxone	1	Nepal
BaDinh Pharmaceutical Biological JS Co, Viet Nam	2	levonorgestrel, mifepristone	1	Viet Nam
Biologici Italia Laboratories, Italy	2	gentamicin, oxytocin	1	Zimbabwe
Bryntsalov – A ZAO, Russia	2	dexamethasone phosphate, oxytocin	1	Tajikistan
Medicamen Biotech Ltd, India	2	amoxicillin, zinc sulfate	1	Tajikistan
MinhDan Pharmaceutical JS Co, Viet Nam	2	ampicillin, ceftriaxone	1	Viet Nam
National Health Care Pvt Ltd, Nepal	2	amoxicillin, zinc sulfate	1	Nepal
Ningbo Dahongying Pharmaceutical Co Ltd, China	2	gentamicin, oxytocin	1	Uganda
Pymepharco Co, Viet Nam	2	dexamethasone phosphate, gentamicin	1	Viet Nam
S.R. Drug Laboratories Pvt Ltd, Nepal	2	amoxicillin, zinc gluconate	1	Nepal
Sanavita Pharmaceuticals GmbH, Germany	2	ampicillin, gentamicin	1	Tajikistan
Square Pharmaceuticals Ltd, Bangladesh	2	gentamicin, zinc sulfate	1	Kenya
Stada-VN JV Co Ltd, Viet Nam	2	levonorgestrel, mifepristone	1	Viet Nam
Tablets India Ltd, India	2	gentamicin, oxytocin	1	Nepal
Viet Nam China Pharmaceutical JS Co (VCP), Viet Nam	2	ampicillin, ceftriaxone	1	Viet Nam
Famy Care Ltd, India	1	levonorgestrel	**3**	Madagascar, Tanzania, Zimbabwe
Laboratoires Pharmaceutiques Rodael, France	1	zinc sulfate	**3**	Tajikistan, Uganda, Zimbabwe
Aurobindo Pharma Ltd, India	1	ampicillin	2	Uganda, Zimbabwe
Cadila Healthcare Ltd, India	1	dexamethasone phosphate	2	Nepal, Uganda
Cipla Ltd, India	1	levonorgestrel	2	Madagascar, Nepal
Intas Pharmaceuticals Ltd, India	1	gentamicin	2	Tanzania, Zimbabwe
Ranbaxy Laboratories Ltd, India	1	ceftriaxone	2	Nepal, Nigeria
Zhejiang Ruixin Pharmaceuticals Co Ltd, China	1	oxytocin	2	Burkina Faso, Uganda

Batches

It was rare to find the same batches among collected samples, even in a single country. Only three of the total 202 batches were sampled in two different sampling sites: 1) a batch of magnesium sulfate injection in two separate sites in Tanzania, 2) another batch of magnesium sulfate injection in Kenya and in Uganda, and 3) a batch of levonorgestrel tablets in Madagascar and in Uganda.

3.1.3 Sampling sites

A total of 82 collection sites in the 10 countries were included in the survey. As requested by the survey protocol, all sites were at the first level of distribution chain; 73% of the sites where in the private sector, 22% in the public sector and 5% NGO stores. The numbers and types of collection sites in individual countries with numbers of collected samples are shown in Table 8. Samples were collected in central medical stores, stores of distributers, importers or directly purchasing hospitals and treatment centres in the public sector, in NGO stores, and in warehouses of importers, distributors, wholesalers, retailers or manufacturers in the private sector. Most of the sampling sites were located in capital cities; in four countries samples were collected also in other cities: in Viet Nam apart from Hanoi the collectors went to five other cities, in Nepal, Nigeria and Uganda apart from the capital to one additional city.

Table 8 Numbers of collection sites in individual countries with numbers of collected samples

Country	*Number of sampling sites*	Public		NGO		Private	
		Number of sites	Number of samples	*Number of sites*	Number of samples	*Number of sites*	Number of samples
Burkina Faso	***8***	*5*	10	*0*	0	*3*	3
Kenya	***5***	*0*	0	*1*	4	*4*	15
Madagascar	***4***	*1*	2	*0*	0	*3*	13
Nepal	***10***	*5*	9	*0*	0	*5*	16
Nigeria	***11***	*0*	0	*0*	0	*11*	17
Tajikistan	***6***	*1*	1	*0*	0	*5*	24
Tanzania	***6***	*1*	7	*0*	0	*5*	15
Uganda	***11***	*1*	6	*3*	5	*7*	15
Viet Nam	***15***	*3*	7	*0*	0	*12*	21
Zimbabwe	***6***	*1*	7	*0*	0	*5*	8
Total	***82***	***18** (22%)*	**49** (24%)	***4** (5%)*	9 (4%)	***60** (73%)*	147 (72%)

3.1.4 Storage and transportation conditions

The sample collectors were instructed to record the storage conditions at the sampling sites on the sample collection forms. The adherence to this requirement was very good, information on storage conditions was missing on only 2 of 205 forms (1%). An overview of the recorded storage conditions is presented in **Table 9**. Compliance with the storage conditions declared by manufacturers is discussed further below in relation to individual products, where relevant.

Table 9 Storage conditions at sampling sites, as recorded by collectors

Storage conditions	Number (%) of samples*	Temperature	Medicines concerned
Controlled	169 (83%)	2 – 8°C (9 samples)	Oxytocin
		15 – 25°C (94 samples)	All tested medicines, including 3 oxytocin samples
		25.6 – 28°C (4 samples)	Dexamethasone phosphate, mifepristone, levonorgestrel, oxytocin
		No information on temperature provided on the sampling form (62 samples)	All tested medicines except mifepristone, including 6 oxytocin samples
Not controlled	34 (17%)	In 11 cases the actual temperature as measured by collectors was 25 – 30°C	All tested medicines, including 3 oxytocin samples

* For two of the 205 samples no information on storage conditions was recorded on the sample collection form.

The storage instructions for shipment of samples from countries to the testing laboratories were to avoid freezing and to keep all samples at temperature below 25°C, except samples of oxytocin injection which were to be kept between 2°C and 8°C.

Only one incident was recorded: all but one ampoules of one sample of magnesium sulfate injection were broken when delivered to the laboratory, most probably because of freezing. However, sample collectors in the relevant country succeeded in re-sampling the same batch from the same sampling site and re-sending it without any damage. Thus the survey results were not influenced by the event.

As regards samples of oxytocin injection, only the samples from Nepal and Viet Nam were delivered to the testing laboratory at temperature between 2°C and 8°C (7°C for samples from Nepal, 2°C for the sample from Viet Nam). All other oxytocin injection samples were delivered at room temperature.

3.2 Registration status of sampled products

According to the information from national authorities in participating countries, 93% (190 of 205) of collected samples were from products with a valid registration by the national regulatory body, or products under re-registration; this was the case for all samples collected in Kenya, Madagascar, Nigeria, Tanzania and Viet Nam. In Burkina Faso, Nepal, Tajikistan, Uganda and Zimbabwe some collected samples were of unregistered products supplied centrally based on a global tender, as donations or on a special import permit.

All samples of amoxicillin, mifepristone and ceftriaxone were registered. For other medicines, there was always found at least one sample of an unregistered product.

Table 10 shows the numbers and proportions of samples of registered and unregistered products by country, together with the mechanism of placing unregistered products on the market and information on medicines concerned.

Table 10 Registration status of samples

Country	Total samples	Registered or under re-registration	Un-registered	Mechanism of placing of unregistered medicines on the market	Medicines concerned
Viet Nam	**28**	28	0	Not applicable	Not applicable
Tanzania	**22**	22	0		
Kenya	**19**	19	0		
Nigeria	**17**	17	0		
Madagascar	**15**	15	0		
Nepal	**25**	24	1	Global tender	Oxytocin
Tajikistan	**25**	24	1	Donation	Zinc sulfate
Uganda	**26**	24	2	Donation (1) Special import permit (1)	Oxytocin, magnesium sulfate
Burkina Faso	**13**	9	4	Global tender	Oxytocin, gentamicin (3 different products)
Zimbabwe	**15**	8	7	Donation (6), Special import permit (1)	Oxytocin, magnesium sulfate, gentamicin, procaine benzylpenicillin, ampicillin, dexamethasone phosphate, zinc sulfate
Total	**205**	**190** (93%)	**15** (7%)		

3.3 WHO prequalification status of sampled products

Only selected medicines of specific formulations are invited for WHO prequalification. Of the medicines included in the survey, the following were included in an invitation for expression of interest for prequalification at the time of this survey:

- Oxytocin injection 10IU, 1mL **[7]**;
- Magnesium sulfate injection 500mg/mL, in 2mL and 10mL ampoule **[7]**;
- Ceftriaxone injection 1g **[8]**;
- Dexamethasone injection 4mg/mL **[8]** ;
- Levonorgestrel tablets 0.75mg (pack of two); 1.5mg (pack of one) **[7]**; and
- Zinc sulfate dispersible tablets 10mg, 20mg; oral liquid 10mg per unit of dosage forms; tablets 10mg, 20mg. **[9]**

At the time of writing this report, no products containing oxytocin or magnesium sulfate were prequalified. WHO-prequalified products containing ceftriaxone, dexamethasone phosphate, levonorgestrel or zinc sulfate are listed in **Table 11**.

Table 11 WHO-prequalified products relevant to this quality survey

INN	Formulation and strength	Applicant	Manufacturing site	Packaging	Date of prequalification
Ceftriaxone	Powder for injection 500mg	Roche	Basel, Switzerland	Glass vials 5mL	29-May-2002
Ceftriaxone	Powder for injection 250mg	Roche	Basel, Switzerland	Glass vials 5mL	29-May-2002
Ceftriaxone (as sodium)	Powder for injection 1g	Egyptian International Pharmaceutical Industries Co (EIPICO)	Tenth of Ramadan City, Egypt	Glass vial 1g	16-May-2014
Ceftriaxone (as sodium)	Powder for injection 0.5g	Egyptian International Pharmaceutical Industries Co (EIPICO)	Tenth of Ramadan City, Egypt	Glass vial 0.5g	16-May-2014
Dexamethasone phosphate (as sodium salt)	Solution for injection 4mg/mL	Kern Pharma S.L.	Terrassa (Barcelona), Spain	Glass ampoule 1mL (3 or 100 ampoules per carton)	13-Aug-2014
Levonorgestrel	Tablets 750µg	Famy Care Ltd	Ahmedabad, Gujarat, India	PVC/PVDC/Alu blister 1x2	14-Jun-2013
Levonorgestrel	Tablets 1.5mg	Famy Care Ltd	Ahmedabad, Gujarat, India	Al/PVC/PVDC blister 1x1	21-Oct-2013
Levonorgestrel	Tablets 0.75mg	Gedeon Richter Plc	Budapest, Hungary	Al/PVC blister 1x2	20-Aug-2010
Levonorgestrel	Tablets 0.75mg	Cipla Ltd	Verna, Goa, India	Al/PVC/PE/PVDC blister 1x2	08-Apr-2014
Zinc (as sulfate monohydrate)	Dispersible tablets 20mg	Laboratoires Pharmaceutiques Rodael, France	Route de Socx, Bierne, France	Alu/PVDC/PVC blister 10x10	04-Dec-2012
Zinc (as sulfate monohydrate)	Dispersible tablets 20mg	Alkem Laboratories Ltd	Amaliya, Daman, India	Al/PVC/PVDC blister 1x10, 10x10	19-Feb-2014

Source: WHO prequalification list **[10],** as at 31 August 2014.

Of the 205 samples collected, 11 were from the following prequalified products:

- Levonorgestrel tablets 0.75mg, Cipla India – 2 samples (Madagascar, Nepal)
- Levonorgestrel tablets 0.75mg, Famy Care, India – 3 samples (Madagascar, Tanzania Zimbabwe);
- Levonorgestrel tablets 0.75mg, Gedeon Richter, Hungary – 3 samples (Tajikistan, Uganda); and
- Zinc sulfate dispersible tablets 20 mg, Laboratoires Pharmaceutiques Rodael, France – 3 samples (Tajikistan, Uganda, Zimbabwe).

WHO-prequalified samples accounted for 53% of all levonorgestrel-containing samples (8 of 15) and 14% of all zinc-containing samples (3 of 22) tested in this survey.

No samples of prequalified products containing ceftriaxone or dexamethasone phosphate were collected.

3.4 Compliance with specifications

3.4.1 Overview of results

Number of samples tested with conclusive results

The expiry dates of the samples collected in this survey ranged from January 2014 to January 2018 (sample collection took place in September – November 2013). All samples were within their shelf life at the time of collection and testing.

Conclusive results were obtained for all except one of the total of 205 samples tested. For one sample of zinc sulfate effervescent tablets the assay results were inconclusive because the analytical method was not suitable for effervescent tablets due to interference of some excipients. As the survey focused on zinc sulfate dispersible tablets, no specific analytical method suitable for effervescent tablets was developed, and this sample was excluded from the evaluation of survey results.

Overall rate of compliance with specifications

Of a total of 204 samples evaluated, 157 (77%) complied with the specifications set for this survey. The outcomes of laboratory testing are summarized in **Table 12**. The remaining 47 samples were non-compliant. This represented 40 different products for which at least one sample did not comply with specifications, i.e. 27% of 149 evaluated products.

No failures were found for procaine benzylpenicillin injection, amoxicillin dispersible tablets, zinc tablets, zinc syrup and mifepristone tablets. The highest proportion of non-compliant samples was for oxytocin injection (64%), and relatively high failure rates were also recorded for gentamicin injection (41%), ampicillin injection (35%) and dexamethasone phosphate injection (32%). A substantially lower proportion of non-compliant samples was found for levonorgestrel tablets (14%), magnesium sulfate injection (11%) and ceftriaxone injection (7%). Detailed results for individual medicines are provided in Section 3.4.2.

Rates of compliance in countries

At least one non-compliant sample was found in each of the participating countries. The proportion of non-compliant samples was lowest in Zimbabwe (7%, 1 of 15 samples). It ranged from 14 to 20% in Tanzania, Tajikistan, Uganda, Nepal), and from 29 to 35% in Viet Nam, Burkina Faso, Kenya, Madagascar and Nigeria (**Table 12**). Bearing in mind that the numbers of collected samples varied in individual countries and were generally quite low, these percentages should not be considered as representative of the failure rates in the different countries.

Table 12 Breakdown of testing outcomes for each medicine by country

Country / Medicine*	Burkina Faso	Kenya	Madagascar	Nepal	Nigeria	Tajikistan	Tanzania	Uganda	Viet Nam	Zimbabwe	Overall failure rate per medicine
	Number of non-compliant samples / Number of collected samples										
Oxytocin injection	1 / 2	1 / 1	1 / 1	3 / 3	2 / 3	1 / 3	2 / 3	3 / 3	0 / 1	0 / 2	**14 / 22 (64%)**
Magnesium sulfate injection	1 / 1	0 / 2	0 / 3	0 / 3	0 / 3	0 / 3	0 / 2	0 / 1	1 / 3	0 / 1	**2 / 19 (11%)**
Gentamicin injection	1 / 3	1 / 3	2 / 2	1 / 2	1 / 3	0 / 3	1 / 4	1 / 3	3 / 3	1 / 2	**12 / 29 (41%)**
Procaine benzyl-penicillin injection	0 / 1	NC	0 / 2	NC	NC	NC	0 / 1	0 / 1	NC	0 / 1	**0 / 6 (0%)**
Ampicillin injection	1 / 3	1 / 2	1 / 3	0 / 3	1 / 1	2 / 3	0 / 2	1 / 3	2 / 3	0 / 3	**9 / 26 (35%)**
Ceftriaxone injection	0 / 3	1 / 4	0 / 3	0 / 3	1 / 3	0 / 3	0 / 3	0 / 3	0 / 3	0 / 2	**2 / 30 (7%)**
Dexamethasone phosphate injection	NC	1 / 1	1 / 2	1 / 3	1 / 2	1 / 3	0 / 2	0 / 2	1 / 3	0 / 1	**6 / 19 (32%)**
Amoxicillin dispersible tablet	NC	NC	NC	0 / 2	NC	0 / 3	NC	0 / 4	NC	NC	**0 / 10 (0%)**
Zinc containing products	NC	0 / 3	NC	0 / 3	0 / 2	0 / 2	0 / 4	0 / 3	0 / 2	0 / 2	**0 / 21 (0%)**
Levonorgestrel tablet	NC	1 / 3	0 / 2	0 / 2	NC	0 / 1	0 / 1	0 / 2	1 / 2	0 / 1	**2 / 14 (14%)**
Mifepristone tablet	NC	NC	NC	NC	NC	NC	NC	NC	0 / 8	NC	**0 / 8 (0%)**
Total failure rate per country	**4 / 13 (31%)**	**6 / 19 (32%)**	**5 / 15 (33%)**	**5 / 25 (20%)**	**6 / 17 (35%)**	**4 / 25 (16%)**	**3 / 22 (14%)**	**5 / 26 (19%)**	**8 / 28 (29%)**	**1 / 15 (7%)**	**47 / 204 (23%)**

NC Not collected
* The table does not differentiate between different strengths and dosage forms.

Locally manufactured versus imported products

The failure rates for locally manufactured and imported samples were similar, amounting to 18% (7 of 39 locally manufactured samples) and 24% (40 of 165 imported samples) respectively. No comparison could be made at individual country level due to the different proportions of locally manufactured and imported medicines sampled (see Section 3.1.2).

In summary, all samples of domestically produced amoxicillin dispersible tablets – collected in Nepal and Uganda – and all samples of domestically produced zinc-containing products – collected in Kenya, Nepal, Nigeria, Tanzania, Viet Nam and Zimbabwe – complied fully with the specifications set for this survey. There were also no failures found for locally produced ceftriaxone or mifepristone samples, all collected in Viet Nam.

The seven samples that did not comply were all from Viet Nam, where 24 of the 39 locally manufactured samples were collected. They included one sample each of magnesium sulfate injection, levonorgestrel tablets and dexamethasone injection, and two samples each of gentamicin injection and ampicillin injection.

Registered versus unregistered products

Thirteen of the 15 samples of unregistered products (corresponding to 14 products), which were supplied in line with specific national regulations, complied with specifications; two oxytocin injection samples did not. The two samples were produced by different manufacturers, one sample was imported to Burkina Faso and the other to Nepal.

For registered products, 144 of 189 evaluated samples complied with specifications while 45 were non-compliant. At least one non-compliant registered sample was collected in each of the 10 participating countries.

WHO-prequalified products

All 11 samples of WHO-prequalified products fully complied with specifications.

Outcomes of specific tests

Table 13 shows the numbers of samples that failed specific quality tests. No failures were found for procaine benzylpenicillin injection, amoxicillin dispersible tablets, zinc-containing tablets and syrup and mifepristone tablets; these medicines are therefore not shown in the table.

Table 13 Number of samples which failed specific quality tests

	Oxytocin injection	Magnesium sulfate injection	Gentamicin injection	Ampicillin injection	Ceftriaxone injection	Dexamethasone phosphate injection	Levonorgestrel tablets
Total samples tested	22	19	29	26	30	19	14
Non-compliant samples	**14**	**2**	**12**	**9**	**2**	**6**	**2**
Overall failure rate	64%	11%	41%	35%	7%	32%	14%
Number of samples failed in:							
Visible particles	3	0	0	n.p.	n.p.	0	n.a.
Assay	8	0	**6**	3	**2**	**5**	0
Related substances	**14**	n.a.	n.a.	**8**	0	n.a.	0
pH	0	**2**	2	0	0	0	n.a.
Extractable volume	0	n.p.	n.p.	n.a.	n.a.	0	n.a.
Uniformity of mass	n.a.	n.a.	n.a.	1	0	n.a.	n.a.
Water content	n.a.	n.a.	n.a.	0	0	n.a.	n.a.
Composition of gentamicin	n.a.	n.a.	4	n.a.	n.a.	n.a.	n.a.
Free dexamethasone	n.a.	n.a.	n.a.	n.a.	n.a.	3	n.a.
Dissolution	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	**2**
Content uniformity	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	1

Notes: Some samples failed more than one test.
Cells shaded green indicate the most frequently failed test for each medicine.
Cells shaded grey indicate the tests that were not applicable according to the specification used in the survey (n.a.) or that were not performed (n.p.) for the respective medicine.

3.4.2 Results for individual medicines

Details and tests results of the samples for medicine tested are listed in Appendices 3-13. Within each appendix, the samples are sorted according to the countries in which they were collected. The results for each of the medicines included in the survey are presented below.

3.4.2.1 Oxytocin injection (Appendix 3)

Twenty-two samples (22 batches) of oxytocin injection produced by 15 manufacturers were tested for appearance, identity, assay, related substances, pH value, and extractable volume according to the Ph. Int. monograph. Ten collected samples were of the strength 10IU/mL and 12 of the strength 5IU/mL, all contained 1 mL of solution in ampoules.

Eight samples (36% of collected samples) produced by four manufacturers fully complied with the specifications. Fourteen samples (64%) from another 11 manufacturers failed one or more test.

There were three manufacturers from which several oxytocin samples were collected. From one manufacturer five samples were collected and all complied. From the second manufacturer there were two samples collected, and one complied while the other did not. From the third manufacturer two samples were collected and both failed.

Markedly substandard sample

One sample – the only oxytocin sample from that particular manufacturer – was found to be substantially sub-standard. This sample, which came from one collection site and was identified by a single batch number, was visibly non-homogenous and contained five different types of ampoules (see **Figure 2**). In 26 of 40 ampoules collected for this sample visible particles were observed. One type of ampoules did not contain any oxytocin. In the other four types of ampoules varying amounts of oxytocin (31.0 – 68.7%) and related substances (up to 16 peaks >2% and 12 peaks >5%) were found. Because of the extreme non-homogeneity this sample was not considered in the further evaluation of assay results and related substances test shown in the remainder of this section.

Figure 2 Appearance of different types of ampoules collected for one oxytocin injection sample at one collection site and identified by the same batch number

Content and related substances

Assay and related substances test results were evaluated for 13 non-compliant samples of oxytocin injection from a total of 10 different manufacturers.

Oxytocin was identified in all 13 samples. In seven samples (6 manufacturers) the content of oxytocin was found below the acceptance limit of 90.0%. The two lowest values were 52.0% and 78.6% of the labelled amount, the other five ranged between 85.2% and 89.8%. All seven samples also contained related substances above the acceptance limits. Visible particles were found in one of these samples.

In the remaining six samples (6 manufacturers) the oxytocin content was within the acceptance limits; however, related substances were found above the acceptance limits. In one of these samples also visible particles were recorded.

To illustrate the differences in related substances, **Figures 3 and 4** show the examples of HPLC chromatograms of a sample in which no related substances were detected and another with a high amount of related substances.

Figure 3 HPLC chromatogram of a oxytocin injection sample with no related substances detected

(The product does not contain a preservative.)

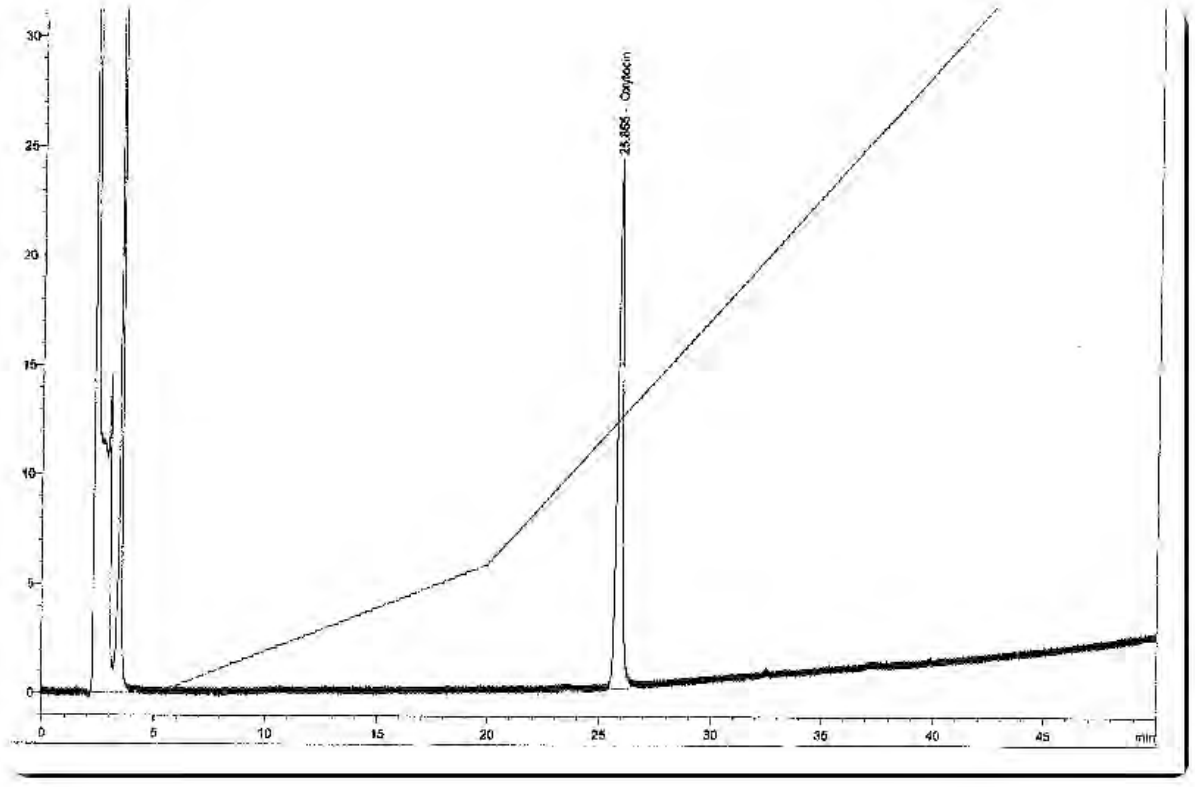
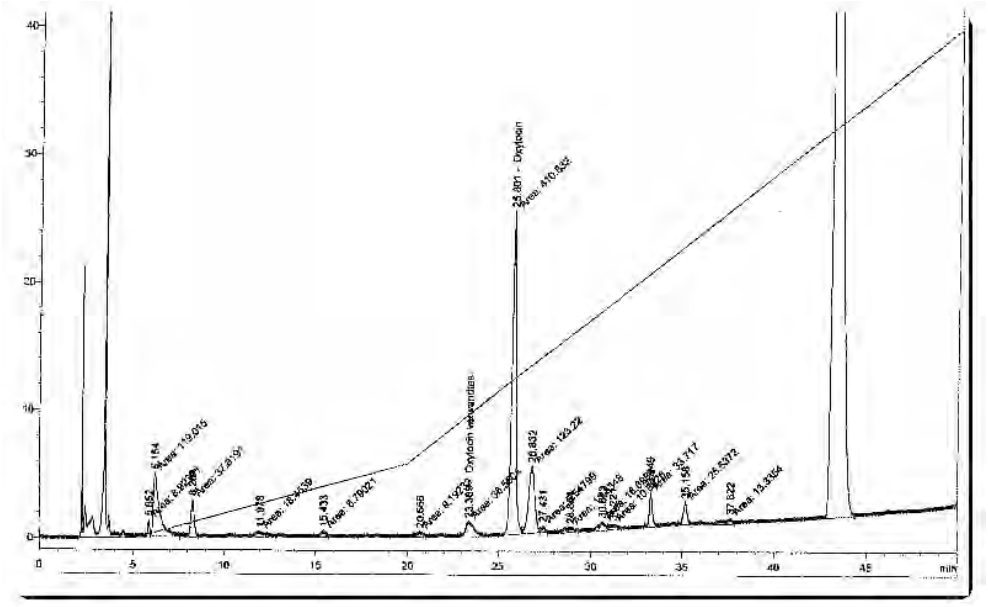


Figure 4 HPLC chromatogram of an oxytocin injection sample with a high amount of related substances detected

(The product contains chlorobutanol, retention time around 43 minutes)



According to the Ph. Int. monograph for oxytocin injection **[11]** the content of related substances was evaluated by comparison of the area of individual peaks with the area of oxytocin peak in the diluted injection solution. Any peak with a retention time corresponding to the peak of chlorobutanol – which may be present in some formulations as a preservative – was excluded. For one sample containing phenol as a preservative, the phenol peak was excluded. The numbers of related substances peaks above 2% and above 5% were assessed against the acceptance limits of "not more than one peak above 2% and no peak above 5%". Numbers of related substance peaks above these limits found in individual samples are shown in Appendix 3.

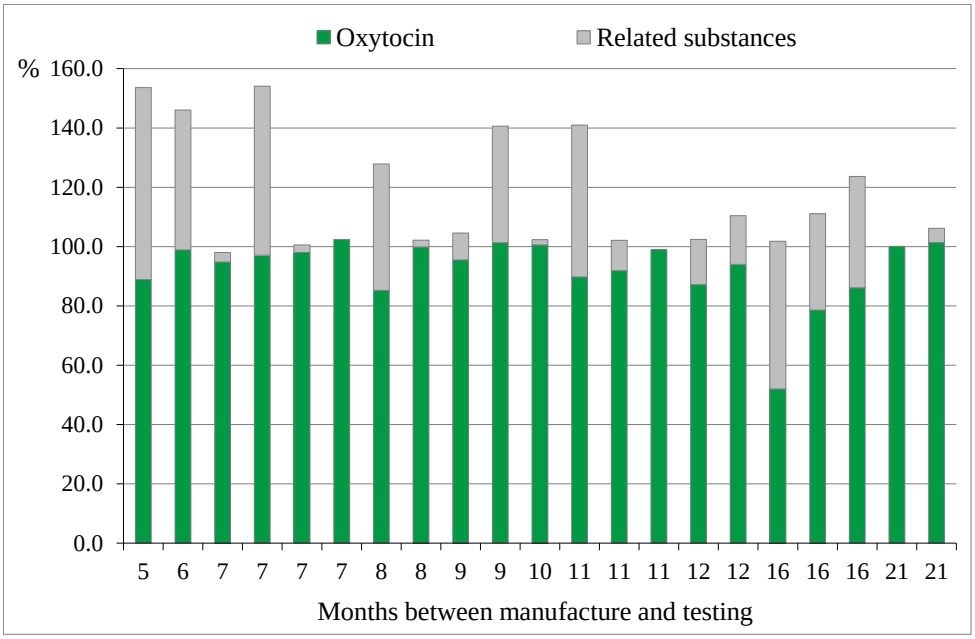
To obtain an indicative picture of the amount of related substances, and to hypothesize to which extent the related substances can be degradation products, the areas of related substances peaks were summed up and presented together with the content of oxytocin as a proportion of the declared content of oxytocin. The results were plotted for individual samples against time elapsed between manufacture and testing (see **Figure 5**).

In all eight samples which fully complied with specifications, the sum of oxytocin and related substances contents gave results very close to 100% (98.0 – 106.2%).

Of 13 samples with a higher related substances content, seven had a sum of oxytocin and related substances contents substantially over 100% (123.6 – 154.1%). Among these seven samples, four had an oxytocin content below the acceptance limit of 90.0%, while three complied with specifications. For the remaining six samples the sum of oxytocin and related substances contents were close to 100% of the labelled amount; three of these samples failed in oxytocin content, three complied).

The data do not show a clear relation between the content of oxytocin or the sum of oxytocin and related substances and time passed from manufacture to testing date.

Figure 5 Content of oxytocin and related substances in individual samples presented as a percentage of the declared oxytocin content against time elapsed between manufacture and testing



Origin of oxytocin

Definitions of oxytocin and labelling requirements differ between pharmacopoeias. The Ph. Int., Ph. Eur. and BP define oxytocin as "a synthetic cyclic nonapeptide having the structure of the hormone produced by the posterior lobe of the pituitary gland that stimulates contraction of the uterus and milk ejection in receptive mammals". There is no labelling requirement with respect to the origin.

The USP defines oxytocin as "a nonapeptide hormone having the property of causing the contraction of uterine smooth muscle and of the myoepithelial cells within the mammary gland. It is prepared by synthesis." The monograph for oxytocin injection requires that the product label states the animal source if naturally derived, or states that it is synthetic.

Substantial numbers of samples produced by Chinese, Indian and Vietnamese manufacturers were collected in the survey. Therefore the definitions and requirements of the Chinese Pharmacopoeia 2010 (CPh), Indian Pharmacopoeia 2014 (IP) and Vietnamese Pharmacopoeia IV (VP) are also provided here for comparison. The IP defines oxytocin as "a cyclic nonapeptide hormone obtained by a process of fractionation from the posterior lobe of the pituitary gland of healthy oxen or other mammals or by synthesis that has the property of stimulating contraction of the uterus and milk ejection in receptive animals." The monograph for oxytocin injection requires that the product label states either the animal species from which it is obtained or whether it is synthetic. The monograph for oxytocin injection of CPh defines oxytocin as "obtained from posterior of pork or cattle or prepared by synthesis" and does not contain any requirement for information on the product label. There is no oxytocin monograph in VP.

Labels of collected samples were examined for the information on the oxytocin origin. It was found that 21 of 22 samples referred to a synthetic origin (either explicitly stated or by reference to BP quality of oxytocin). For one sample from a Chinese manufacturer no information regarding the origin of oxytocin was provided on the label.

Presence of preservatives

It was noted from the label information as well as from the chromatograms obtained in the HPLC assay and related substances tests that in some samples a preservative was present. **Table 14** combines information on preservatives on the label and findings from testing. The substantially substandard sample containing five different ampoule types of different content was not included in this overview.

There were six samples with no preservative stated on the label and no corresponding peak detected, and seven samples with declared and detected preservatives.

In two samples chlorobutanol was detected but not stated on the label. In six samples a small peak with the retention time of chlorobutanol was detected. Five of them did not have any preservatives stated on the label and the small peaks may be indicative of related substances. The sixth sample had chlorobutanol stated as a preservative, but the respective peak was much smaller than in other samples stating the presence of chlorobutanol on their labels.

Table 14 Presence of preservatives in collected oxytocin injection samples

	No preservatives detected	Phenol detected	Chlorobutanol detected	Only small peak with the retention time of chlorobutanol detected
No preservatives stated on the label	**6 samples from 2 manufacturers**	-	2 samples from 2 manufacturers	5 samples from 3 manufacturers
Presence of phenol stated on the label	-	**1 sample**	-	-
Presence of chlorobutanol stated on the label	-	-	**6 samples from 5 manufacturers**	1 sample

Storage conditions

Most of the labels of collected samples contained instructions to protect the product from light and to avoid freezing. However, the manufacturers' instructions on storage temperature differed. They are shown in **Table 15** together with the information on the product shelf-life.

Table 15 Storage temperature declared by manufacturers of collected oxytocin injection samples and the shelf-life[7]

Storage temperature declared by manufacturers	Number of manufacturers	Shelf-life
2 – 8 °C	3	1x 2 years; 2x 3 years
2 – 15 °C	1	3 years
8 – 20 °C	1	3 years
8 – 25 °C	1	2 years
Below 25 °C	3	2x 2 years; 1x 3 years
Not exceeding 30 °C	2	1x 2 years; 1x 3 years
Store in a cool place	3	1x 2 years; 2x 3 years
Do not freeze (no other instruction on temperature given on the label)	1	2 years

Table 16 compares the storage temperatures at the collection sites with the temperature declared by manufacturers, as well as testing outcomes of the samples collected in these sites. The substantially substandard sample containing five different ampoule types of different content, which was collected in the site where temperature was not controlled and the manufacturer's storage instruction was only "Do not freeze", was not included in this table.

Table 16 Oxytocin injection samples – storage conditions and outcomes of testing for collected samples

Temperature at collection sites as recorded by collectors	Storage temperature requested by manufacturers (number of samples)	Number of compliant samples	Number of non-compliant samples	Tests failed
2 – 8°C	2 – 8°C	4		
	Below 25°C	1		
	2 – 8°C		2	Assay and related substances
	2 – 8°C		1	Related substances only
	Cold place		1	Assay and related substances
17.6 – 24°C	Cold place		1	Related substances only
	Below 25°C		1	Assay and related substances
	Below 30°C		1	Related substances only
25.6°C	Below 25°C		1	Assay and related substances
Controlled (No temperature information recorded)	2 – 8°C	1		
	2 – 15°C	1		
	8 – 20°C	1		
	8 – 25°C		1	Related substances only
	8 – 25°C		1	Assay and related substances
	Below 25°C		1	Related substances only
Not controlled	Not exceeding 30°C		1	Related substances only
	Cold place		1	Assay and related substances
Total	`	**8**	**13**	

[7] As only few package leaflets specified the shelf-life, it was derived from dates of manufacture and expiry of collected products.

3.4.2.2 Magnesium sulfate injection (Appendix 4)

Nineteen samples (17 batches) of magnesium sulfate injection produced by 14 manufacturers were tested for appearance, identity, assay, and pH value according to the Ph. Int. monograph. Thirteen collected samples were of the strength 500mg/mL and contained 10mL (10 samples) or 2mL (3 samples) of solution in ampoules. Three samples were of the strength 250mg/mL and contained 10mL (2 samples) or 5mL (1 sample) of solution in ampoules. Three samples were of the strength 150mg/mL and contained 10mL of solution in ampoules.

Magnesium sulfate injection is defined in the Ph. Int., BP, USP, IP and CPh as a sterile solution of magnesium sulfate heptahydrate, and the labelled amount corresponds to this compound. The VP does not contain a monograph for magnesium sulfate injection but the magnesium sulfate substance is also defined as heptahydrate. The Ph. Int. provides in addition the information on the strength in the current WHO Model List of Essential Medicines, which is 500mg of magnesium sulfate heptahydrate per mL, corresponding to the concentration of magnesium ions approx. 2 mmol Mg^{2+}/mL. The WHO Model List of Essential Medicines **[4]** includes magnesium sulfate injection and does not mention that it is in the form of heptahydrate.

The information on labels of collected samples differed:

- Labels of 8 samples clearly declared the amount of magnesium sulfate heptahydrate;
- Labels of 2 samples stated the amount of magnesium sulfate and the concentration of magnesium ions in mmol/mL (which clarified that it was in heptahydrate form);
- Labels of 5 samples stated the amount of magnesium sulfate and referred to BP or IP (which meant that it was heptahydrate form); and
- Labels of 4 samples (including two produced in Viet Nam) stated only the amount of magnesium sulfate.

The assay results for all samples were calculated as the amount of magnesium sulfate heptahydrate, and as there were no deviations from specifications it was concluded that all samples contained magnesium sulfate heptahydrate.

Sixteen samples (14 batches, 13 manufacturers) fully complied with the specifications. One sample could not be tested for pH value due to insufficient amount of sample. However, two other batches from the same manufacturer complied in pH value and there was no reason to expect non-compliance of this batch; it was therefore also considered compliant. Two samples (2 batches, 2 manufacturers), i.e. 11% did not comply in pH value, the values of 7.2 and 7.3 were above the acceptance limit of 5.5 – 7.0. The results of other tests complied with specifications.

There were four manufacturers from which several magnesium sulfate samples were collected. One manufacturer had three compliant samples included in this survey, two had two compliant samples, and one manufacturer had one compliant and one non-compliant sample.

3.4.2.3 Gentamicin injection (Appendix 5)

Twenty-nine samples (29 batches) of gentamicin injection produced by 23 manufacturers were tested for appearance, identity, assay, composition of gentamicin, and pH value according to the BP monograph. Twenty-seven collected samples were of the strength 40mg/mL, for 26 of them the ampoules contained 2mL and were labelled 80mg/2mL, one sample contained 1mL in ampoules and was labelled 40mg/1mL. Two remaining samples were of lower strength and contained 20mg/2mL. In line with pharmacopoeias, the strength was expressed as the amount of gentamicin, and each injection solution contained gentamicin sulfate.

In all collected samples gentamicin was identified. Seventeen samples (59%) produced by 15 manufacturers complied with the specifications. Twelve samples (41%) produced by 11 manufacturers did not comply either in the assay or the gentamicin composition test, or in pH value. Each of these non-compliant samples failed one test only.

There were four manufacturers from which several gentamicin samples were collected. From one manufacturer four samples were collected and two complied while two did not. From three manufacturers two samples were collected; for one manufacturer both samples complied, for two manufacturers one sample failed and one complied.

Content of gentamicin

The microbiological assay according to the BP monograph was performed to determine the content of gentamicin. Results of 22 samples were found within the acceptable limits, results for one sample were just around the lower limit with an indicative average of 95.3%. As BP has the strictest limits compared to other pharmacopoeias (see 4.10) this sample was considered compliant.

Six of 29 samples (representing 6 batches and 6 manufacturers) gave a non-compliant result; they were retested twice and the non-compliance was confirmed. The BP evaluation of results using fiducial limits is quite complex, and simple average contents from three tests were therefore counted for these six samples to provide an indicative picture. For five samples the indicative results obtained were below 97.0% (87.8 – 95.3%), for one sample above 110.0% (114.1%).

Composition of gentamicin

The HPLC method according to the BP monograph was performed to determine the percentage content of gentamicin components C_1, C_{1a}, C_2 and C_{2a} with the following acceptance limits:

- C_1: 25.0 – 50.0%;
- C_{1a}: 10.0 – 35.0%; and
- $C_2 + C_{2a}$: 25.0 – 55.0%.

Of the 29 samples, four (representing 4 batches, 4 manufacturers) were found non-compliant with this test. For all four the content of the component C_1 was found to be below the acceptance limit (results in the range 23.8 – 24.8%); one also deviated in the content of the component C_{1a}, which was 35.5%.

There were two noticeable groups of samples that had different chromatographic profiles in this test. **Figure 6** shows the pattern of a chromatogram observed with samples from eight manufacturers. This pattern corresponded to the chromatogram obtained with the reference substance Gentamicin BPCRS.

Figure 6 Typical HPLC chromatogram obtained with gentamicin injection samples of 8 manufacturers and reference substance Gentamicin BPCRS

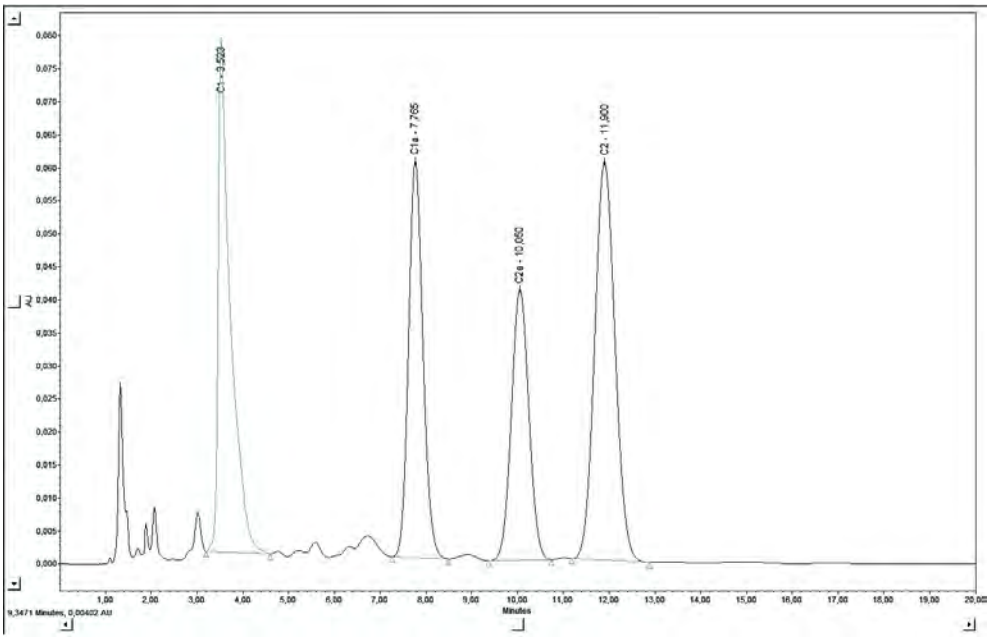
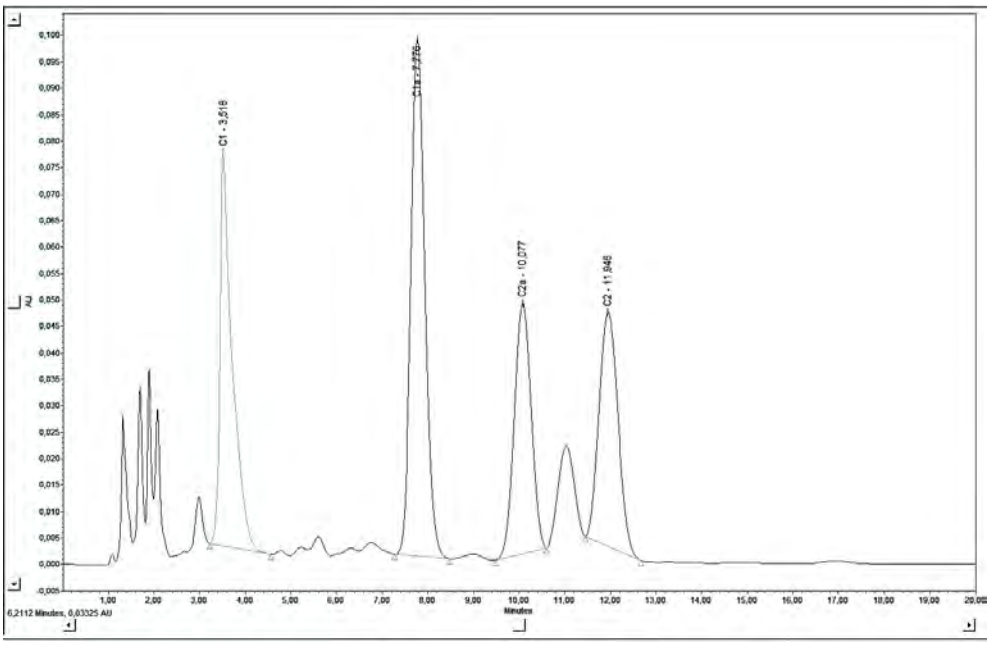


Figure 7 shows an example of chromatogram typical for samples from 15 other manufacturers. There was an additional peak observed between the components C_{2a} and C_2, which is not mentioned in the BP monograph but did not interfere with evaluation of compliance with this test. The peak was therefore not further identified or evaluated.

Figure 7 Typical HPLC chromatogram obtained with gentamicin injection samples of 15 other manufacturers



pH

Two samples of 29 (representing 2 batches from 2 manufacturers) did not comply in pH value. In both samples pH value was 5.6, i.e. just above the acceptance limit of 3.0 – 5.5.

3.4.2.4 Procaine benzylpenicillin injection (Appendix 6)

Six samples (6 batches, 3 manufacturers) of procaine benzylpenicillin powder for injection were tested for appearance, identity, contents of benzylpenicillin and procaine, related substances, and uniformity of mass according to the BP (Veterinary) monograph for procaine benzylpenicillin injection in suspension form. This monograph was chosen because it included a HPLC method for assay and related substances test, while the Ph. Int. monograph used UV spectrophotometry and the USP monograph used iodometric titration for assay of penicillins. Other than the BP veterinary monograph no pharmacopoeia included the related substances test. The BP monograph applied to the suspension dosage form, while the collected samples were in the form of powder for injection. Therefore tests for water content and pH value according to the USP monograph for penicillin G procaine for injectable suspension were added in the testing protocol for this medicine.

Three collected samples (3 batches, 3 manufacturers) contained procaine benzylpenicillin in the strength 1 MIU (2 samples) and 3 MIU (1 sample). The remaining three samples (3 batches, 2 manufacturers) contained the combination of procaine benzylpenicillin 3 MIU and benzylpenicillin sodium 1 MIU (Fortified Procaine Penicillin). All samples were tested using the method described in the BP monograph. Samples of Fortified Procaine Penicillin could not be evaluated according to the specifications in this monograph due to the difference in composition. A monograph for the combination of procaine benzylpenicillin and benzylpenicillin sodium could not be found in any of the pharmacopoeias used for this survey (Ph. Int., BP, USP). However, it was found in the Chinese Pharmacopoeia and as the three samples were produced by Chinese manufacturers, the CPh monograph specifications were used for their evaluation.

In all six collected samples procaine benzylpenicillin was identified, and all complied with the respective specifications.

Three of six samples were produced by the same manufacturer, and two samples were produced by another manufacturer; the third manufacturer had a single sample included in the survey.

3.4.2.5 Ampicillin injection (Appendix 7)

Twenty-six samples (26 batches) of ampicillin powder for injection produced by a total of 17 manufacturers were tested for appearance, identity, assay, related substances, pH value, water content, and uniformity of mass according to the BP monograph. Twelve samples were of the strength 1g/vial, 12 of the strength 500mg/vial and two of the strength 250mg/vial. Samples contained ampicillin sodium and their strength was expressed as the amount of ampicillin in line with pharmacopoeias.

Ampicillin was identified in all collected samples. Fourteen samples produced by 12 manufacturers fully complied with the specifications. For three samples from two manufacturers it was not possible to complete the uniformity of mass test due to insufficient number of vials. For these samples, 18 or 19 vials were tested (instead of 20 vials). All tested vials deviated from the respective average mass by less than 5% (acceptance limits: minimum 18 vials should be within ± 10% and maximum 2 within ± 20% from the average mass). In addition, samples of other batches from these manufacturers were collected and fully complied. Therefore, 17 samples, i.e. 65% of collected samples were considered compliant.

Nine samples (35%) produced by seven manufacturers did not comply in the assay and/or the related substances test and/or the uniformity of mass test.

There were five manufacturers from which several ampicillin samples were collected. From one manufacturer four samples were collected and two complied while two did not. From two

manufacturers three samples were collected; for one manufacturer all samples complied, for the other two samples failed and one complied. From two manufacturers two samples were collected and all complied.

Content and related substances

The results of the assay and related substances test were evaluated for nine non-compliant samples. In three samples (3 batches, 3 manufacturers) the content of ampicillin was found to be below the acceptance limit of 95.0%; the contents were 93.3%, 93.9% and 94.3% of the labelled amount. In two of these three samples the results of the test for related substances also did not comply with the specifications due to one secondary peak in each sample that was above the acceptance limit of 2% (3.6% and 3.1%).

In six samples (6 batches, 5 manufacturers), the ampicillin content was within the acceptance limits. However, the results of the test for related substances did not comply with the limits of the BP monograph (maximum 4.5% for a peak corresponding to ampicillin dimer and 2% for any secondary peak). In two samples (2 manufacturers) ampicillin dimer was found to be above the limit (4.7% in each). Both these samples contained also one secondary peak above the acceptance limit of 2% (2.6% and 5.3%) and one of them also failed the test for uniformity of mass – one vial was out of the acceptance limit. In the four remaining samples (3 manufacturers) one secondary peak was found above the acceptance limit of 2% (ranging from 2.2% to 4.0%).

In all eight samples that failed the related substances test, the secondary peak found above the acceptance limit of 2% eluted at the same relative retention time (approx. 3.36). To illustrate results of the test for related substances in ampicillin injection samples, **Figures 8 and 9** show example HPLC chromatograms of a compliant sample and a sample with peaks of ampicillin dimer and a secondary peak above the limits.

Figure 8 Example of HPLC chromatogram of an ampicillin sample compliant with specifications

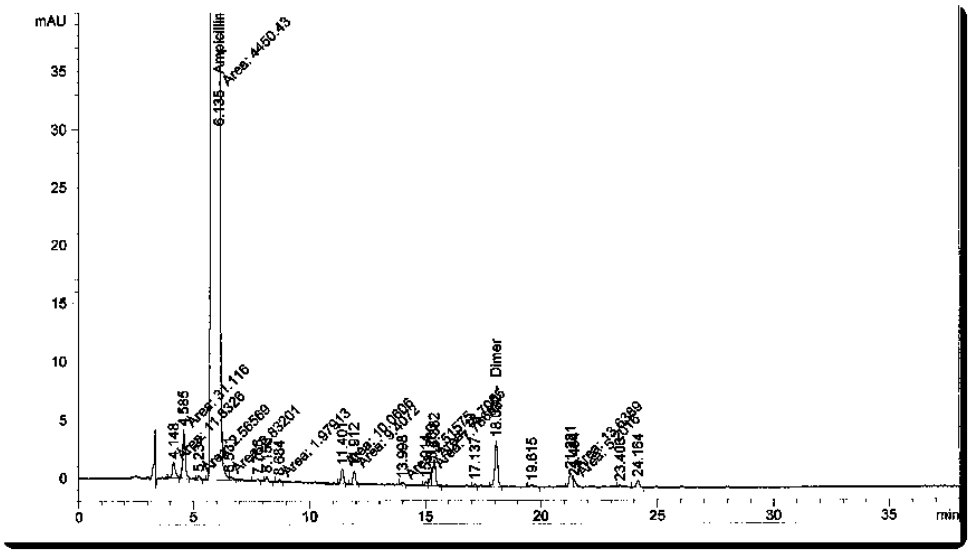
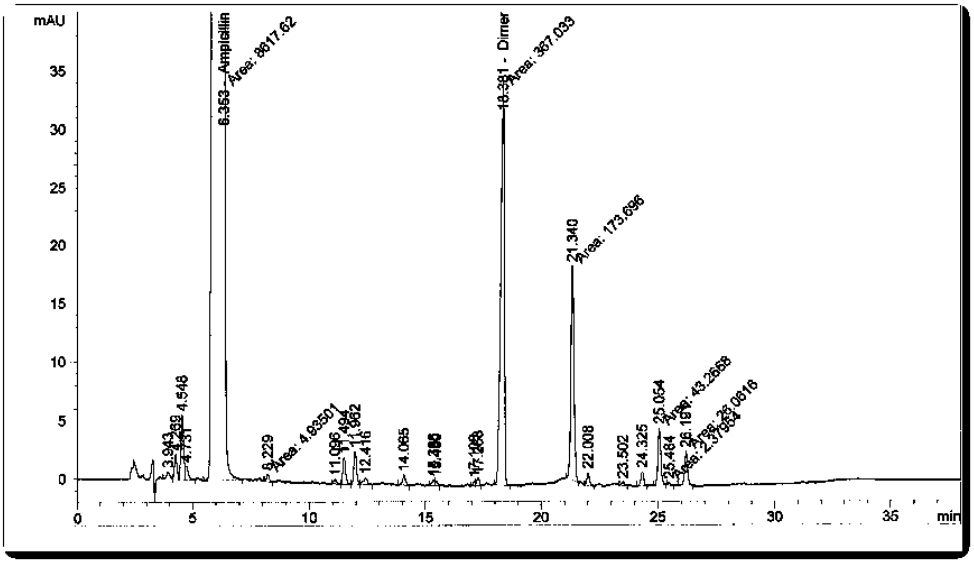


Figure 9 Example of HPLC chromatogram of an ampicillin sample with peaks of ampicillin dimer and a secondary peak above the limits



Most of the labels of collected samples contained the instruction to store the product in a cold and dry place, in some cases protection from light was recommended or the temperature below 25°C or 30°C was specified. Nineteen samples were stored at the collection sites at controlled temperatures (for six of them the temperature was not recorded on the sample collection form, 13 were stored at 17.6 – 25°C). Seven samples were stored at the site without temperature control (in four of them sample collectors recorded an actual temperature of 25 – 29°C). Only one of these seven samples failed the test for related substances although it passed the assay, the other six samples fully complied with specifications.

3.4.2.6 Ceftriaxone injection (Appendix 8)

Thirty samples (each from a different batch) of ceftriaxone powder for injection produced by 24 manufacturers were tested for appearance, identity, assay, related substances, pH value, water content and uniformity of mass according to the BP monograph. The strength of 26 samples was 1g/vial, two were of the strength 500mg/vial and two of the strength 250mg/vial. Samples contained ceftriaxone sodium and their strength was expressed as the amount of ceftriaxone in line with pharmacopoeias.

In all collected samples ceftriaxone was identified. Twenty-eight samples (93%) produced by 24 manufacturers fully complied with the specifications. Two samples (7%) produced by two manufacturers failed the assay. In these samples the content of ceftriaxone was found to be below the acceptance limit of 92.0%; namely 90.7% and 91.2% of the labelled amount. The results of the other tests, including the related substances test, complied with specifications.

There were four manufacturers from which several ceftriaxone samples were collected. From two manufacturers three samples were collected; for one manufacturer all samples complied, for the other manufacturer one sample failed and two complied. From two other manufacturers two samples were collected; for one manufacturer both samples complied, while for the other one sample complied and one failed.

It was noted that for the two manufacturers that had non-compliant ceftriaxone samples in this survey, some samples of other medicines were found compliant in this survey.

3.4.2.7 Dexamethasone phosphate injection (Appendix 9)

Nineteen samples (each from different batches) of dexamethasone phosphate injection produced by 14 manufacturers were tested for appearance, identity, assay, free dexamethasone, pH value and extractable volume according to the BP monograph. All samples were of the strength 4mg/mL and contained 1 mL or 2 mL of solution in ampoules.

The WHO Model List of Essential Medicines **[4]** includes dexamethasone injection and defines it as an injection containing 4mg/mL dexamethasone phosphate (as disodium salt). Similarly, pharmacopoeias express the strength of this medicine as the amount of dexamethasone phosphate which is present in the form of dexamethasone phosphate sodium salt.

While the information about the strength on labels was clear for 14 samples, it was not precise for five samples:

- the labels of 3 samples declared that each mL contains 4mg of dexamethasone sodium phosphate;
- the label of 1 sample declared that each mL contains dexamethasone sodium phosphate equivalent to 4mg dexamethasone; and
- the label of 1 sample declared that each ampoule contains 4mg of dexamethasone.

In line with pharmacopoeias, the assay results for all samples were calculated on the basis of the amount of dexamethasone phosphate.

In all collected samples dexamethasone phosphate was identified. Thirteen samples (68%) produced by 10 manufacturers complied with the specifications. Six samples (32%) produced by five manufacturers did not comply in the assay and/or the test for free dexamethasone.

There were two manufacturers from whom three samples were collected; for one manufacturer all samples complied, for the other manufacturer one sample complied and two failed. From a third manufacturer two samples were collected and both complied.

Content of dexamethasone phosphate and free dexamethasone

The content of dexamethasone phosphate was found to be within acceptable limits for twelve samples. Results for one sample were just around the upper limit of 105.0% (average 105.1%). As the BP has stricter limits than some other pharmacopoeias (see 4.10) this sample was considered compliant.

In five samples (4 manufacturers) the content of dexamethasone phosphate was found below the acceptance limit of 95.0%; the findings were in the range 64.4% – 92.8% of the labelled amount.

In two of the five samples with a low dexamethasone phosphate content, the content of free dexamethasone was found above the acceptance limit of 0.5% (1.2% for the sample with 82.1% of dexamethasone phosphate and 0.7% for the sample with 92.8%). Free dexamethasone was not detected in three other samples with a low content of dexamethasone phosphate.

One sample failed only in the test for free dexamethasone. In this sample 0.8% of free dexamethasone was found, while it contained 104.8% of dexamethasone phosphate.

As regards storage conditions, most manufacturers' instructions required to store the product in a cool, dry place, protected from light, while some specified temperature below 25°C or below 30°C. **Table 17** shows the storage conditions at the sampling sites, testing results, and storage instructions as declared on the product packaging where available, for the six samples that failed any of the tests.

Table 17 Storage conditions at the sites where non-compliant samples were collected and results found

Sample code	Storage conditions at sampling sites	Assay 95.0 – 105.0%	Free dexamethasone ≤ 0.5%	Storage conditions declared by manufacturers
KE/DEX/ 17/09-09-13	Controlled: 23°C, RH 60%	**64.4%**	Not detected	Store in a dry place, below 30°C, protect from light
MG/DEX/ 13/110913	Controlled: 19.1°C, RH 33.6%	**84.6%**	Not detected	Not available
NP/DEX/ D3/30Aug2013	Not controlled	**82.1%**	**1.2%**	Store in a cool and dark place
NG/DEX/ 13/081013	Controlled	**88.8%**	Not detected	Store below 25°C, protect from light
TJ/DEX/ 2/300813	Controlled temperature	**92.8%**	**0.7%**	Not available
VN/DEX/ 03/2409013	Controlled: 22°C, RH 54%	104.8%	**0.8%**	Keep in dry place, below 25°C, protect from light

3.4.2.8 Amoxicillin dispersible tablets (Appendix 10)

Ten samples (each from a different batch) of amoxicillin dispersible tablets produced by eight manufacturers were tested for appearance, identity, assay, weight variation, disintegration, dissolution and dispersion fineness according to the USP monograph. Five collected samples were of the strength 125mg, four of the strength 250mg and one of the strength 500mg. Samples contained amoxicillin trihydrate and their strength was expressed as the amount of amoxicillin in line with pharmacopoeias.

In all ten collected samples amoxicillin was identified and none of the samples failed to comply with the specifications for any of the conducted tests.

There was one manufacturer from which three amoxicillin samples were collected.

3.4.2.9 Zinc containing products (Appendix 11)

Seventeen samples (all from different batches) of zinc sulfate tablets and one sample of zinc gluconate dispersible tablets produced by 14 manufacturers were collected in this survey. The zinc sulfate tablets were in the form of dispersible tablets (15 samples), conventional tablets (1 sample) and effervescent tablets (1 sample). Fourteen samples of zinc sulfate dispersible tablets and one sample of zinc sulfate conventional tablets were of the strength 20mg; one sample of zinc sulfate dispersible tablets, the sample of zinc sulfate effervescent tablets and the sample of zinc gluconate dispersible tablets were of the strength 10mg.

The 18 samples were tested for appearance, identity, assay, weight variation, disintegration, and content uniformity according to the USP monograph. The test for fineness of dispersion according to Ph. Eur. was added to the testing protocol for dispersible tablets.

Four samples (4 batches) of zinc sulfate syrup produced by two manufacturers were tested for appearance, identity, assay, pH value, and specific gravity according to the USP monograph. All four samples were of the strength 10mg/5mL.

The Ph. Int. requires that labels of zinc sulfate tablets and syrups state that the active ingredient is in the form of zinc sulfate monohydrate and the strength is indicated in terms of the equivalent amount of elemental zinc. The WHO Model List of Essential Medicines [4] includes zinc sulfate oral dosage form and does not mention the monohydrate form or indicate the strength as elemental zinc. However,

WHO guidelines for production of zinc sulfate tablets and zinc oral solution **[6]** clearly indicate the content of zinc sulfate monohydrate and require labelling in terms of both zinc sulfate monohydrate and elemental zinc. Also the IP monograph for zinc sulfate dispersible tablets indicates the strength as elemental zinc present as zinc sulfate monohydrate.

USP and BP define zinc sulfate tablets as containing zinc sulfate monohydrate and expect calculation of the content as zinc sulfate monohydrate. CPh and VP do not contain a monograph for zinc sulfate dispersible tablets but zinc sulfate substance is defined as heptahydrate in both these pharmacopoeias.

The information on labels of 21 samples differed but was clear in principle:

- Labels of 18 samples (dispersible tablets and syrups) declared the amount of zinc sulfate monohydrate as well as its equivalent in terms of elemental zinc in line with WHO guidelines **[6]**.
- Labels of two samples (syrups) declared the amount of elemental zinc contained as zinc sulfate monohydrate,
- The label of one sample (effervescent tablets) declared the amount of zinc sulfate heptahydrate and its equivalent in terms of elemental zinc.

The label of one sample (conventional tablets) was not clear:

- The label on the secondary packaging (card box) stated zinc sulfate monohydrate 20mg, the label on the primary packaging (blister) stated zinc sulfate 20mg, and in the package leaflet the recommended dosage was expressed as zinc.

In line with the Ph. Int. and WHO guideline **[6]** the assay results for all samples were calculated in terms of elemental zinc.

As explained in section 3.4.1, the sample of zinc sulfate effervescent tablets could not be tested using methods for dispersible tablets and was therefore excluded from the evaluation. There were no problems in testing of zinc gluconate dispersible tablets and this sample was included in the evaluation.

In all collected samples zinc was identified and none of 21 evaluated samples failed to comply with the specifications.

There were five manufacturers from which several zinc samples were collected. From one manufacturer three samples were collected. From another two manufacturers two samples of dispersible tablets and from the last two manufacturers two samples of syrup were collected.

3.4.2.10 Levonorgestrel tablets (Appendix 12)

Fourteen samples (13 batches) of levonorgestrel tablets produced by nine manufacturers were tested for appearance, identity, assay, related substances and content uniformity according to the BP monograph. The test for dissolution according to Ph. Int. monograph was added to the testing protocol for this medicine. Thirteen samples were of the strength 0.75mg, one sample was of the strength 1.5mg.

In all collected samples levonorgestrel was identified. Twelve samples (86%) produced by seven manufacturers fully complied with the specifications. Two samples (14%) produced by two manufacturers did not comply with the content uniformity and/or dissolution.

One sample failed the content uniformity test. The acceptance limits for this test are: not more than one individual content outside the limits of 85-105% of the average content and none outside the limits

of 75-125%. In the failing sample the contents of three of 10 tablets were found out of the limits of 85-115% of the average content; one of the three tablets was outside of 75-125%. This sample failed also in the dissolution test performed according to the Ph. Int. monograph: for 6 tablets tested, the minimum dissolved amount found was 9%, the maximum 11% and the mean 10% of the amount declared on the label. The second sample failed the dissolution test only: for 6 tablets tested the minimum dissolved amount was 43%, the maximum 56% and the mean 50%.

There were three manufacturers from which several levonorgestrel samples were collected. From two manufacturers three samples were collected and all complied. From one manufacturer two samples were collected and also both complied.

3.4.2.11 Mifepristone tablets (Appendix 13)

Eight samples (from 8 batches) of mifepristone tablets produced by five manufacturers were collected. All samples were of the strength 10mg. There were three manufacturers from which two mifepristone samples were collected.

The samples were tested for appearance, identity, assay, related substances, uniformity of mass and disintegration. The specifications and methods were provided by one of the manufacturers of the collected mifepristone tablet samples, and the methods were re-validated by the testing laboratory.

In all eight collected samples mifepristone was identified, and none of the samples failed to comply with the specifications.

In one sample it was noted that all blisters were labelled with manufacturing and expiry dates but the batch number was missing. For the purposes of evaluation of testing results within this survey, this was classified as a GMP issue and not a quality defect. A levonorgestrel sample collected from this manufacturer was labelled properly. Regulators in the country of collection were informed.

4. Discussion

4.1 Testing methods and data quality

Standardized laboratory testing methods and specifications according to established pharmacopoeias (Ph. Int., BP and USP) were used in this survey to reveal quality of collected samples. Testing according to official pharmacopoeial monographs made it possible to compare products from different manufacturers. It should be kept in mind that individual products may be registered in countries with methods and specifications which differ from those set for this survey, and that non-compliance in this survey does therefore not necessarily imply non-compliance with the specifications approved in the country of collection. Some differences will be discussed further for individual medicines.

The reliability of results was assured by testing at WHO-prequalified quality control laboratories.

Samples were collected, stored and transported in compliance with the survey protocol, which prevented quality deterioration during sampling and transportation before laboratory testing. The only deviation from instructions of the survey protocol occurred in the transportation of oxytocin samples. As described in section 3.1.4, a temperature between 2°C and 8°C was requested regardless of the fact that the storage conditions declared by some manufacturers allowed higher storage temperatures; however only the samples from Nepal and Viet Nam were delivered to the testing laboratory at 2 – 8°C. The other samples were delivered at room temperature; their transportation was organized by a courier service and took 4-5 days with a temperature below 25°C ensured. A comparison of testing results for oxytocin samples from Nepal and Viet Nam with the results of other oxytocin samples does not point to a deterioration of quality due to transportation conditions. It was therefore considered that this deviation from the protocol did not influence the results of this survey.

No sample was collected after its expiry date, and all samples were tested before their expiry date.

For a vast majority of samples sufficient amount of units were collected allowing proper performance of requested tests. There were only four of 204 samples for which insufficient amount of sample did not allow completion of a test:

- One sample of magnesium sulfate injection where pH value could not be tested, and
- Three samples of ampicillin injection where uniformity of mass test was carried out with 18 or 19 vials instead 20.

As explained in sections 3.4.2.2. and 3.4.2.5 there were no reasons to expect non-compliance of these samples if tests were fully performed. The insufficient amount of units for these four samples did not influence the overall outcomes of the survey. However in retrospect, the sample size specifically for ampicillin injection samples should probably have been slightly higher than the 20 vials requested by the survey protocol.

4.2 Limitations of methodology

The survey was not designed to investigate the quality of the target medicines as made available to patients, i.e. throughout the distribution chain and in all regions within a country. Samples were collected only at the first level of the distribution chain to eliminate any potential influence of inappropriate storage and transportation conditions, and to find out the quality of products as manufactured.

Relatively small numbers of samples were collected as the availability of products was rather limited.

Neither the selection of sampling sites nor selection of samples from each site could have been done according to a randomized sampling procedure. Hence, it cannot be claimed that the samples collected and tested were representative of all target medicines used in the selected countries at the time of the survey. Additional medicines could be channelled via other first level distribution sites or via the same sites at different time periods. Nevertheless, the findings provided an understanding of the quality of the target medicines at the first level of distribution chain.

4.3 Selection of participating countries

The selection of countries for the survey aimed to identify products of good quality (or products the quality of which can be improved in a short period of time), which had already been on some markets of EWEC countries and could be recommended also for use in other countries. Therefore, in selecting countries the survey focused on those where many of the target medicines were registered, which had relatively long experience in medicines regulation, and which were located in a variety of geographic regions (see Section 2.3). Because of the risk of not identifying enough relevant products in some countries, the selection of countries for this survey only partly overlapped with the initial group of pathfinder countries[8].

Local production of target medicines may significantly contribute to their availability. In the majority of selected countries local pharmaceutical production exists. Within this survey medicines produced by local manufacturers were collected particularly in Viet Nam and to a lesser extent in Kenya, Nepal, Nigeria, Tanzania, Uganda and Zimbabwe.

4.4 Availability of target medicines for sample collection in surveyed countries

The sample collectors were asked to focus on medicines and dosage forms specified in the protocol only, and to collect three samples for each medicine, if possible from different manufacturers to reflect the UNCoLSC recommendation No. 4 which asks for availability of target medicines from at least three sources.

Collection of samples only at the first distribution level and instructions to exclude medicines produced by manufacturers under supervision of an SRA (e.g. innovator products) from the collection (see Section 2.5) might slightly underestimate the availability of the target medicines in countries.

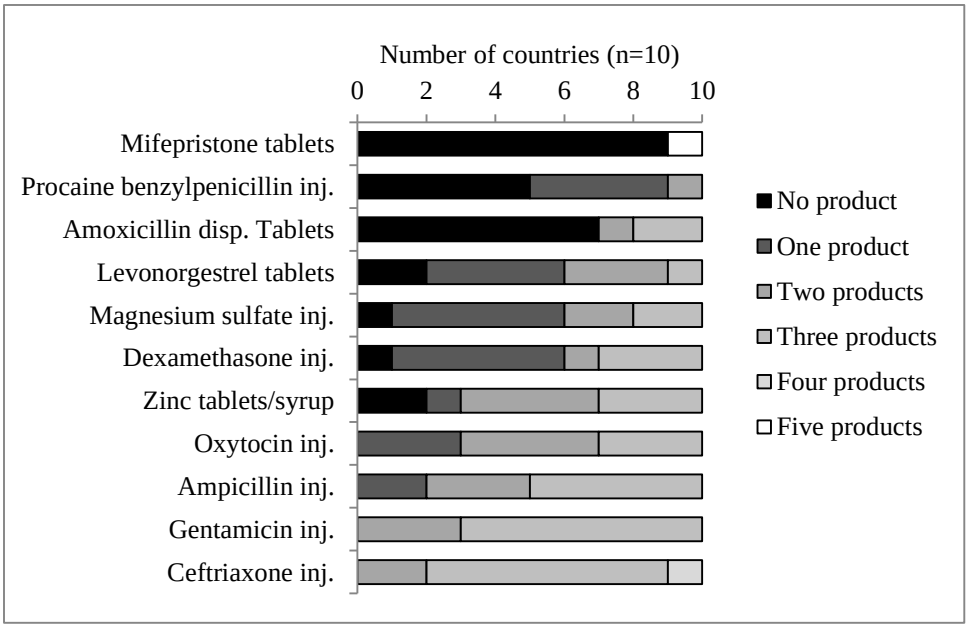
Despite the restrictions resulting from the given protocol, there were no major problems with collection of samples of injections containing ceftriaxone, ampicillin or gentamicin in any of the surveyed countries. In the case of oxytocin injection, it was difficult to collect three samples but still at least one sample was collected in each participating country. Samples of magnesium sulfate injection, dexamethasone phosphate injection, zinc dispersible tablets/syrup and levonorgestrel tablets were not collected at all in one or two countries, and in the other countries it was difficult to collect three samples. An even more limited presence was observed for the remaining medicines. Procaine benzylpenicillin injection in the strength of 1 MIU was found in one country only, and higher strengths were only collected in four other countries. Samples of amoxicillin dispersible tablets were collected in three countries only (other dosage forms e.g. powders for suspension and capsules were available but not requested to be collected within this survey). Samples of mifepristone tablets were found in one country only.

[8] DRC, Ethiopia, Nigeria, Senegal, Sierra Leone, Tanzania, Uganda

Summarizing information on numbers of products collected in countries is shown in Figure 10. This figure specifically highlights numbers of countries where none or only one product[9] was collected and which therefore deserve special attention.

In the case of betamethasone injection only the innovator product was available in some countries and thus no samples were collected within the survey.

Figure 10 Availability of different products for collection in countries



A relation between the local economic situation of the participating countries and the availability of target medicines was not seen. According to the World Bank classification, eight of the participating countries are classified as low income and two countries (Nigeria, Viet Nam) as lower-middle income. In Nigeria fewer samples were found than in some low income countries (see Table 5 on page 28) while the higher number of samples collected in Viet Nam may be due to local production of some of the target medicines.

4.5 Medicines' strengths available for sample collection in surveyed countries

For oxytocin injection, magnesium sulfate injection and amoxicillin dispersible tablets samples of the strengths defined by UNCoLSC were not available in some countries and lower strengths were collected. In the case of oxytocin injection (recommended strength 10IU/mL), only samples of the strength 5IU/mL were collected in five countries (Burkina Faso, Nepal, Tajikistan, Tanzania, Viet Nam). For magnesium sulfate injection (recommended strength 500mg/mL) only samples of the strength 250mg/mL were collected in Tajikistan, and only samples of the strength 150mg/mL were collected in Viet Nam. For amoxicillin dispersible tablets (recommended strengths 500 and 250mg) only samples of the strength 125mg were collected in Uganda.

[9] See footnote 2 on page 17

In the case of procaine benzylpenicillin injection, which was difficult to find at all within the survey, samples of the recommended strength 1 MIU/vial were found only in Madagascar. All other samples were of higher strength (3 MIU/vial or 3 MIU combined with benzylpenicillin 1 MIU in a vial).

The variety of collected strengths indicates differences in therapeutic practice. Therefore, to introduce the strengths recommended by UNCoLSC, a change of therapeutic guidelines would be necessary. Manufacturers would most probably react on changed demands.

This survey did not evaluate the appropriateness of pack sizes for each of the products e.g. tablets, nor inclusion of diluents for the injectable.

4.6 Information on the strength and API on the label

For several samples of magnesium sulfate injection, dexamethasone injection and zinc sulfate tablets/syrup; some inconsistencies were found with respect to the form of the active pharmaceutical ingredient (API) contained in the products and the expression of their strength. In general, in the case of APIs present in the form of hydrates, salts or derivatives, the label statement should clearly indicate the API form in which the content of API (strength) is expressed and the API form which is present in the product. An example of a clear statement on the label was ampicillin injection, where the strength was explicitly expressed as the amount of ampicillin, which was present in the product as ampicillin sodium salt[10].

In the case of magnesium sulfate injection, according to pharmacopoeias products generally contain magnesium sulfate heptahydrate, and the labelled amount (strength) corresponds to this compound. On the labels of four of 19 samples the content of magnesium sulfate was stated without specification of the hydrated form.

For dexamethasone phosphate injection the pharmacopoeias express the strength as the amount of dexamethasone phosphate which is present in the form of dexamethasone sodium phosphate. For five of 19 samples the information was not precise (see Section 3.4.2.7).

In the case of zinc sulfate tablets and syrup, according to pharmacopoeias, products generally contain zinc sulfate monohydrate and the labelled amount corresponds to this compound. Some pharmacopoeias (Ph. Int. and IP) require also the indication of the strength in terms of the equivalent amount of elemental zinc. The information on the label of one sample of tablets was not clear – on the secondary packaging zinc sulfate monohydrate 20mg was stated, while on the blisters zinc sulfate 20mg was declared and yet the recommended dosage in the package leaflet was expressed as zinc.

The WHO Model List of Essential Medicines **[4]** uses the name dexamethasone injection but defines clearly that it contains 4mg/mL dexamethasone phosphate (as disodium salt). In the case of magnesium sulfate injection and zinc sulfate oral dosage forms it does not mention the hydrate form. However, WHO guidelines for production of zinc sulfate tablets and zinc oral solution **[6]** clearly indicate the content of zinc sulfate monohydrate and require labelling in terms of both zinc sulfate monohydrate and elemental zinc.

It can therefore be concluded that correct labelling is an issue, and that more effort should be invested by NMRAs in its control. In clinical practice these inaccuracies very probably do not cause any confusion but they may be a problem in quality control testing. The exact specification of strength is also an issue in UNCoLSC recommendations, which do not always provide sufficient clarity on the API form to which the recommended strengths are related.

[10] Example: *"Ampicillin powder for injection: 500 mg ampicillin (as sodium salt) in vial"*

4.7 Manufacturers

In total, samples of 106 manufacturers from 22 countries were collected.

There were several manufacturers whose samples were found in more than one country (see Table 7 on page 31). It was interesting to see that frequently countries were not geographically close or even in the same region. For products that have been WHO-prequalified or registered by a stringent regulatory authority this can be explained by the fact that they are often supplied by international organizations and may be broadly distributed. However, numerous Chinese and Indian manufacturers supplied countries in different regions, and this indicated their interest and potential in exporting of products to more countries. Provided that these companies produce good quality medicines, they can be considered as potential suppliers also to additional EWEC countries.

Some of the manufacturers supplied several of the target medicines (see Table 7 on page 31). The most frequent combinations of medicines from one manufacturer were ampicillin injection and ceftriaxone injection, oxytocin injection and gentamicin injection, and amoxicillin dispersible tablets and zinc dispersible tablets. This confirms both the technological and therapeutic specialization. These manufacturers also deserve special attention as potential suppliers.

Overall, samples produced by 105 manufacturers from 22 countries were tested and evaluated. For 74 manufacturers from 21 countries all collected samples complied. For 17 manufacturers from four countries some collected samples complied, some did not. In the case of 14 manufacturers from six countries, none of the collected samples complied with the specifications set for this survey (for 12 manufacturers only one sample was collected, for two manufacturers there were two samples).

4.8 Storage conditions in sites of sample collection

Information about storage conditions was available for 99% of collected samples. According to the reports obtained from collectors, storage conditions were controlled for 82% of collected samples. No major deviations from expected storage conditions were observed.

For 17% of samples, storage conditions were not controlled. In some sites the actual temperature as measured by collectors was between 25°C and 30°C. No clear relation was found between storage conditions and quality deterioration of samples. Available information did not suggest damage to samples stored at sites without proper control of storage conditions. There are many possible reasons to explain this observation (e.g. small number of samples, short duration of storage, no extreme deviations from expected storage conditions etc.).

4.9 Overall quality findings

Of 204 samples tested, 157 (77%) complied with the specifications set for this survey. These samples represented 109 different products and were produced by 91 manufacturers from 21 countries. No failure was found for samples of procaine benzylpenicillin injection (including Fortified Procaine Penicillin), amoxicillin dispersible tablets, zinc tablets, zinc syrup and mifepristone tablets.

On the other hand, there were 47 (23%) samples which failed one or more tests. These samples represented 40 different products and were produced by 31 manufacturers from seven countries.

Extreme, moderate and minor deviations

With due respect to the limitations of the applied approach, an attempt has been made to differentiate deviations from specifications which most likely impact the therapeutic effect of the product. For this purpose, the category of extreme deviations was defined as

- the content of API deviating by more than 20% from the declared content, and/or
- for tablets, an average dissolution value of tested units below pharmacopoeial Q value minus 25%.

This approach was used in earlier reports on the quality of antimalarials **[12]** and anti-tuberculosis medicines **[13]**.

Other deviations were considered moderate, except failures to comply in assay with the strict BP limits of 95.0 – 105.0% when the content complied with limits of other pharmacopoeias (90.0 – 110.0%). These deviations were classified as minor. This classification was applied in situations where there was no failure in any other test.

Moderate deviations therefore covered failures which were not classified as extreme or minor, such as content of API 80.0 – 90.0% or 110.0 – 120.0%, presence of related substances in cases when the content of API was within acceptance limits, pH value out of acceptance limits, failure in mass uniformity test or presence of visible particles.

When applying this approach to the results of this survey, only five of 204 samples were classified as extremely deviating:

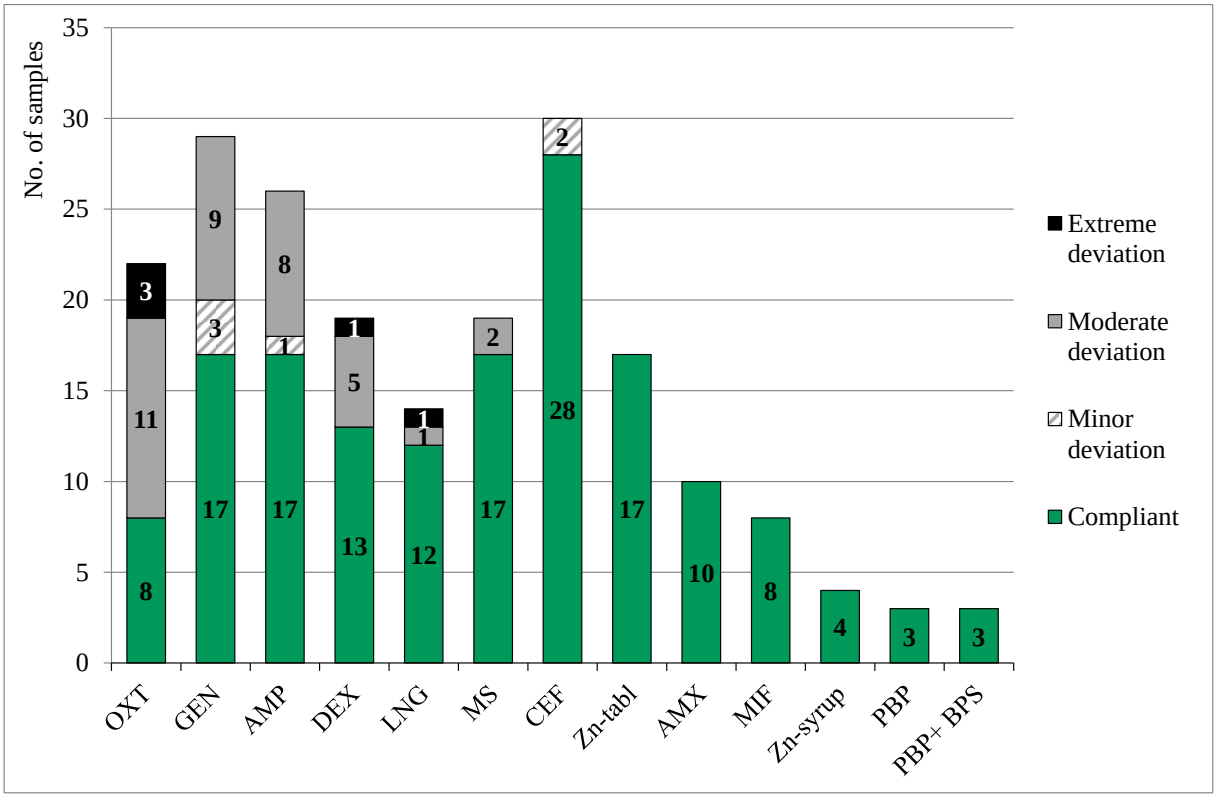
- 3 samples of oxytocin injection (the extremely non-homogeneous sample in which individual ampoules contained 0-68.7% of oxytocin, and 2 samples with the content 52.0% and 78.6% of the labelled amount of API),
- 1 sample of dexamethasone phosphate injection containing 64.4% of the labelled amount of API, and
- 1 sample of levonorgestrel tablets which failed the content uniformity test and which had an average dissolution value for tested units of 10% of the API amount declared on the label.

Of the remaining 42 non-compliant samples, 36 were considered moderately deviating from the specifications. Deviations of six samples were classified as minor. These were three samples of gentamicin injection, one sample of ampicillin injection and two samples of ceftriaxone injection, which failed in the assay only. The content of API found in these six samples was below the lower acceptance limit of BP but above the lower acceptance limit of USP (see also section 4.10).

It has to be kept in mind that even if some deviations from specifications are considered moderate they are still failures. They most likely indicate that the manufacturers have problems to operate in compliance with GMP and with adherence to international quality standards or with product formulation, and that, as a result, the quality of the products may not be assured.

Figure 11 provides a graphical summary of numbers of compliant and non-compliant samples per individual tested medicine. Deviations of non-compliant samples are classified as extreme, moderate and minor.

Figure 11 Samples with no deviations, and with minor, moderate and extreme deviations



Quality of products included in the survey

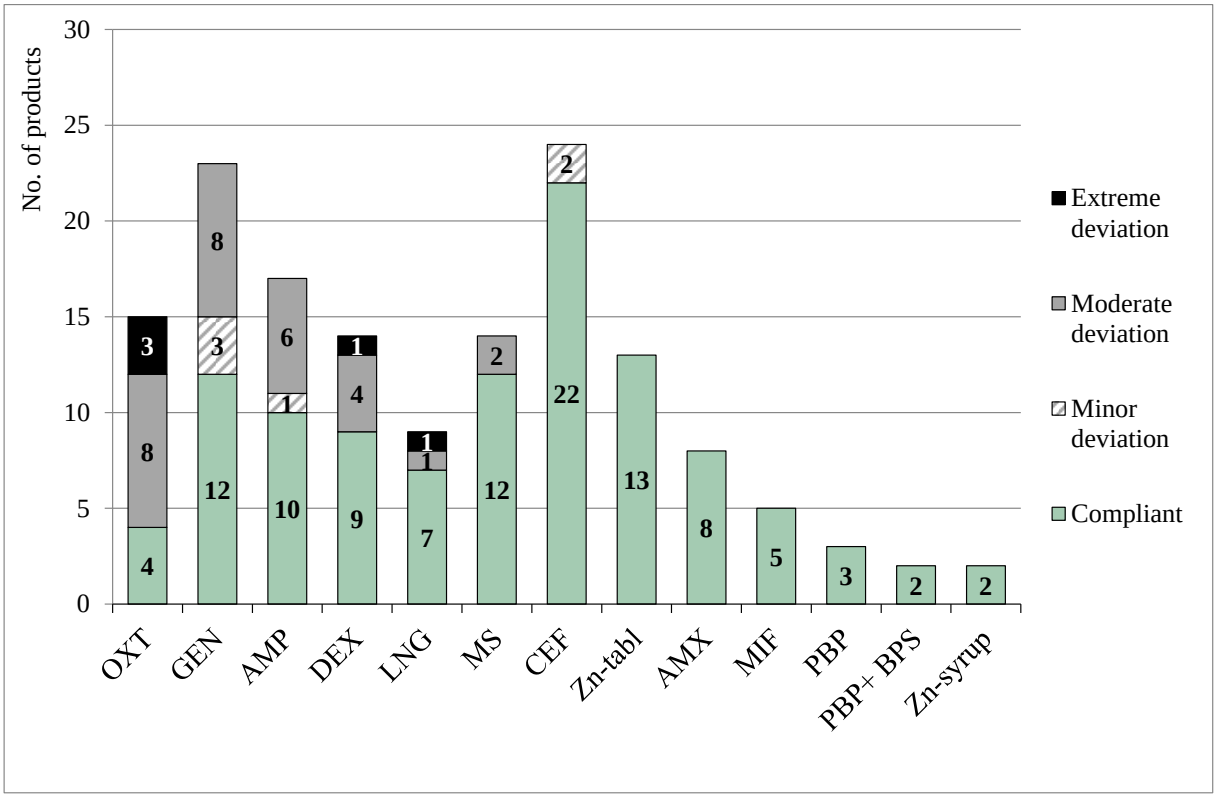
To obtain a picture of the quality of the finished products sampled in this survey, each product[11] where at least one sample did not meet its specifications was classified as non-compliant (irrespective of the number of collected batches). The severity of non-compliance was classified in the same way as for the respective samples.

This approach has some limitations. As no root cause analysis could be done, the classification of products is indicative. On one hand it can lead to overestimation of the number of products which are seen as problematic. Conversely, it does not provide assurance that products without any non-compliant sample can be definitively seen as being of good quality.

Results of this classification for products are presented in Figure 12. As there were only small differences between numbers of samples and numbers of products, the results of this classification are rather similar to the classification of samples shown in Figure 11. The products that appear to be most liable to quality defects and deserve special attention are oxytocin, followed by gentamicin, ampicillin and dexamethasone phosphate, and to a lesser extent also magnesium sulfate and levonorgestrel. Amoxicillin, zinc, mifepristone and procaine benzylpenicillin seem to be less problematic, as no non-compliance was identified. Due to the relatively small numbers of samples and products, these conclusions should be interpreted with caution.

[11] See footnote 2 on page 25

Figure 12 Products with no deviations, and with minor, moderate and extreme deviations



Quality in relation to countries of collection

At least one failing sample was detected in each of the participating countries. The numbers of collected samples were in general quite low, and the results should not be used to compare failure rates between countries.

Without consideration of other factors the findings do not enable any conclusions about the level of regulatory market control. Nevertheless, it is possible to differentiate between countries with very low level of out-of-specification results (Zimbabwe; 7%), countries with medium occurrence (Tanzania, Tajikistan, Uganda, Nepal; range 14 – 20%) and countries with relatively high level of presence of non-compliant samples (Viet Nam, Burkina Faso, Kenya, Madagascar, Nigeria; range 29 – 35%) (data in Table 12 on page 37). These findings were communicated to the respective NMRAs for consideration of further actions.

Quality in relation to domestic production

Of a total of 39 locally manufactured samples, 32 were compliant and seven were not. These samples represent a total of 32 locally manufactured products, including seven products with non-compliances.

All non-compliant samples were collected in Viet Nam – apart from Nigeria the only other participating country with a sizeable domestic production – where 24 samples of eight locally manufactured target medicines were collected. For six samples the deviation from specifications was moderate and for one sample it was minor. In the case of gentamicin injection, dexamethasone phosphate injection and levonorgestrel tablets the deviations were seen only against testing specifications set for this survey, i.e. the relevant BP monographs; according to information obtained from Vietnamese regulators the samples would comply with specifications registered in Viet Nam.

The most often found locally produced medicine was zinc (tablets or syrup), which was collected in Viet Nam and five other countries. A total of 21 zinc-containing samples (tablets and syrup) produced

by a total of 11 local manufacturers were included in the survey, and all complied with specifications. Also, all three samples of amoxicillin dispersible tablets (each from a different manufacturer) locally produced in Uganda and Nepal complied with specifications.

Table 18 shows the breakdown of numbers of locally manufactured products for each medicine by country, and the number of products with at least one non-compliant sample.

Table 18 Quality of domestically produced products

Number of products with at least 1 non-compliant sample / number of collected domestically produced products

	Magnesium sulfate injection	Genta-micin injection	Ampi-cillin injection	Ceftri-axone injection	Dexa-metha-sone injection	Amoxi-cillin disp. tablets	Zinc tablets/ syrup	Levonor-gestrel tablets	Mife-pristone tablets
Kenya	0	0	0	0	0	0	**0 / 2**	0	0
Nepal	0	0	0	0	0	**0 / 2**	**0 / 3**	0	0
Nigeria	0	0	0	0	0	0	**0 / 2**	0	0
Tanzania	0	0	0	0	0	0	**0 / 2** (4 samples)	0	0
Uganda	0	0	0	0	0	**0 / 1**	0	0	0
Viet Nam	**1 / 1** (2 samples – 1 complied) Moderate deviation	**2 / 2** Both moderate deviations	**2 / 3** Minor and moderate deviations	**0 / 2**	**1 / 3** Moderate deviation	0	**0 / 1** (2 samples)	**1 / 2** Moderate deviation	**0 / 5** (8 samples)
Zimbabwe	0	0	0	0	0	0	**0 / 2**	0	0

White cells indicate compliant testing results; cells shaded green indicate some deviation from specifications.

In summary, no major quality issues were identified with locally manufactured products. Moderate or minor non-compliances were found in 18% of the locally manufactured samples. The non-compliances were detected by the use of standards that in some cases were stricter than domestic ones. There were no extreme findings. For comparison, the occurrence of non-compliant samples among imported products was 24%, including some with extreme deviations. Except for the products manufactured in Viet Nam, the production of the locally manufactured medicines included in this survey was not highly technologically demanding and thus easier to produce for local manufacturers in an acceptable quality.

In spite of the relatively good quality of the locally manufactured products, it is worth noting that none of them was found in other surveyed countries, outside the country of production.

Quality in relation to registration status

Collectors evaluated registration status of collected samples, i.e. if sampled products were authorised by the competent NMRA for marketing and distribution in the country of collection. In the case that they found a sample of unregistered product they investigated the basis on which those products were supplied and placed on the market. Relatively few unregistered products were found at the first

distribution level in participating countries, which was a positive observation. Of a total of 149 evaluated products, 14 were not registered in the country of collection. All these products were placed on the market legally using various specific mechanisms and all of them were imported. This indicated that other mechanisms than normal registration processes are used to control supply of needed medicines.

No samples of unregistered products were collected in Kenya, Madagascar, Nigeria, Tanzania and Viet Nam. In each of these countries collectors were not able to find some of UNCoLSC target medicines. This could indicate that these countries either applied rigorous registration policies, or that missing products were supplied through other channels, or that these products (mostly procaine benzylpenicillin injection, amoxicillin dispersible tablets and mifepristone tablets) were not seen to be needed (e.g. according to current treatment guidelines).

Each of the other countries applied a policy of making unregistered products available under certain conditions. The mechanisms through which unregistered products entered the distribution in the surveyed countries included donations, central supplies based on a global tender, and special imports permits.

For samples of unregistered products, extreme quality deficiencies were not observed, and samples largely complied with specifications set for this survey. Bearing in mind that only small numbers of samples of unregistered products were evaluated, it could be concluded that quality of unregistered products did not substantially deviate from that of registered products. In this survey, unregistered (but supplied in line with specific national regulations) products could be even considered of better quality. Only two of 14 unregistered products were moderately deficient (14%), while 39 of 135 registered products (29%) had some non-compliant result, including extreme deviations in some cases. This can be the result of effective quality assurance policies of donors and other importers, and/or it may reflect an effective regulatory management of these special situations in countries, ensuring the availability of medicines in emergency situations.

Table 19 shows the breakdown of numbers of unregistered products for each medicine collected in individual countries and the number of products with at least one non-compliant sample.

Table 19 Quality of products unregistered in the country of collection

Numbers of non-compliant unregistered products / number of collected unregistered products

	Oxytocin injection	Magne-sium sulfate injection	Genta-micin injection	Procaine benzyl-penicillin	Ampicillin injection	Dexa-methasone injection	Zinc tablets/ syrup	Levo-norgestrel tablets
Burkina Faso	**1/2 Moderate deviation**	0	**0/2**	0	0	0	0	0
Nepal	**1/1 Moderate deviation**	0	0	0	0	0	0	0
Tajikistan	0	0	0	0	0	0	**0/1**	0
Uganda	0	**0/1**	0	0	0	0	0	**0/1**
Zimbabwe	**0/1**	**0/1**	**0/1**	**0/1**	**0/1**	**0/1**	**0/2**	0

White cells indicate compliant testing results; cells shaded green indicate some deviation from specifications.

Quality in relation to WHO prequalification

Eleven samples of four WHO-prequalified products (produced by four manufacturers) all complied fully with specifications. Although very few products from the target list were prequalified, and even though there were not many samples of WHO-prequalified products collected in the survey, the results helped to provide additional assurance that prequalification is an effective mechanism to guarantee product quality.

The survey included 14 samples produced by six manufacturers who went successfully through WHO prequalification with other products not targeted in this survey, but in related dosage forms. None of these 14 samples failed to comply with specifications set for this survey, which may indicate that the WHO prequalification experience contributed to the overall quality of the products of these manufacturers.

4.10 Quality of individual sampled medicines

Oxytocin injection

Oxytocin samples had the highest failure rate of the medicines tested in this survey and because of this the results deserve further analysis. Of the total of 22 samples, 14 (representing 11 products) did not comply with the specifications set for this survey.

Three samples from three products were found extremely deviating. One of these was visibly substandard, containing different ampoules with varying amounts of oxytocin and related substances. Some ampoules did not contain any oxytocin at all, and in the majority of ampoules visible particles were found. It was the only oxytocin sample from that particular manufacturer. Four samples of other medicines were collected from this manufacturer – three of them complied and one did not. The findings indicated extreme non-compliance with GMP principles, and the regulators in the country of collection were informed.

The content of oxytocin below the acceptance limit of 90.0% was found frequently (7 samples); in two of these samples representing two products the deviation was extreme (52.0 and 78.6% of the labelled amount). As the content of related substances in all these samples was above the limit, one can hypothesize about the degradation of oxytocin and presence of degradation products.

However, an excessive amount of related substances was also seen in six other samples in which oxytocin content was within the acceptance limits. This finding suggests that there are other possible sources of related substances, e.g. impurities from raw materials – be it API or excipients. Some characteristic peaks repeatedly occurred in products from different manufacturers which might indicate that they were API-related. The data did not show any clear relation between the content of oxytocin and related substances in individual samples. In some samples the sum of oxytocin and related substances was well above 100%, suggesting the possibility of a large overage of API in manufacture. Such practice is not normally acceptable and should be controlled by regulators during the registration process.

Results of the test for related substances may provide an indication of medicines quality, but USP and BP monographs for oxytocin injections do not include this test, and limits for related substances are specified only in the substance monographs. Such a focus on quality of API may not be sufficient for countries with less advanced regulation, which control mainly the final products.

If the results of oxytocin products are evaluated according to USP or BP, the samples that failed only in the related substances test would have passed all tests. The related substances present in the samples

were not identified or qualified, and it was not possible to correlate their presence with any biological effect. However, irrespective of pharmacopoeial criteria, the presence of excessive amounts of related substances indicates weaknesses in registration processes, because the identification and qualification would be normally requested by regulators during assessment of data submitted for registration.

In the context of related substances, the labelled information on the origin of oxytocin was evaluated. A majority of pharmacopoeias searched in this survey (Ph. Int., Ph. Eur., BP, USP) define oxytocin as synthetic (USP still requires that the product label states the animal source if naturally derived). IP and CPh admit oxytocin of synthetic and animal origin. Although it was not always explicitly stated, from the references to pharmacopoeial standards it could be concluded that all except one of the samples tested contained synthetic oxytocin. The sample for which no information on oxytocin origin was available was produced in China and contained 52% of oxytocin and a high amount of related substances. As there was no sample with a declared content of oxytocin of animal origin, it was not possible to compare the presence of related substances/impurities between products containing naturally derived and synthetic oxytocin.

In relation to the results of the related substances test, the preservative content in collected samples was also evaluated. Normally single use injection dosage forms do not need preservatives, but as the innovator oxytocin product (produced by Sandoz/Novartis) contains chlorobutanol, some generic products follow this composition. Some collected samples contained a preservative, mostly chlorobutanol, in one case phenol (see Table 14 on page 43 and Appendix 3). There were some inconsistencies between the testing results and information about a preservative content on the label; however the requirements on the statement of preservatives on labels might differ in countries. In some cases, peaks of related substances might be covered by a preservative peak or mistaken for a preservative, and thus the content of related substances might have been underestimated.

The quality of oxytocin products may deteriorate in inappropriate storage conditions. Normally it is recommended to store oxytocin at 2°C to 8°C, but manufacturers' instructions on labels varied substantially. In spite of this fact, the shelf-lives were similar, i.e. two or three years (see Table 15 on page 44). It would be useful to verify to which extent manufacturers' instructions for higher storage temperatures were based on reliable stability studies. No clear relation was found between non-compliance in oxytocin content or related substances on one hand and storage temperature or time elapsed from manufacture on the other hand.

In three of 22 samples visible particles were found in addition to other deviations. This indicated problems in GMP compliance of the respective manufacturers.

As sterility and bacterial endotoxins tests were not performed in this survey, evidence of GMP compliance would be important before recommending any of these products to other countries.

Magnesium sulfate injection

Testing of magnesium sulfate injection samples produced by 14 manufacturers did not reveal any major problems. Of 19 samples only two (representing two products) failed in pH value, the results of all other tests complied with specifications. The pH value of these two samples was slightly above the upper acceptance limit of 7.0 (see Appendix 4). The acceptance limits for pH value in magnesium sulfate injection monographs in various pharmacopoeias (BP, Ph. Int., USP, CPh, IP) were compared and it was found that all except CPh required a pH value in the range 5.5 – 7.0. The CPh acceptance range was 5.0 – 7.0. Thus the upper limit was identical in all searched pharmacopoeias and there was no reason to deviate.

Deviations of these two samples from specifications are considered moderate, however, they may indicate some problems in GMP compliance of manufacturers. As sterility and bacterial endotoxins tests were not performed in this survey, GMP inspections would be important before recommending any of these products to additional countries.

Gentamicin injection

Of the total of 29 samples, 12 (produced by a total of 11 manufacturers) each failed one test. The deviations were classified as moderate.

In six samples (corresponding to six products) the content of gentamicin did not comply with BP specifications of 97.0 – 110.0% used in this survey (see Appendix 5). The acceptance limits for the content of gentamicin in injection differed between pharmacopoeias. The limits in IP and VP were 95.0 – 110.0%, in CPh 90.0 – 110.0 % and in USP 90.0 – 125.0%. A microbiological assay is used in all monographs. According to the limits of USP only two samples would moderately deviate from specifications, i.e. the samples with an average content of 87.8% and 87.9%.

In four other samples (four products) the composition of gentamicin deviated from specifications as they had a slightly lower content of component C_1; one of them also had a slightly higher content of component C_{1a} (see Appendix 5). Limits for gentamicin components are specified in various pharmacopoeias as follows:

BP, IP, VP:	C_1: 25.0-50.0%;	C_{1a}: 10.0-35.0%;	C_2+C_{2a}: 25.0-55.0%
CPh:	C_1: 25.0-50.0%;	C_{1a}: 15.0-40.0%;	C_2+C_{2a}: 20.0-50.0%
USP (for API only):	C_1+C_{2b}: 25.0-50.0%;	C_{1a}: 10.0-35.0%;	C_2+C_{2a}: 25.0-55.0%
Ph. Eur. (for API only):	C_1: 25.0-45.0%;	C_{1a}: 10.0-30.0%;	$C_2+C_{2a}+C_{2b}$: 35.0-55.0%

As there are small differences even among individual pharmacopoeias, the deviations found in four tested samples were considered moderate.

Finally, there were two samples (representing two products) which failed in pH value while the results of all other tests complied with the specifications. The pH value of these two samples was found slightly above the upper acceptance limit of 5.5 (see Appendix 5). The limits for pH value also differ between pharmacopoeias:

BP, USP, VP:	3.0 – 5.5
IP:	3.0 – 5.0
CPh:	3.5 – 6.0

Therefore this deviation was considered moderate.

As sterility and bacterial endotoxins tests were not performed in this survey, evidence of GMP compliance would be important before recommending these products to additional countries.

Procaine benzylpenicillin injection

It was very difficult to find samples of procaine benzylpenicillin injection in the surveyed countries. Only three samples of procaine benzylpenicillin injection (representing three products) and three samples of procaine benzylpenicillin with benzylpenicillin sodium injection (representing two products) were therefore collected. These were produced by three manufacturers from two countries.

All collected samples complied with the specifications set for this survey. However it should be kept in mind that such a small number of tested samples cannot provide a representative picture of the quality of this medicine. As sterility and bacterial endotoxins tests were not performed in this survey,

evidence of GMP compliance would be important before recommending these products to other countries.

Ampicillin injection

For nine of 26 samples (representing seven products) some moderate deviations from specifications were found.

Three samples (representing three products) had an ampicillin content slightly below the lower acceptance limit of 95.0% (see Appendix 7). The acceptance limits for the content of ampicillin in injection monographs in various pharmacopoeias were compared. The HPLC method was used in all monographs; CPh, IP, VP had the same limits as BP, while the USP limits were 90.0 – 115.0%. The three samples would therefore comply with USP specifications for assay.

Eight samples (representing six products) failed the related substances test. In all samples one secondary peak above the acceptance limit of 2% was found; in two of them also ampicillin dimer was found slightly above the acceptance limit of 4.5% (see Appendix 7). No relation was found between the storage conditions at the respective sampling sites and these findings. From the comparison of monographs in various pharmacopoeias it was seen that apart from BP only CPh included the test for related substances in the injection monograph (with the same limits as BP). VP had limits for related substances for the ampicillin substance but not for the dosage form. The USP and IP monographs for ampicillin substance and injection did not include a test for related substances. Three of these eight samples claimed BP quality on their labels, thus compliance with the specification of the BP monograph was expected.

One sample failed both the related substances test and the test for uniformity of mass, which might indicate some problems in GMP compliance of the manufacturer.

Taking into account the requirements of different pharmacopoeias, only one sample would not comply with any of them (the sample that failed the test for uniformity of mass). The other 25 collected samples would comply with the USP specifications. Five of the nine non-compliant samples would comply also with the IP and VP specifications.

As sterility and bacterial endotoxins tests were not performed in this survey, evidence of GMP compliance would be important before recommending any of these products to additional countries.

Ceftriaxone injection

Testing of ceftriaxone injection samples, which were produced by 24 manufacturers from eight countries, did not reveal any major problems. Of 30 samples only two (representing two products) were non-compliant with the specifications set for this survey; the content of ceftriaxone was below the acceptance limit of 92.0% (see Appendix 8). The results of other tests, including the related substances test, were within the specifications set for this survey.

The acceptance limits for the content of ceftriaxone in injection monographs in various pharmacopoeias were compared and were found to differ, even if the HPLC method was used in all of them. Only BP and VP specified the limits as 92.0 – 108.0%. In CPh the limits were 90.0 – 110.0% and in USP and IP 90.0 – 115.0%. As the content of ceftriaxone in both samples was above 90.0% they would comply with USP, CPh and IP. Therefore, for the purposes of this survey, the deviations of these two samples were considered minor. As sterility and bacterial endotoxins tests were not performed in this survey, evidence of GMP compliance would be important before recommending any of these products to additional countries.

Dexamethasone phosphate injection

Of 19 samples of dexamethasone phosphate injection, six (representing five products) failed to comply with the specifications set for this survey.

In five of them (corresponding to four products) the content of dexamethasone was below the lower acceptance limit of 95.0%; in one sample the deviation was extreme (64.4% of the labelled amount), in three samples the content was between 80.0 – 90.0% and in one sample it was 92.8%. The acceptance limits for the content of dexamethasone phosphate in injection monographs in various pharmacopoeias were compared and it was found that only IP required the same limits as BP, i.e. 95.0 – 105.0%. The limits in CPh and VP were 90.0 – 110.0% and those of USP were 90.0 – 115.0%.

In three samples (representing three products) the content of free dexamethasone was above the acceptance limit of 0.5% (see Appendix 9). Again, the limits for the content of free dexamethasone differed between pharmacopoeias. Only CPh includes this test in the dosage form monograph and has the same limit as BP. In USP, IP and VP no test for free dexamethasone is included in the dosage form monograph, limits are specified only for the substance (IP and VP: 0.5%; USP: 1.0%).

Taking into account the requirements of various pharmacopoeias, four of six samples (those with an API content below 90.0%) would not comply with specifications of any of them. Two of six samples would comply if evaluated according to USP or VP specifications.

No clear relation was found between the storage conditions at sampling sites as reported by collectors and the findings for the non-compliant dexamethasone phosphate injection samples.

As sterility and bacterial endotoxins tests were not performed in this survey, evidence of GMP compliance would be important before recommending any of these products to additional countries.

Amoxicillin dispersible tablets

Although amoxicillin-containing medicines were available in the surveyed countries in various forms (as syrup, as capsules or in combination with clavulanic acid), amoxicillin in the form of dispersible tablets was available only in three of 10 surveyed countries. Ten samples corresponding to eight products were collected, and all complied with the specifications set for this survey.

Zinc-containing products

A total of 16 samples of zinc sulfate tablets (representing 12 products), one sample of zinc gluconate tablets and four samples of zinc sulfate syrup (representing two products) were tested. All of them complied with the specifications set for this survey.

Levonorgestrel tablets

Twelve of 14 collected samples of levonorgestrel tablets (representing seven products) complied with the specifications set for this survey. Two samples (corresponding to two products from different manufacturers) did not comply. One failed the test for content uniformity, an important test for this product which is administered in low dose and the effect of which depends on one or two tablets. Both non-compliant samples failed the dissolution test, which was performed using methods described in the Ph. Int., the only pharmacopoeia consulted within this survey which includes a dissolution test for levonorgestrel tablets.

Interpretation of the observed dissolution test results has its limitations. The dissolution test should in principle control the consistency of produced batches with the batch which was clinically tested during product development. Dissolution conditions used for a particular product should be sufficiently discriminating to reveal any changes in manufacture which could influence bioavailability of the

product. While conditions are not necessarily identical for different products, manufacturers should prove that their conditions are suitable for the particular product and regulators should assess this during the registration process. Therefore the dissolution test is not often part of pharmacopoeial monographs, however, it should be included in product dossiers and performed by manufacturers of solid dosage forms.

Both products failed this test quite clearly. The dissolved amount for six tablets was 9 – 11% for one sample and 43 – 56% for the other, compared with a required Q value of 75%. No failures were detected for the other seven products using the dissolution conditions of the Ph. Int. monograph. Even if the above-mentioned limitations are considered, the results are worrying. The product with the average dissolved amount of 10% was considered extremely deviating and that with the mean of 50% (25% below the Q value) moderately deviating. These results were communicated to regulators in countries of collection for further action.

Mifepristone tablets

Mifepristone tablets in the strength 10mg or 20mg were not found in any of the surveyed countries except in Viet Nam. In a few countries the 200mg strength was registered, but this was not one of the products identified by UNCoLSC. In Viet Nam eight samples produced by five domestic manufacturers were collected and all samples complied with the specifications set for this survey.

4.11 Regulatory actions

Non-compliant results were communicated to the focal persons in the respective countries, together with the certificates of analysis issued by the testing laboratories. The specifications approved in individual countries were reviewed and discussed. Adoption of any regulatory action was the responsibility of regulators in participating countries. As no deviations from specifications were observed for any WHO-prequalified products, or for any products produced by manufacturers of other prequalified products, the involvement of WHO inspectors from the prequalification team was not necessary.

Participating regulatory authorities reacted in various ways. Some authorities used the information as a signal and started their own investigation as a basis for potential regulatory action. Other authorities immediately initiated discussion with the respective manufacturers and adopted regulatory actions. Some authorities took strict regulatory actions even if deviations from pharmacopoeial specifications were not serious.

4.12 Recommendations from survey wrap-up meeting

Each focal person was provided with detailed testing results for all samples collected in the respective country. The outcomes of the survey, possible regulatory actions and possible ways to contribute towards fulfilling the UNCoLSC goals were discussed in a meeting with representatives of NMRAs from participating countries.

The following recommendations to increase the availability of good quality medicines identified by UNCoLSC were agreed:

To regulators in countries

- Identify registered products which are considered to be of acceptable standard for other countries and be ready to share up-to date assessment and/or inspection reports with other regulators;

- Identify products with pending applications for registration and products which are placed on the market using special mechanisms (donations, special imports, conditional approvals, specific treatment programmes etc.), and consider arrangements for their registration and regular availability;
- Apply innovative regulatory pathways to accelerate availability of products for which there are currently less than three sources – e.g. use of assessment and inspection reports of other regulators to accelerate the decision making-process – and apply different models of collaborative registration;
- To verify medicines quality, organize post-marketing surveillance studies (laboratory testing), planning should be based on an assessment of risks related to substandard quality;
- With respect to specific medicines (see also the corresponding recommendations to manufacturers):
    - Review stability studies of oxytocin products which declare storage conditions above 8°C and indicate those which are stable under more harsh conditions; in some cases verification of data during GMP inspection may be considered,
    - Review registered gentamicin products according to current specifications,
    - Review ampicillin products that have been registered for a long time; perform these reviews on a risk basis (during variations or in case of emerging problems),
    - Check proper package labelling for dexamethasone products with respect to the content of API,
    - For amoxicillin dispersible tablets, consider task-shifting – respecting local conditions and organization of the dispensing system – to make products available through a lower level of health care professionals (prescription by nurses, assistants etc.),
    - Clarify requirements for the demonstration of taste acceptability for zinc sulfate dispersible tablets/syrup for the purposes of registration (if relevant),
    - Clarify requirements for demonstration of bioequivalence for levonorgestrel tablets and mifepristone tablets for the purposes of registration (if relevant).

To manufacturers

- Review the list of countries lacking three sources of medicines targeted by UNCoLSC and consider applications for registration;
- Agree to sharing of assessment and inspection reports among regulators in order to accelerate registrations;
- Consider possibility of assistance by WHO or other party to develop needed products, complete regulatory data and comply with GMP;
- With respect to specific medicines*:*
    - Be prepared to document properly the stability of oxytocin products (using a stability-indicating method) and adjust shelf-life and storage conditions accordingly; include ‘drug development’ information in regulatory dossiers explaining the sourcing of oxytocin and justifying the use of excipients/preservatives;
    - Do not apply overage for oxytocin products;

  - Consider the possibility that demonstration of bioequivalence in vivo for amoxicillin dispersible tablets may be required in some of the surveyed countries in the future; and
  - Be prepared to demonstrate taste acceptability of zinc sulfate dispersible tablets/syrup to the majority of regulators; well-designed taste acceptability study represent the ideal solution but pharmacovigilance or market consumption data may satisfy some regulators.

To WHO

- Make publicly available a list of manufacturers deemed to be prospective suppliers of products of good quality, and a list of countries lacking three sources of the medicines targeted by UNCoLSC;
- Help to organize expert support for product assessment or to resolve inspection issues, if required;
- Support countries in dealing with complaints on poor efficacy of generic ceftriaxone injection;
- Make publicly available a model protocol for zinc taste-masking studies;
- Consider extending the eligibility for WHO prequalification from zinc sulfate products to zinc products containing other salts than sulfate.

To UNCoLSC

- Clarify the need for procaine benzylpenicillin injection and consider the possibility to replace it with ampicillin injection if necessary;
- Clarify to which extent dexamethasone and betamethasone injections are therapeutic alternatives, or whether availability of both is recommended.

5. Conclusions

The survey was conducted in good compliance with the pre-established protocol. The data generated can be seen as robust. Apart from providing a snapshot picture on the quality of collected samples, the survey generated some information about the availability of the target medicines. The results do not provide a representative picture of the markets in surveyed countries or of the quality of production of individual manufacturers. Sample collection was subordinated to the objective to identify good quality products, and only relatively small numbers of samples were collected. The selected testing criteria cannot demonstrate product quality to the full extent. Nevertheless, the data collected made it possible to obtain a good picture of the quality of the investigated segment of medicines and their availability.

The outcomes related to the availability of the target medicines underestimate the reality due to the sampling methodology used. Several medicines (ceftriaxone injection, gentamicin injection, ampicillin injection, oxytocin injection) were relatively well available in all countries, others (zinc containing products, dexamethasone phosphate injection, magnesium sulfate injection, levonorgestrel tablets) were only available in some of the countries, and some products (procaine benzylpenicillin injection, amoxicillin dispersible tablets, mifepristone tablets) were frequently not available at all. In each country at least one of the medicines recommended by UNCoLSC could not be identified for collection. For betamethasone injection, which was also among selected medicines, no samples were available in any country. In some countries the innovator product was available but the sample collectors respected the instructions in the protocol to exclude innovator products. The medicines that were less frequently available deserve special attention in future efforts of UNCoLSC.

In spite of its limitations, the survey confirmed that a comprehensible approach is necessary to improve the availability and quality of UNCoLSC target medicines. It appeared that the lack of availability of certain medicines in individual countries was driven by a low demand from local physicians, and therefore updates of therapeutic treatment guidelines and training of physicians are necessary.

Some medicines were available in different strengths than recommended by UNCoLSC (e.g. oxytocin injection, magnesium sulfate injection) or in different dosage forms (e.g. amoxicillin products). This illustrates the differences in current therapeutic use. Some medicines (such as amoxicillin dispersible tablets) were not available even in countries with the potential of local production.

To improve availability, UNCoLSC should clearly specify the needed medicines by their dosage form and strength – with clarification to which API form the strength relates – and possible alternatives in the list of commodities. This will enable countries and manufacturers to understand the needs and to act accordingly. For certain categories of medicines that are relatively easy to produce and control (e.g. zinc products), availability can be facilitated by local production and pragmatic regulatory requirements.

Although the small number of collected samples of individual products limits the adoption of valid conclusions, the total number of over 200 tested samples provides a relatively good understanding of the overall situation regarding quality. It should be remembered that this survey focused on identifying good quality medicines, generating a systematic bias which likely provided a more optimistic picture than is justified by the market reality.

The overall proportion of samples that did not comply with the testing specifications was relatively high (23%, 47 of 204 samples). Considering the prevalence of products for which at least one deviation was found in any collected sample, the proportion of failing products was even higher (27%, 40 of 149 products). The high rate of non-compliance can be partially explained by relatively strict

testing criteria, involving testing against pharmacopoeial specifications rather than manufacturers' specifications approved in countries of collection. The extent of failing samples and products indicates that international quality and GMP standards are not yet fully adopted by the respective manufacturers nor consistently implemented by national regulatory bodies.

Extreme quality failures were present to a much lesser extent. Five of 204 samples (2%) or five of 149 products (3%) had extreme deviations indicating a potential lack of expected efficacy due to the low content of active principle or its limited release from the dosage form.

Some categories of medicines were consistently of acceptable quality in all tested parameters. No failure was found for samples of procaine benzylpenicillin injection, amoxicillin dispersible tablets, zinc tablets/syrup and mifepristone tablets. The number of tested samples for these medicines was quite low, though.

For samples of ceftriaxone injection, gentamicin injection, magnesium sulfate injection and ampicillin injection only moderate deviations from the specifications set for this survey were found.

A low proportion of failing samples was found for levonorgestrel tablets (14%, 2 of 14 samples), but the poor dissolution seen in two products was considered an important quality defect for this medicine. Testing for dissolution should therefore be included in the specifications for levonorgestrel tablets and routinely tested by manufacturers.

Quality problems were identified for dexamethasone phosphate injections and in particular for oxytocin injections. The quality of these medicines therefore deserves further attention. Dexamethasone phosphate injections deviated from specifications in API content, which in one sample was extremely low. In the case of oxytocin injection, the testing confirmed the vulnerability of oxytocin to quality deterioration and pointed to existing problems with GMP compliance and quality of raw materials. This survey was conducted at the first level of the distribution chain and did not demonstrate any association between storage conditions and the quality of oxytocin products. However, oxytocin samples from different manufacturers exhibited a surprising variety of approved storage temperatures (from 2 – 8°C to below 30°C) although the shelf-life of products was comparable. The differences can be partially explained by optimization of the formulation but may still be considered as excessive. It is recommended to focus on well documented stability studies, including verification of data, during inspections and during review of oxytocin product dossiers for registration.

Even if the number of collected samples varied in individual countries and was low in general (ranging from 13 in Burkina Faso to 28 in Viet Nam), it was possible to observe differences in the proportions of quality-compromised products found in countries. These accounted for 7% of collected samples in Zimbabwe and were in the range of 14–20% in Nepal, Tajikistan, Tanzania and Uganda, and in the range of 29 – 35% in Burkina Faso, Kenya, Madagascar, Nigeria and Viet Nam. These findings may reflect market complexity as well as differences in the level of regulatory scrutiny and applied standards.

The survey stressed the need of harmonization of pharmacopoeial requirements in several respects, including the recommendations for product labelling. Differences between requirements in various pharmacopoeias have a major influence on the interpretation of results and can lead to contradicting opinions on product quality. An example is the test for related substances, which is not included in all pharmacopoeial monographs for finished pharmaceutical products, meaning that medicines with high levels of impurities or degradation products can comply with certain pharmacopoeial monographs but not others. In countries with less advanced regulation, which control chiefly the finished products, it would not be wise to rely on the assured quality of the API used for manufacture without testing the

finished product for impurities. Thus, testing of related substances in finished products is considered important.

In general, the quality of UNCoLSC target medicines collected during the survey was not very satisfactory. Therefore, after implementation of regulatory actions and other corrective measures, it is worth continuing to organize similar studies in the future to monitor the improvement in applicable quality standards and to generate additional useful data.

The survey provided a broad picture of manufacturers whose products were available in the selected countries. Products from a total of 106 manufacturers from 22 countries were sampled; some products were available in several countries and some manufacturers produced several of the target medicines. In an effort to collect samples from as many manufacturers as possible, one sample per manufacturer was typically collected, which did not allow to take far-reaching conclusions on the overall quality of production of individual manufacturers. However, it was possible to arrive at a certain differentiation between more or less promising manufacturers for further investigation. Readers of the report can make their own judgement by looking at the testing results in the Appendices 3 – 13.

Tested samples originated both from local production (19%) and from importation (81%). Locally manufactured products were collected for nine of 11 tested medicines. The highest number of samples from local manufacturers (24 of 28 samples) was collected in Viet Nam, one of two participating countries with a sizeable domestic production, the other being Nigeria. Deviations from specifications were observed for locally manufactured Vietnamese products; however, the deviations were never extreme and according to information obtained from Vietnamese regulators, some of the samples would comply with the specifications registered in Viet Nam.

All samples of domestically produced amoxicillin dispersible tablets and zinc containing products complied fully with the specifications set for this survey. In summary, no major quality issues for domestically produced products were identified. With the exception of products collected in Viet Nam, the locally manufactured medicines were not highly technologically demanding and thus easier to produce for local manufacturers in an acceptable quality.

Thorough assessment and registration are the best way of gaining assurance about the quality, safety and efficacy of medicines before they are placed on the market and used in therapeutic practice. However, the survey showed that 9% of products collected for testing were imported without registration. This documents that other mechanisms that bypass normal registration processes are used to supply needed medicines. Different pathways, such as donations or special import permits or centralized supply based on a global tender, were used in participating countries to make products available without registration. In general the quality of unregistered (but supplied in line with specific national regulations) medicines tested in this survey was good; two of 14 unregistered products (14%) failed to comply with specifications, compared to 39 of 135 registered products (29%). In Zimbabwe, where the highest proportion of unregistered samples was collected (7 of 15 products), all samples complied with specifications. The only sample found in Zimbabwe with a deviation – which was minor – was registered. This can be partially explained by effective quality assurance mechanisms of donors and partially by effective regulatory control of these alternative pathways. The results of the survey thus indicate that the use of alternative regulatory pathways does not necessarily increase the risk of sub-standard quality of imported products.

Although the number of sampled WHO-prequalified medicines was small (11 samples of 4 products), the survey confirmed their consistently good quality. The zero failure rates of WHO-prequalified products suggest that the WHO prequalification reliably assures uniform quality standards.

It should be remembered that the quality testing performed in this survey helped to understand only certain quality parameters. Other important ones, such as bioavailability, taste acceptability or consistent production of defined quality, must be verified by different regulatory instruments. As several observations indicated problems with GMP compliance, special attention should be given to strengthening the implementation of GMP in producing countries.

The survey met its primary and secondary objectives. It generated information which led to a better understanding of the availability and quality of UNCoLSC target medicines in selected EWEC countries. It also contributed towards evidence-based regulatory actions in some countries. The results of the survey enable NMRAs and WHO to focus on selected manufacturers and to confirm to which extent good quality confirmed by testing is also supported by compliance with GMP and proper regulatory documentation.

The meeting held with regulators from participating countries to discuss and analyse the outcomes of the survey proved to be important to interpret the findings and come to regulatory actions. The meeting participants agreed on conclusions and recommendations which should be implemented in practice and could contribute to achieving the UNCoLSC goals and to strengthening regulatory systems. More intensive cooperation and information exchange among regulators would help to eliminate poor quality medicines. This can be achieved through exchanging assessment and inspection reports, cooperation in sample testing and/or consultations before adoption of regulatory actions against substandard medicines. Regulatory cooperation and harmonization of regulatory requirements and procedures can also help to improve regulatory efficiency and incentivize manufacturers to register more UNCoLSC-relevant medicines in the respective countries.

Lessons were also learned for the organization of similar surveys in future. Notably, to gain a better picture of the availability of target medicines the sample collectors could be asked to gather more information about all target products in stock at the time of the survey or procured over a defined period of time.

6. References

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3 MIMS Drug Information System (Available at: http://www.mims.com/)

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Appendices

Appendix 1 Survey protocol

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

1. Glossary of terms and abbreviations

Country codes (for the purposes of coding samples):

Burkina Faso = BF
Kenya = KE
Madagascar = MG
Nepal = NP
Nigeria = NG
Tajikistan = TJ
Tanzania = TZ
Uganda = UG
Viet Nam = VN
Zimbabwe = ZW

Medicines abbreviations (for the purposes of coding samples):

Amoxicillin = AMX
Ampicillin = AMP
Betamethasone = BET
Ceftriaxone = CEF
Dexamethasone = DEX
Gentamicin = GEN
Levonorgestrel = LNG
Magnesium sulfate = MS
Mifepristone = MIF
Oxytocin = OXT
Procaine benzylpenicillin = PBP
Zinc sulfate = ZS

Sample	for the purposes of this project means a product in given presentation (identified by the name, content of APIs, dosage form, strength, batch number and manufacturer) collected at the specific collection site. That means that the same product characterized by the same name, content of APIs, the same dosage form, strength, batch and from the same manufacturer collected in two different sites represents two samples.
API	Active pharmaceutical ingredient
CHX	Chlorhexidine
CMS	Central medical store
CWG	Chlorhexidine Working Group
EWEC	Every Woman Every Child
GMP	Good Manufacturing Practice
HPLC	High performance liquid chromatography
INN	International Nonproprietary Names for pharmaceutical substances
NGO	Non-governmental organization
NMRA	National medicines regulatory authority
ORS	Oral Rehydration Salts
PQT	WHO Prequalification Team
UNCoLSC	United Nations Commission on Life-Saving Commodities for Women and Children
WHO	World Health Organization

2. Background

The United Nations Commission on Life-Saving Commodities for Women and Children (UNCoLSC) was set up in response to the call in the UN Secretary-General's Global Strategy for Women's and Children's Health for increasing access to and appropriate use of medicines, medical devices and health supplies that effectively address leading avoidable causes of death during pregnancy, childbirth and childhood. The Commission's report, published on 26 September 2012, identified 13 essential and overlooked commodities that, if more widely accessed and properly used, could save the lives of millions of women and children and made 10 recommendations for how to get these commodities to those who need them most.

The target commodities include:

Maternal health commodities

1. Oxytocin injection 10IU, 1mL – *post-partum haemorrhage*
2. Misoprostol 200µg tablet – *post-partum haemorrhage*
3. Magnesium sulfate injection 500mg/mL, 2mL, 5mL and 10mL ampoules – *eclampsia and severe pre-eclampsia*
    a. ± Calcium gluconate injection 100 mg/mL in 10-mL ampoule (*for treatment of magnesium toxicity*)

Newborn health commodities

4. Injectable antibiotics – *newborn sepsis*
    a. Gentamicin injection 40mg/mL in 1mL ampoules or 2mL ampoules (80mg/2mL)
    b. Gentamicin injection 20mg/mL in 1mL ampoules.
    c. Gentamicin injection 10mg/mL in 2mL ampoules (20mg/2mL)
    d. Procaine benzylpenicillin injection 1g in a vial (*1g is equivalent to 1 000 000 IU, i.e. 1 MIU; water suspensions or powder for suspension)*
    e. Ceftriaxone injection 250mg, 500mg or 1g in a vial
    f. Ampicillin injection 250mg, 500mg or 1g in a vial
5. Antenatal corticosteroids – *preterm respiratory distress syndrome*
    a. Betamethasone injection 5.7mg/mL (3mg/mL as betamethasone sodium phosphate + 2.7mg/mL as betamethasone acetate) in 1mL ampoule (aqueous vehicle)
    b. Betamethasone injection 4mg/mL in 1mL or 8mg in 2 mL ampoules (as betamethasone phosphate disodium salt)
    c. Dexamethasone injection 4mg/mL in 1mL ampoules (as dexamethasone phosphate disodium salt)
6. Chlorhexidine digluconate gel or solution containing 4% chlorhexidine (i.e. 7.1% chlorhexidine digluconate) – *newborn cord care*
7. Resuscitation devices – *newborn asphyxia*
    a. Resuscitator manual, Neonatal with mask, bag and valve
    b. Electric suction pump less than 100mm Hg, 1 bottle
    c. Suction catheter, CH08, l50 cm, conical tip
    d. Suction bulb

Child health commodities

8. Amoxicillin 250mg or 500mg dispersible tablet – *pneumonia*
9. oral rehydration salts (ORS) – *diarrhoea*
10. Zinc sulfate – *diarrhoea*
    a. 10mg or 20mg dispersible tablet
    b. 10mg/5mL syrup

Reproductive health commodities

11. Female condoms – *family planning/ contraception*
12. Contraceptive implants –*family planning/ contraception*
    a. Levonorgestrel 75mg/rod x 2 rods implant
    b. Etonogestrel 68mg /rod x 1 rod implant
13. Emergency contraception – *family planning/ contraception*
    a. Levonorgestrel 1.5mg or 0.75mg tablet
    b. Ulipristal acetate 30mg tablet
    c. Mifepristone 10mg or 25mg tablet

UNCoLSC focuses on 49 world's poorest countries identified under the "Every Woman Every Child" (EWEC) movement, i.e.:

Afghanistan, Bangladesh, Benin, Burkina Faso, Burundi, Cambodia, Central African Republic, Chad, Comoros, Democratic Republic of Congo, Côte d'Ivoire, Eritrea, Ethiopia, The Gambia, Ghana, Guinea, Guinea-Bissau, Haiti, Kenya, Democratic Republic of Korea, Kyrgyz Republic, Lao PDR, Liberia, Madagascar, Malawi, Mali, Mauritania, Mozambique, Myanmar, Nepal, Niger, Nigeria, Pakistan, Papua New Guinea, Rwanda, Sao Tome and Principe, Senegal, Sierra Leone, Solomon Islands, Somalia, Tajikistan, Tanzania, Togo, Uganda, Uzbekistan, Viet Nam, Yemen, Zambia and Zimbabwe.

UNCoLSC recommendation No. 4, for which WHO Prequalification of Medicines Programme is responsible, relates to quality strengthening and requests to identify manufacturers of quality-certified and affordable products. The target is to ensure that, by 2015, quality-certified and affordable products from at least three manufacturers per commodity are marketed in each of 49 countries.

One of the first activities under this recommendation is to perform an initial quality survey of the most commonly available forms of the life-saving medicines in selected EWEC countries.

3. Objectives

This quality survey focuses on medicines defined as target commodities in the UNCoLSC project and primarily aims to identify products which are of good quality (or the quality of which can be improved in short period of time). The quality of identified products will be further verified through the evaluation of level of compliance of identified manufacturers with Good Manufacturing Practices (GMP) and assessment of products' dossiers and, in case of need, technical assistance will be provided to promising manufacturers.

The secondary objective of the survey is to evaluate the quality of products currently available in selected countries at the first level of distribution chain (e.g. central medical stores, non-governmental organizations (NGO) central stores, warehouses of importers or major distributors).

The results of this survey are expected also to assist responsible authorities in the surveyed countries in meeting the target mentioned above and may be informative to the authorities of other EWEC countries.

Limitations of the survey

Due to time and resource constraints and the need to focus on the objectives of the UNCoLSC project, this survey cannot evaluate quality of target medicines throughout the distribution chain to assess the effect of storage and transportation conditions and evaluate the risk of patients' exposure to substandard medicines.

It is obvious that the survey findings will be relevant only to tested samples and extrapolation to other produced batches (or even within a tested batch) will be limited. Therefore any conclusion on quality of products will be done in conjunction with outcomes of evaluation of manufacturers' GMP compliance and assessment of products' dossiers.

4. Methodology

4.1 Selection of medicines and countries for sampling and testing

This survey is focusing on medicines included among target commodities of UNCoLSC project, not on medical devices.

To optimize use of resources available for this survey benefit-risk analysis has been performed. Based on it, medicines deemed to be of assured quality because of production in stringent regulatory systems as well as those which are already in focus of international NGOs or other organizations are not involved in laboratory testing. Also some low-risk medicines such as oral rehydration salts are excluded.

Search on availability of targeted medicines was performed in medicines registers of 13 EWEC countries. In the case of Kenya, Madagascar and Uganda registers were downloaded from the National Medicines Regulatory Authority (NMRA) website, for Viet Nam the MIMS Drug Information System[1] was searched, and registers from Burkina Faso, Democratic Republic of Congo, Kyrgyzstan, Nigeria, Senegal, Tajikistan, Tanzania, Uzbekistan and Zimbabwe were obtained from the respective NMRAs with help of WHO regional offices.

Based on the information gathered, it was decided that quality testing would not be performed on the following products:

- In the case of **ulipristal acetate 30mg tablets** and **etonogestrel 68mg/rod implant**, only innovator products are available. As the respective innovator companies (HRA Pharma, France and N.V. Organon, Netherlands) are under stringent regulatory supervision, these products do not need to be included in the quality survey.
- For **levonorgestrel 75mg/rod implant**, either the product from the innovator company (Bayer Schering, Finland) is available or the product from Shanghai Dahua Pharmaceutical Co. Ltd China, the development of which was supported by the organization fhi360. The first one is well under control and the second one is currently under WHO review. Because of that none of these products is included in this quality survey.
- Production of good quality **misoprostol 200µg tablets** has been in long term focus of the Concept Foundation. In 2011 Concept Foundation performed a quality survey of misoprostol products and identified potential causes of substandard quality. They are currently working with six manufacturers on improvement of their production of misoprostol tablets. None of these manufacturers is placing yet the improved product on the market. It is considered that potential suppliers of good quality misoprostol tablets are already under control and there is no need to include misoprostol tablets in this quality survey.
- **Calcium gluconate injection 100mg/mL** is recommended to be used for treatment of magnesium toxicity when magnesium sulfate injection is used for treatment of eclampsia. Therefore both products are recommended to be co-packed. Because of that calcium gluconate

[1] http://www.mims.com/

injection will not be tested in this phase of the project. When a manufacturer of good quality magnesium sulfate injection will be identified, negotiations will be initiated regarding possible production of combined product with calcium gluconate injection.

For the other medicines from the list of UNCoLSC target commodities a risk assessment has been performed based on:

- Estimate of probability of occurrence of a quality problem (taking into account complexity of manufacture, stability of product, suitability of specifications to control potential problems),
- Exposure of patients to the product (way of dispensing and extent of exposed population), and
- Seriousness of potential harm (vulnerability of target population, risks related to product′s dosage form and route of administration and to therapeutic properties, such as therapeutic index, risk of therapeutic failure, acute versus chronic use, development of resistance).

The outcomes of this risk assessment are provided in Annex 1.

Based on the risk assessment outcomes and on additional market information, the following two medicines with the lowest risk score were excluded from the sampling and testing. In case need emerges in the future, they can be tested later.

- **Chlorhexidine** digluconate gel or solution containing 4% chlorhexidine (i.e. 7.1% chlorhexidine digluconate) is a new formulation which has been submitted by PATH on behalf of the Chlorhexidine Working Group (CWG) to WHO Expert Committee on the Selection and Use of Essential Medicines for inclusion in the WHO Model List of Essential Medicines.[2] The product is available from Lomus Pharmaceuticals in Nepal. In 2012 UNICEF Supply Division procured Chlorhexidine digluconate 7.1% solution from Galentic Pharma Pvt. Ltd., India. In addition Purna Pharma, Belgium and Sirmaxo Pharma, India are also suppliers of 5% chlorhexidine through UNICEF Supply Division and indicate their willingness to start producing 7.1% chlorhexidine digluconate when demand for this product increases. CWG is also encouraging local manufacture of chlorhexidine for umbilical cord care in low and middle income countries to increase product availability. Therefore it is considered that potential suppliers of this product have been already identified and CWG is following the availability of this product.
- For **Oral Rehydration Salts**, most of the products registered in screened countries were products with composition slightly different from the composition recommended by WHO and UNICEF[3] since 2006 (2.6g/l sodium chloride + 13.5g/l glucose anhydrous + 1.5g/l potassium chloride + 2.9g/l trisodium citrate dehydrate; total osmolarity 245mOsmol/l). The identified companies, Cosmos Kenya, Medipharm Industries Ltd Uganda, Shelys Tanzania and CHI Pharmaceuticals Nigeria, which produce newly recommended low osmolarity composition may be inspected in connection with other products of interest within UNCoLSC. Thus the verification of quality by laboratory testing is not considered necessary at this phase of the project.

Taking into account the above considerations and availability, the following medicines were selected for sampling and testing within this survey (focusing **only** on specified dosage forms and strengths):

- Oxytocin injection 10IU (if not available, then a lower strength) in 1mL ampoules

[2] http://www.who.int/entity/selection_medicines/committees/expert/19/applications/chlorhexidine/en/index.html
[3] http://www.who.int/entity/maternal_child_adolescent/documents/fch_cah_06_1/en/

- Magnesium sulfate injection 500mg/mL (if not available, then a lower strength) in 2mL, 5mL or 10mL ampoules
- Gentamicin injection 40mg/mL or 20mg/mL or 10mg/mL in 1mL or 2mL ampoules
- Procaine benzylpenicillin injection 1 MIU (= 1g) in a vial (if not available, then 3 MIU); *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 5.7mg/mL (3mg/mL as betamethasone sodium phosphate + 2.7mg/mL as betamethasone acetate) in 1 mL ampoules or 4mg/mL (as betamethasone sodium phosphate) in 1mL or 2 mL ampoules
- Dexamethasone injection 4mg/mL (as dexamethasone sodium phosphate) in 1mL ampoules
- Amoxicillin 250mg or 500mg (if not available, then a lower strength) dispersible tablet
- Zinc sulfate 10mg or 20mg dispersible tablet or 10mg/5mL syrup
- Levonorgestrel 1.5 mg or 0.75mg tablet
- Mifepristone 10mg or 25mg tablet.

Countries for collection of samples have been selected from 49 EWEC countries having in mind the following:

- Countries should have on the market majority of selected medicines and higher number of registered products on the market would make sampling feasible;
- Countries with longer experience in medicines regulation may have on their markets good quality products which can be recommended for use and registration in other countries;
- Countries from various geographic regions should be represented;
- Countries where the NMRA is willing to cooperate in collection of samples for the project should be selected.

Based on the information gathered and considering advice from other WHO HQ units as well as WHO regional and country offices the following countries were selected for collection of samples:

- Burkina Faso
- Kenya
- Madagascar
- Nepal
- Nigeria
- Tajikistan
- Tanzania
- Uganda
- Viet Nam
- Zimbabwe.

NMRAs of the selected countries were contacted, requested to cooperate within the survey, identify a focal person for this survey and notify him/her to WHO-PQ focal point.[4] Appropriate arrangements with the NMRAs in selected countries regarding cooperation and reimbursement of activities done by NMRAs were agreed.

Nominated focal persons in countries are responsible for:

- Identification of the appropriate sampling sites and preparation of the list of products available in the country for surveyed medicines,
- Preparation of a national sampling plan (see Annex 2),
- Organization of sampling in the country and transportation of samples to the pre-specified testing laboratories,
- Participation in analysis of outcomes of quality monitoring of products and recommendation of corrective actions in the country, if necessary.

Before national sampling plans are finalized and sampling starts, a meeting has been organized by PQT with participation of focal persons from the selected countries to

- Explain the UNCoLSC project and quality survey,
- Discuss and, if needed, modify the survey protocol to reflect local conditions,
- Discuss availability and quality of selected medicines in the respective countries and finalize national sampling plans,
- Provide detailed instructions for collection and transportation of samples.

4.2 Survey period

The preparatory work on the survey started in March 2013. The survey should be completed in the beginning of 2014 as indicated in Table 1.

[4] Dr Jitka Sabartova - e-mail: sabartovaj@who.int, phone: +41 22 7913376, fax: +41 22 7914730. World Health Organization, HIS/EMP/QSM, Prequalification of Medicines Programme, 20 Avenue Appia, CH-1211 Geneva 27, Switzerland.

Table 1 Timeframe for the quality survey

Activity	Timeframe	Responsibility
• Search on availability of medicines included among UNCoLSC project target commodities in registers of EWEC countries • Risk assessment of targeted medicines	March – May 2013	PQT
• Selection of countries and medicines to be included in the quality survey	May 2013	PQT in cooperation with regional offices
• Preparation of survey protocol • Sending letters to NMRAs in selected countries • Preparation of APWs with NMRAs to cover national expenditures	May - June 2013	PQT
• Selection of laboratories for performance of tests	June 2013	PQT
• Organization of meeting with focal persons from selected countries	August 2013	PQT in cooperation with WHO office in the country where meeting takes place
• Collection of samples by NMRAs	September – November 2013	NMRAs
• Testing of samples by selected laboratories	December 2013 – April 2014	Testing laboratories
• Compilation and evaluation of results • Discussions in PQT to identify products for further quality verification within UNCoLSC project	February – June 2014	PQT
• Organization of meeting with the participating countries to discuss final results and actions needed	July 2014	PQT in cooperation with WHO office in the country where meeting takes place
• Preparation of the final report	August 2014	PQT

4.3 Selection of sample collection sites

To obtain information about the quality of products as supplied by manufacturers and avoid any influence of inappropriate storage conditions, samples will be collected at the first level of distribution chain, e.g. in central medical stores, NGO central stores, warehouses of importers or major distributors or other facilities supplied directly within various programmes.

Focal persons in selected countries have identified sites at the first level of distribution chain where medicines selected for this survey can be collected and prepared the lists of products which were available in these sites for selected medicines. These lists have been discussed in the meeting with focal persons.

4.4 Sample collection

For the purposes of this project, a sample means an item collected from each medicine's presentation (identified by the name, content of APIs, dosage form, strength, batch number and manufacturer) at the same collection site. That means that a product of the same name, content of APIs, the same dosage form, strength, batch and from the same manufacturer collected in two different sites represents two samples.

Samples will be collected by the staff of NMRA in the respective country. Samples should be collected in the countries during the second half of August 2013 and sent to testing laboratories by 6 September 2013.

In principle, three samples should be collected per each of the 12 selected medicines in each country and total number of samples per country should not exceed 36 samples.

Number of dosage units to be collected per sample is specified for each medicine in the national sampling plan template (Annex 2). As only unopened original packages shall be collected, the number of units per sample will be dependent on the pack size. If there is less tablets available for the particular batch than requested, sample should not be collected and another batch should be selected.

To fulfil the objectives of this quality survey, samples from as many manufacturers as possible should be collected. The following principles should be applied when selecting products for sampling:

- Only dosage forms and strengths specified in the list of medicines for sampling will be collected,
- If there are more strengths or pack sizes per a medicine recommended within the project and available for the particular product in the country, it is sufficient to collect one of them. In principle, the lower strengths and biggest pack sizes should be collected.
- Samples of products from various manufacturers should be collected rather than several batches produced by one manufacturer. If more than three brands are available for sampling:
    - the most likely quality assured products should be collected, but
    - it is not necessary to collect samples from products manufactured in countries with stringent regulatory systems.

  The selection of products for sampling has been discussed in detail in the meeting of focal persons.

Based on the information prepared by focal persons on products available at identified sample collection sites, specific products to be sampled in each country has been discussed in the meeting with focal persons and national sampling plans have been finalized.

Sampling will be recorded using the sample collection form (Annex 3). Whenever the required information is not available, it should be indicated by "NA" in the appropriate space on the sample collection form, where also any abnormalities should be recorded. In order to avoid confusion, each sample will be identified by a unique sample code (for coding system see the sample collection form, Annex 3) specified in the sample collection form as well as on all the original packages belonging to the respective sample (legible and not covering basic sample information). Packages belonging to one sample and sample collection form will be kept together (e.g. inserted in a dedicated envelope/bag/sack marked with the appropriate sample code and trade name of the product).

During sample collection the storage conditions at the site should be evaluated and described in the sample collection form (see Annex 3).

Collected samples should be taken to the NMRA as quickly as possible and time period when they are kept outside the conditions recommended by the manufacturer should be short. For oxytocin injection it is recommended to use cold box for transportation from sampling sites to NMRA premises.

In the case that manufacturer's batch certificates of analysis are available, the copy should be collected with samples and kept with the sample collection form. Any other available results of analysis of the collected batch (pre- or post-shipment, testing by procurers or NMRAs) should also be collected with samples and kept with the sample collection form.

Detailed instructions for collection of samples are listed in Annex 2. The focal person in each country will arrange for training of collectors to be familiar with the national sampling plan and detailed instructions for collection of samples and ensure that they are adhered to.

4.5 Storage and dispatch of samples

- The samples should be kept in the original packaging and under storage conditions specified on the label. Because of different labelled storage conditions for oxytocin products, it is recommendable to keep all oxytocin samples between 2°C and 8°C.
- For transportation all samples should be packed adequately and transported in such a way as to avoid damage and contamination during transportation. Any residual space in the container should be filled with a suitable material.
- A packing list should be prepared listing all samples in the shipment (product names, manufacturers, batch numbers and exact quantities). If more than one parcel/box is used, a packing list should be prepared showing the contents of each parcel/box.
- Each shipment should be accompanied by the following documents (further referred to as "accompanying documents"):
  - A simple covering letter,
  - Packing list(s),
  - Copies of sample collection forms and,
  - Copies of manufacturer's and any other available certificates of analysis, if accessible (in the case that search for these certificates would delay dispatch of samples, they may be sent to testing laboratories and WHO contact point separately later).
- Samples with the accompanying documents should be sent straightforward to the assigned testing laboratories **by a courier service**.
  - For each shipment it should be clearly indicated that samples are sent for laboratory testing purposes only, will not be used on humans or animals, have no commercial value and will not be placed on the market. Low price just for customs purposes should be indicated to avoid problems with the customs clearance.
  - As there may be slight differences among storage conditions for products with the same API from different manufacturers, the following transportation conditions should be requested from the courier service:
    - Freezing of all samples has to be avoided
    - Tablets and powders for injection should be kept below 25°C
    - Injections should be kept between 2°C and 8°C
- The contact points in laboratories and in WHO[4] should be informed about the shipment and the tracking number as provided by the courier service.

4.6 Records on collection and dispatch of samples

Records on collection and dispatch of samples are the following:

- National sampling plan,
- Accompanying documents (covering letter, packing list(s), copies of sample collection forms and, copies of manufacturer's and any other available certificates of analysis, if accessible),
- Shipment documents.

Three sets of these records should be prepared:

- One set of records is retained by the NMRA,
- Second set should be sent to WHO contact point,[4]

- Third set should be sent together with samples to the contact points in the respective laboratories. It is not necessary to send national sampling plan to each testing laboratory.

4.7 Testing laboratories

Three WHO-prequalified quality control laboratories were selected for testing of samples collected within this survey: InphA GmbH - Institute for Pharmaceutical and Applied Analytics, Official Medicines Control Laboratory (OMCL), Bremen, Germany; National Quality Control Laboratory (NQCL), Nairobi, Kenya; and SGS Lab Simon S.A., Wavre, Belgium. Table 2 shows the division of samples among laboratories.

Table 2 Laboratories performing quality testing

Testing laboratory	**Address**	**Medicines tested**
InphA GmbH Institute for Pharmaceutical and Applied Analytics, Official Medicines Control Laboratory (OMCL), Bremen, Germany	Emil-Sommer-Str. 7 D-28329 Bremen GERMANY	Oxytocin injection Procaine benzylpenicillin injection Ampicillin injection Ceftriaxone injection Betamethasone injection Levonorgestrel tablet Mifepristone tablet
National Quality Control Laboratory (NQCL), Nairobi, Kenya	Hospital Road KNH Complex School of Pharmacy Building, 2nd Floor P.O. Box 29726-00202 – KNH Nairobi KENYA	Magnesium sulfate injection Dexamethasone injection Amoxicillin dispersible tablet Zinc sulfate dispersible tablet or syrup
SGS Lab Simon S.A., Wavre, Belgium	Vieux Chemin du Poète 10 B-1301 Wavre BELGIUM	Gentamicin injection

WHO Prequalification of Medicines Programme will cover all testing costs.

4.8 Tests to be conducted

Laboratory testing of all collected samples will be performed according to the testing protocol agreed with the testing laboratories (Annex 4).

In principle, the following tests are included depending on formulation and specifications:

- Appearance
- Identification
- Assay
- Test for related substances
- For tablets – uniformity of mass (weight variation) / content uniformity, disintegration / dissolution, fineness of dispersion
- For syrups – pH, specific gravity (relative density)
- For injections – pH, extractable volume, visual inspection
- For powders for injection – uniformity of mass, water content, pH after reconstitution

Given that sterility testing can never provide 100% certainty about the sterility of the batch and is resource demanding, and that quality of identified products will be further verified within GMP inspections, sterility test is not included in this survey. For similar reasons and because there are only small volume parenteral products selected for this survey, test for bacterial endotoxins is not included as well.

4.9 Test methods and specifications

Testing methods and specifications are compendial methods of the International Pharmacopoeia or British Pharmacopoeia or US Pharmacopoeia. When a monograph is available in more pharmacopoeias, the ability of the respective specifications and methods to reveal quality problems has been considered and the monograph was selected accordingly. In some cases tests from another pharmacopoeia were added to provide more complete picture about the quality of a particular medicine. Detailed testing protocol is attached as Annex 4.

4.10 Receipt and testing of samples by a testing laboratory

The testing laboratories should ensure that:

- Each sample will be inspected to ensure that the labelling is in conformance with the information contained in the sample collection form. An electronic databank (photos of tablets and packaging) is recommended;
- Samples are stored according to the respective label requirements;
- Quality testing is conducted in line with this protocol, with the agreed testing protocol and in compliance with WHO standards recommended for quality control laboratories;[5]
- Analytical Test Reports (Annex 5) are prepared. In the case that non-compliant results are found and confirmed after application of a laboratory out-of-specification procedure, they are reported without delay to WHO contact point;[4]
- Records of testing of each sample, accompanying document/s and retention samples are kept for at least six months if the sample complied with the analytical test requirements, or for at least one year or until the expiry date (whichever is longer) if it did not comply.

5. Data management, analysis and publication

Any non-compliant result found in the survey will be communicated without delay and investigated with the respective NMRA and manufacturer.

The testing results will be provided to all NMRAs involved in the survey. The outcomes of the survey will be discussed by national authorities and WHO, and corrective actions, if necessary, will be recommended. The 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.

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[5] Good practices for pharmaceutical quality control laboratories. In: *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty fourth report. Geneva, World Health Organization. WHO Technical Report Series, No. 957, 2010, Annex 1.
http://www.who.int/prequal/info_general/documents/TRS957/GPCL_TRS957_Annex1.pdf

Annex 1 to Survey protocol

Risk assessment of targeted medicines

Scale: 0=low risk, 1=medium risk, 2=high risk

	Problem occurrence - probability			Exposure		Potential harm			**Risk score**
	Complexity of manufacture	Stability	Specifications controlling potential problems	Way of dispensing	Extent of exposed population	Vulnerability of target population	Dosage form and administration	Therapeutic properties (therapeutic index, risk of therapeutic failure, acute vs chronic use, resistance)	
Oxytocin injection 10IU, 1mL	2	2	1	2	1	2	1	2	**13**
Ampicillin injection 250mg, 500mg or 1g in a vial	2	2	1	1.5	0.5	2	1	1.5	**11.5**
Gentamicin injection 40mg/mL in 1mL or 2mL ampoules or 20mg/mL in 1mL ampoules or 10mg/mL in 2mL ampoules (20mg/2mL)	2	1	1	1.5	0.5	2	1	2	**11**
Procaine benzylpenicillin injection 1g in a vial (1000000 IU)	2	1	1	1.5	0.5	2	1	2	**11**
Ceftriaxone injection 250mg, 500mg or 1g in a vial	2	1	1	1.5	0.5	2	1	1.5	**10.5**
Betamethasone injection 5.7mg/mL (3mg/mL as betamethasone sodium phosphate + 2.7mg/mL as betamethasone acetate) in 1mL ampoule or 4mg/mL in 1mL or 8mg in 2 mL	2	1	1	1.5	0	2	1	1	**9.5**

	Problem occurrence - probability			Exposure		Potential harm			**Risk score**
	Complexity of manufacture	Stability	Specifications controlling potential problems	Way of dispensing	Extent of exposed population	Vulnerability of target population	Dosage form and administration	Therapeutic properties (therapeutic index, risk of therapeutic failure, acute vs chronic use, resistance)	
ampoules (as betamethasone phosphate disodium salt)									
Dexamethasone injection 4mg/mL in 1mL ampoules (as dexamethasone phosphate disodium salt)	2	1	1	1.5	0	2	1	1	**9.5**
Amoxicillin dispersible tablet 250mg or 500mg	1	2	1	1	1	2	0	1	**9**
Magnesium sulfate injection 500mg/mL, 2mL and 10mL ampoules	1	1	1	1.5	0	2	1	0	**7.5**
Zinc sulfate dispersible tablet 10mg or 20mg or **Zinc sulfate syrup** 10mg/5mL	1	1	1	1	2	1	0	0	**7**
Levonorgestrel tablet 1.5 mg or 0.75 mg	1.5	1	1	0.5	1	0.5	0	1	**6.5**
Mifepristone tablet 10mg or 25mg	1	1	1	0.5	1	0.5	0	1	**6**
Oral rehydration salts	0	1	1	0	2	1	0	0	**5**
Chlorhexidine gel 4%	1	0	0	0	2	1	0	0	**4**
Chlorhexidine solution 4%	0.5	0	0	0	2	1	0	0	**3.5**

Annex 2 to Survey protocol

National Sampling Plan

Country: _____

Focal Person: _____

MEDICINES TO BE COLLECTED (*please, focus **only** on specified dosage forms and strengths, if more strengths are available for the particular product, it is not necessary to collect all of them*):

- Oxytocin injection 10IU (in 1mL ampoule)
- Magnesium sulfate injection 500mg/mL (in 2mL or 5mL or 10mL ampoule)
- Gentamicin 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 (1000000 IU) in a vial
- Ampicillin injection 250mg, 500mg or 1g in a vial
- Ceftriaxone injection 250mg, 500mg or 1g in a vial
- Betamethasone injection
    - 5.7mg/mL (3mg/mL as betamethasone sodium phosphate + 2.7mg/mL as betamethasone acetate) in 1 mL ampoule (aqueous injection) or
    - 4mg/mL in 1mL ampoule or 8mg in 2 mL 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 or 25mg tablet

NAMES AND ADDRESSES OF THE SITES, WHERE SAMPLES SHALL BE COLLECTED (first level of distribution chain, e.g. in central medical stores, NGO central stores, warehouses of importers):

	Facility name	**Address**	**Facility type** 1. Private / public 2. CMS / NGO / importer/…
1.			
2.			
3.			
4.			
5.			

NUMBER OF SAMPLES TO BE COLLECTED PER PRODUCT:

In principle, **three samples should be collected per each of the 12 selected products in each country.**

TOTAL NUMBER OF SAMPLES PER COUNTRY:

Total number of samples per country **should not exceed 36 samples**.

NUMBER OF UNITS TO BE COLLECTED PER SAMPLE**:**

Numbers of units to be collected per sample are **specified for individual medicines in the form below.**

Medicine Dosage form	Strength	Minimum no. of units to be collected per sample	Manufacturer	Sampling site	Batch no	Pack size	No. of units collected per sample	Sample code
Oxytocin inj. 10IU (if not available, collect 5IU)	10IU	30 ampoules						
	10IU	30 ampoules						
	10IU	30 ampoules						
Magnesium sulfate inj. 500mg/mL	500mg/mL	15 ampoules						
	500mg/mL	15 ampoules						
	500mg/mL	15 ampoules						
Gentamicin inj. • **40mg/1mL or** • **80mg/2mL or** • **20mg/1mL or** • **20mg/2mL**		44 ampoules of 1mL 25 ampoules of 2mL						
		44 ampoules of 1mL 25 ampoules of 2mL						
		44 ampoules of 1mL 25 ampoules of 2mL						
Procaine benzylpenicillin inj. 1g (=1000000 IU) in a vial	1g in a vial	20 vials						
	1g in a vial	20 vials						
	1g in a vial	20 vials						
Ampicillin inj. 250mg, 500mg or 1g in a vial		20 vials						
		20 vials						
		20 vials						
Ceftriaxone inj. 250mg, 500mg or 1g in a vial		20 vials						
		20 vials						
		20 vials						

Medicine Dosage form	Strength	Minimum no. of units to be collected per sample	Manufacturer	Sampling site	Batch no	Pack size	No. of units collected per sample	Sample code
Betamethasone inj. • **5.7mg/1mL** (3mg/mL as betamethasone sodium phosphate + 2.7mg/mL as betamethasone acetate) • **4mg/1mL or 8mg/2mL** (as betamethasone sodium phosphate)		30 ampoules						
		30 ampoules						
		30 ampoules						
Dexamethasone inj. 4mg/1mL (as dexamethasone phosphate disodium salt)	4mg/1mL	30 ampoules						
	4mg/1mL	30 ampoules						
	4mg/1mL	30 ampoules						
Amoxicillin 250mg or 500mg dispersible tablet		100 tablets						
		100 tablets						
		100 tablets						
Zinc sulfate 10mg or 20mg dispersible tablet **or** **10mg/5mL syrup**		100 tablets or 5 bottles						
		100 tablets or 5 bottles						
		100 tablets or 5 bottles						
Levonorgestrel 1.5 mg or 0.75mg tablet		60 tablets						
		60 tablets						
		60 tablets						
Mifepristone 10mg or 25mg tablet		60 tablets						
		60 tablets						
		60 tablets						

INSTRUCTIONS FOR COLLECTORS:

- An item collected from a medicine (identified by the name, content of APIs, dosage form, strength, batch number and manufacturer) at the same collection site is called a sample. **All dosage units of one sample must be of the same batch**, there should not be a mix-up with batches. In the case that in a collection site the required number of packages of the same batch is not available, sample of that particular medicine is not collected from that site.
- **Only dosage forms and strengths specified** in the list of medicines for sampling will be collected.
- If there are more strengths or pack sizes per a medicine recommended within the project and available for the particular product in the country, it is sufficient to collect one of them. In principle, the lower strengths and biggest pack sizes should be collected.
- **Samples of products from various manufacturers should be collected** rather than several batches produced by one manufacturer. If more than three brands are available for sampling:
    - the most likely quality assured products should be collected,
    - it is not necessary to collect samples from products manufactured in countries with stringent regulatory systems.
- Samples collected shall have **at least six months remaining to expiry**. Products with shorter period remaining to expiry date will not be collected.
- **Only unopened original packages shall be collected**.
- Medicine **samples shall not be taken out of the original primary packaging and outer containers** (though removal of blisters from large secondary packs is appropriate). Containers such as **bottles shall not be opened**.
- **Sampling shall be recorded using the sample collection form** (Annex 3). Whenever the required information is not available, it should be indicated by "NA" in the appropriate space on the sample collection form. Any abnormalities should be recorded.
- Each sample will be identified by a **unique sample code** (for coding system see the sample collection form, Annex 3) **specified in the sample collection form as well as on all the original packages belonging to the respective sample** (legible and not covering basic sample information). Packages belonging to one sample and sample collection form will be kept together (e.g. blisters inserted in a dedicated envelope marked with the appropriate sample code and trade name of the product).
- During sample collection the **storage conditions at the site should be evaluated** and described in the sample collection form (see Annex 3). The **date when the batch sampled was received at the sampling site** should be established and recorded in the sample collection form, with relevant documentary evidence, if available.
- Manufacturer's batch **certificates of analysis** will be collected with samples, if available, and kept with the sample collection form. Any other available results of analysis of the collected batch (pre- or post-shipment, testing by procurers or NMRAs) should also be collected with samples and kept with the sample collection form. In case that search for these certificates would delay dispatch of samples, they may be sent to testing laboratories and WHO contact point separately later.
- The **samples should be collected and kept under controlled conditions**, as per label requirements. Collected samples should be taken to the NMRA as quickly as possible and time period when they are kept outside the conditions recommended by the manufacturer should be short. **For oxytocin injection it is recommended to use cold box for transportation from sampling sites to NMRA premises.**
- Samples should be collected in all the countries involved during the second half of August 2013 and the **deadline for sending the last sample to the testing laboratories is 6 September 2013**.

For the instructions for shipment of samples to the testing laboratories, please see Section 4.5 of the protocol.

Annex 3 to Survey protocol

Sample Collection Form*

Country: _____ **Sample code:** _____

(Country code/product abbreviation/sequence number/sampling date ddmmyy)**

Name of location/place where sample was taken:_____

_____

Address (with telephone, fax number and email address, if applicable):

_____

_____

Organization and names of people who took samples:

1. _____

2. _____

Product name of the sample: _____

Name of active pharmaceutical ingredient(s) (INN) with strength:

_____

Dosage form: _____

Package size, type and packaging material of the container: _____

_____

Batch/lot number: _____

Date of manufacture: _____ Expiry date: _____

Regulatory status in the country, registration number, if applicable: _____

_____

Name and address of the manufacturer: _____

_____

Quantity collected (number of tablets and blisters):

_____

Initialise first page:

Product name: _____ **Sample code:** _____

* This sample collection form should always be kept with the sample collected.

** Country codes: Burkina Faso = BF, Kenya = KE, Madagascar = MG, Nepal = NP, Nigeria = NG, Tanzania = TZ, Uganda = UG, Tajikistan = TJ, Viet Nam = VN, Zimbabwe = ZW

Medicines abbreviations: Amoxicillin = AMX, Ampicillin = AMP, Betamethasone = BET, Ceftriaxone = CEF, Dexamethasone = DEX, Gentamicin = GEN, Levonorgestrel = LNG, Magnesium sulfate = MS, Mifepristone = MIF, Oxytocin = OXT, Procaine benzylpenicillin = PBP, Zinc sulfate = ZS

Sample code system can be extended to be appropriate for a particular country collection system.

Date the batch was received at the location:

Storage conditions at the sampling site:

Conditions controlled: Yes No

Temperature and humidity at the place where the sample was stored (at the time of sample collection):

Abnormalities, remarks, observations:

Date:

Signature of person(s) taking samples

1. .....

2. .....

Signature of representative of the establishment where sample(s) was taken (optional)

.....

Note: Samples collected must remain in their original primary packaging, intact and unopened

Annex 4 to Survey protocol

Testing Protocol

	Product	*Tests to be performed and specifications for testing*
1.	**Oxytocin injection** 10IU, 5IU	**Ph. Int.** • Appearance • Identity - HPLC (test B) • pH – 3.0-5.0 • Extractable volume • Assay – HPLC, 90.0-110.0% • Related substances – HPLC, not more than 1 peak above 2%, no peak above 5%
2.	**Magnesium sulfate injection** 500mg of magnesium sulfate heptahydrate/mL	**Ph. Int.** • Appearance • Identity –tests A + B • pH - 5.5-7.0 • Assay – complexometric titration, 90.0-110.0%
3.	**Gentamicin injection/** 40mg/mL, 20mg/mL or 10mg/mL (as gentamicin sulfate)	**BP** • Appearance • Identity – HPLC (test B) • pH - 3.0-5.5 • Assay - microbiological assay, upper fiducial limit of error not less than 97.0%, lower fiducial limit of error not more than 110.0% • Composition of gentamicin sulfate – HPLC, C_1: 25.0-50.0%, C_{1a}: 10.0-35.0%, C_2+C_{2a}: 25.0-55.0%
4.	**Procaine benzylpenicillin injection** 1g of procaine benzylpenicillin in a vial (1000000 IU)	**BP (Veterinary)** • Appearance • Uniformity of mass • Identity - HPLC (confirmed within assay) • Assay – HPLC, 90.0-110.0% total penicillins calculated as procaine benzylpenicillin, procaine 36.0-44.0% of stated amount of procaine benzylpenicillin • Related substances – HPLC, 4-aminobenzoic acid not greater than 0.5%, any other secondary peak not greater than 1% **+ USP tests according to the monograph for Penicillin G procaine for injectable suspension** • Water - K.Fischer method, 2.8-4.2% • pH – 5.0 – 7.5 (after reconstitution as directed on the label)
5.	**Ampicillin injection** 250mg, 500mg or 1g of ampicillin (as ampicillin sodium) in a vial	**BP** • Appearance • Uniformity of mass • Identity – HPLC (confirmed within assay) • pH – 8.0-10.0 • Water – not more than 2.0% • Assay – HPLC, 95.0-105.0% • Related substances – HPLC, ampicillin dimer not greater than 4.5%, any other secondary peak not greater than 2%
6.	**Ceftriaxone injection** 250mg, 500mg or 1g of ceftriaxone in a vial (as ceftriaxone sodium)	**BP** • Appearance • Uniformity of mass • Identity – HPLC (test B) • pH – 6.0-8.0 • Water – not more than 11.0% • Assay – HPLC, 92.0-108.0% • Related substances – HPLC, any secondary peak not greater than 1%, sum of secondary peaks not greater than 5%

	Product	*Tests to be performed and specifications for testing*
7.	**Betamethasone injection** • 5.7mg of betamethasone/mL suspension (as 3.9 mg/mL betamethasone sodium phosphate + 3mg/mL betamethasone acetate) or • 4mg of betametha-sone/mL solution (as betamethasone sodium phosphate)	**USP monograph for Betamethasone sodium phosphate and betamethasone acetate injectable suspension** • Appearance • Identity – TLC (tests A+B) • pH - 6.8-7.2 • Extractable volume • Assay - HPLC, 90.0-115.0% of betamethasone (as betamethasone sodium phosphate) and 90.0-115.0% of betamethasone acetate **BP monograph for Betamethasone injection** • Appearance • Identity – HPLC (confirmed within assay) • pH - 8.0-9.0 • Extractable volume • Assay – HPLC, 92.5-107.5% • Related substances – HPLC, betamethasone not greater than 2.6%, any other secondary peak not greater than 3%, sum of all the secondary peaks not greater than 5%
8.	**Dexamethasone injection** 4mg of dexamethasone phosphate/mL (as dexamethasone sodium phosphate)	**BP monograph for Dexamethasone sodium phosphate injection** • Appearance • Identity – HPLC (test B) • pH - 7.0-8.5 • Extractable volume • Assay – HPLC, 95.0-105.0% • Free dexamethasone – HPLC, not greater than 0.5%
9.	**Amoxicillin dispersible tablet** 250mg or 500mg of amoxicillin (as amoxicillin trihydrate)	**USP monograph for Amoxicillin tablets for oral suspension** • Appearance • Identity –HPLC (confirmed within assay) • Assay – HPLC, 90.0-110.0% • Weight variation • Disintegration – 3 minutes (water 20±5°C) • Dissolution - Q 80%, 30min • Dispersion fineness – sieve No. 25 - 710µm
10	**Zinc sulfate dispersible tablet** 10mg or 20mg of zinc sulfate monohydrate or **Zinc sulfate syrup** 10mg of zinc sulfate monohydrate/5mL	**USP monograph for Zinc sulfate tablets** • Appearance • Identity – tests A+B • Assay - complexometric titration, 95.0-105.0% • Disintegration – 60 seconds • Content uniformity **+ Ph. Eur. test** • Fineness of dispersion – sieve No. 25 - 710µm **USP monograph for Zinc sulfate oral solution** • Appearance • Identity –tests for zinc and sulfate • Assay - complexometric titration, 90.0-110.0% • pH –2.5-4.5 • Specific gravity – 1.18-1.24
11	**Levonorgestrel tablet** 1.5 mg or 0.75 mg	**BP** • Appearance • Identity – HPLC, tests A+B • Assay – HPLC, 95.0-105.0% • Content uniformity • Related substances – HPLC, any secondary peak not greater than 1%, sum of secondary peaks not greater than 2% **+ Ph. Int.** • Dissolution – Q 75%, 30 min
12	**Mifepristone tablet** 10mg or 25mg	**Laboratory validated methods based on methods and specifications kindly provided by one of the manufacturers of collected samples** • Appearance • Identity – HPLC (confirmed within assay) • Assay – HPLC, 90.0-110.0% • Related substances – HPLC, any secondary peak not greater than 1%, sum of secondary peaks not greater than 2% • Uniformity of mass • Disintegration – 15 minutes

Annex 5 to Survey protocol

Content of the Analytical Test Report

The Analytical Test Report shall in accordance with the Good practices for pharmaceutical quality control laboratories[•] provide the following information:

1. Name and address of the laboratory performing the sample testing,
2. Number/code of the Analytical Test Report,
3. Name and address of the originator of the request for testing,
4. Sample code from the sample collection form,
5. Date on which the sample was received,
6. Name of the country where the sample was collected,
7. Sample product name, dosage form, active ingredients, strength, package size, type and packaging material of primary container,
8. Description of the sample (both product and container),
9. Batch number of the sample, expiry date and manufacturing date, if available,
10. Name and address of the manufacturer,
11. Reference to the specifications used for testing the sample, including the limits,
12. Reference to the reference standards used for quantitative determinations,
13. Results of all the tests performed (numerical results, if applicable),
14. Conclusion whether or not the sample was found to be within the limits of the specifications used,
15. Date on which the test was performed, and
16. Signature of the head of the laboratory or authorized person.

• Good practices for pharmaceutical quality control laboratories. In: *WHO Expert Committee on Specifications for Pharmaceutical Preparations*. Forty fourth report. Geneva, World Health Organization. WHO Technical Report Series, No. 957, 2010, Annex 1.
http://www.who.int/prequal/info_general/documents/TRS957/GPCL_TRS957_Annex1.pdf

Appendix 2 Manufacturers of samples collected for individual medicines

Manufacturer	Strength	No. of batches	No. of samples	Country of collection
Oxytocin injection				
Akums Drugs and Pharmaceuticals Ltd, India	5 IU/mL	1	1	Nepal (1)
Biologici Italia Laboratories, Via F.Serpero 2, 20060 Masate, Milano, Italy	10 IU/mL	1	1	Zimbabwe (1)
Bryntsalov - A ZAO, Nagatinskaya str. 1, Moscow, Russia	5 IU/mL	1	1	Tajikistan (1)
Gedeon Richter Plc, Gyömrői út 19-21, Budapest 1103, Hungary	5 IU/mL	1	1	Tajikistan (1)
Hindustan Pharmaceuticals, Barauni - 851 112, India	5 IU/mL	1	1	Nepal (1)
Kwality Pharmaceutical (P) Ltd, Nag kalan, Majitha Road, Amritsar, India	10 IU/mL	1	1	Nigeria (1)
Ningbo Dahongying Pharmaceutical Co Ltd, No.396 Mingzhu Road, Ningbo, Zhejiang, China	10 IU/mL	2	2	Uganda (2)
Nitin Lifesciences Ltd, Rampur Road, Paonta Sahib, Sirmour - 173025, Himachal Pradesh, India	5 IU/mL	1	1	Tajikistan (1)
North China Pharmaceutical Co Ltd (NCPC), No. 217-1 East Heping Road, Shijiazhuang, Hebei, China	10 IU/mL	1	1	Madagascar (1)
Rotexmedica GmbH Arzneimittelwork, 22946 Trittau, Germany	5 IU/mL	3	3	Burkina Faso (1), Tanzania (1), Viet Nam (1)
	10 IU/mL	2	2	Nigeria (1), Zimbabwe (1)
Tablets India Ltd, 179 T.H.Road, Chennai 600081, India	5 IU/mL	1	1	Nepal (1)
Umedica Laboratories Pvt Ltd, Plot 221, GIDC, Vapi 396195, Gujarat, India	10 IU/mL	1	1	Kenya (1)
Vital Healthcare Pvt Ltd, Plot No. H-10, MIDC, Satpur Nashik-422007, India	5 IU/mL	2	2	Tanzania (2)
Zhejiang Ruixin Pharmaceuticals Co Ltd, Kaifa Road, Zhejiang, China	5 IU/mL	1	1	Burkina Faso (1)
	10 IU/mL	1	1	Uganda (1)
Zhejiang Tianfeng Pharmaceutical Factory, No. 518 Daxiang Road, Huzhou, Zhejiang (Jinling Pharmaceutical Co Ltd Group), China	10 IU/mL	1	1	Nigeria (1)
Magnesium sulfate injection				
Dalkhimfarm OAO, Str. Tashketskaya 22, Khabarovsk 680001, Russia	250mg/mL	1	1	Tajikistan (1)
Fresenius Kabi Bidiphar JS Co, Zone 8, Nhon Phu Ward, Quy Nhon City, Binh Dinh Province, Viet Nam	150mg/mL	2	2	Viet Nam (2)
Furen Pharmaceutical Group Co Ltd, (Steyuan Group), XuanWu Economic Development Area, Luyi County, Henan Province, China	500mg/mL	1	1	Nigeria (1)
Harson Laboratories, 12 R.C.Patel Industrial Estate, Akota, Baroda-390020, India	500mg/mL	1	1	Kenya (1)
Hindustan Pharmaceuticals, Barauni - 851 112, India	500mg/mL	3	3	Nepal (3)
Inresa Arzneimittel GmbH, Obere Hardtstrasse 18, 79114 Freiburg, Germany	500mg/mL	1	1	Zimbabwe (1)

Manufacturer	Strength	No. of batches	No. of samples	Country of collection
Laboratoire Aguettant, 1 rue A.Fleming, 69007 Lyon, France	150mg/mL	1	1	Viet Nam (1)
Laboratoire Renaudin, Itxassou, France	500mg/mL	1	1	Burkina Faso (1)
Lincoln Pharmaceuticals Ltd, Trimul Estate, Khatraj Chokdi, Kalol, Gandhinagar, Gujarat, India	500mg/mL	1	1	Nigeria (1)
Martindale Pharmaceuticals, Romford, Essex, Rm3 8UG, UK	500mg/mL	1	1	Nigeria (1)
Moskhimfarmpreparaty OAO, Str. Kamenshiki 9, Semashko, 115172 Moscow, Russia	250mg/mL	1	1	Tajikistan (1)
Nikopharm, str. Engels 1, Makeevka, Donetsk, Ukraine	250mg/mL	1	1	Tajikistan (1)
Pharmaceutical Solution Industry (PSI), PO Box 17476, Jeddah 21484, Saudi Arabia	500mg/mL	1	2	Tanzania (2)
Vital Healthcare Pvt Ltd, Plot No. H-10, MIDC, Satpur Nashik-422007, India	500mg/mL	1	2	Kenya (1), Uganda (1)
Gentamicin injection				
Abbott Healthcare Pvt Ltd, Plot No. 67-70, Sector II, Pithampur 454 775, Dhar, Madhay Pradesh, India	20mg/2mL	1	1	Nepal (1)
Biochem Pharmaceutical Industries Ltd, Survey No.48, Ringanwada Village, Daman (U.T.) 396 210, India	80mg/2mL	1	1	Nepal (1)
Biologici Italia Laboratories, Via F.Serpero 2, 20060 Masate, Milano, Italy	80mg/2mL	1	1	Zimbabwe (1)
CSPC OUYI (Shijiazhuang) Pharmaceuticals Co Ltd, No. 276 West Zhongshan Road, Shijiazhuang, China	80mg/2mL	4	4	Madagascar (1), Kenya (1), Tajikistan (1), Uganda (1)
Fresenius Kabi Bidiphar JS Co, Zone 8, Nhon Phu Ward, Quy Nhon City, Binh Dinh Province, Viet Nam	80mg/2mL	1	1	Viet Nam (1)
Greenfield Pharmaceutical (Jiang su) Co Ltd, No 38, Tai Jiu Road Taizhou, Jiangsu Province, China	80mg/2mL	1	1	Nigeria (1)
Hubei Tianyao Pharmaceutical Co Ltd, No 7 Dufu block, Jianshe Road, Xiangfan, China	80mg/2mL	1	1	Nigeria (1)
Intas Pharmaceuticals Ltd, Matoda-382210, Ahmedabad, India	80mg/2mL	2	2	Tanzania (1), Zimbabwe (1)
Krka d.d., Shmarjeshka cesta 6, 8000 Novo Mesto, Slovenia	40mg/1mL	1	1	Tajikistan (1)
Lek Pharmaceutical and Chemical Co d.d. Verovskova 57, 1526 Ljubljana, Slovenia	80mg/2mL	1	1	Nigeria (1)
Lincoln Pharmaceuticals Ltd, Trimul Estate, Khatraj Chokdi, Kalol, Gandhinagar, Gujarat, India	80mg/2mL	2	2	Tanzania (2)
Medis - Les Laboratoires de Médicaments Stériles SA, Route de Tunis KM7, BP 206, Nabeul 8000, Tunisia	80mg/2mL	1	1	Burkina Faso (1)
Ningbo Dahongying Pharmaceutical Co Ltd, No.396 Mingzhu Road, Ningbo, Zhejiang, China	80mg/2mL	1	1	Uganda (1)
North China Pharmaceutical Co Ltd (NCPC), No 6 Heping East Road, Huayo East Street, Shijiazhuang, Hebei, China	80mg/2mL	1	1	Madagascar (1)
Pymepharco Co, 166-170 Nguyen Hue Street, Tuy Hoa City, Phu Yen Province, Viet Nam	80mg/2mL	1	1	Viet Nam (1)
Rotexmedica GmbH, Group Panpharma, Germany	80mg/2mL	2	2	Burkina Faso (2)
Sanavita Pharmaceuticals GmbH, Lohstr. 2, 59368 Werne, Germany	80mg/2mL	1	1	Tajikistan (1)

Manufacturer	Strength	No. of batches	No. of samples	Country of collection
Shandong Reyoung Pharmaceutical Co Ltd, No. 6 Erlangshan Road, Yiyuan County, Shandong Province, China	80mg/2mL	1	1	Viet Nam (1)
Shandong (Yanzhou) Xier Kangtai Pharmaceutical Co Ltd, Private Economy Garden-Xinyan Town, Yanzhou City, Shandong, China	80mg/2mL	1	1	Kenya (1)
Square Pharmaceuticals Ltd, Pabna Unit, Pabna 6600, Bangladesh	20mg/2mL	1	1	Kenya (1)
Tablets India Ltd, 179 T.H.Road, Chennai 600081, India	80mg/2mL	1	1	Nepal (1)
Vital Healthcare Pvt Ltd, Plot No. H-10, MIDC, Satpur Nashik-422007, India	80mg/2mL	1	1	Tanzania (1)
Zhejiang Tianfeng Pharmaceutical Factory No. 518 Daxiang Road, Huzhou, Zhejiang, China	80mg/2mL	1	1	Uganda (1)
Procaine benzylpenicillin injection				
CSPC Zhongnuo Pharmaceutical (Shijazhuang) Co Ltd, 47 Fengshou Road, Shijiazhuang city, China	3 MIU + benzylpenicillin sodium 1 MIU	1	1	Uganda (1)
	1 MIU	1	1	Madagascar (1)
CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co Ltd, No.188 Gongnong Road, Shijiazhuang, Hebei, China	3 MIU + benzylpenicillin sodium 1 MIU	1	1	Tanzania (1)
North China Pharmaceutical Co Ltd (NCPC), No. 217-1 East Heping Road, Shijiazhuang, Hebei, China	1 MIU	1	1	Madagascar (1)
North China Pharmaceutical Co Ltd (NCPC), No. 388 East Heping Road, Shijiazhuang, Hebei, China	3 MIU + benzylpenicillin sodium 1 MIU	1	1	Burkina Faso (1)
Panpharma SA, France	3 MIU	1	1	Zimbabwe (1)
Ampicillin injection				
Aristo Pharmaceuticals Pvt Ltd, Plot No. 208, New Industrial Area No.2, Mandideep, District Raisen, Madhya Pradesh, India	250mg/vial	2	2	Nepal (2)
	500mg/vial	1	1	Nepal (1)
Aurobindo Pharma Ltd, Unit XII, Survey No. 314, Bachupally Village, Quthubullapur Mandal, Ranga Reddy District, Andhra Pradesh, India	500mg/vial	2	2	Uganda (1), Zimbabwe (1)
CSPC Zhongnuo Pharmaceutical (Shijazhuang) Co Ltd, 47 Fengshou Road, Shijiazhuang, China	500mg/vial	1	1	Uganda (1)
CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co Ltd, No.188 Gongnong Road, Shijiazhuang, Hebei, China	1g/vial	2	2	Madagascar (1), Nigeria (1)
	500mg/vial	1	1	Kenya (1)
Harbin General Pharmaceutical Factory, No. 109 Yuefu Road, Nangang District, Harbin, China	500mg/vial	1	1	Tanzania (1)

Manufacturer	Strength	No. of batches	No. of samples	Country of collection
Karnataka Antibiotics and Pharmaceuticals Ltd, Plot No.14. II Phase, Peenya, Bangalore 560058, India	500mg/vial	2	2	Uganda (1), Zimbabwe (1)
Lincoln Pharmaceuticals Ltd, Trimul Estate, Khatraj Chokdi, Kalol, Gandhinagar, Gujarat, India (manufactured by) *Manufactured at: Makcur Laboratories Ltd, 46/5-6-7, Village Zak, Tal. Dehgam, 382330 Gandhinagar, Gujarat, India*	500mg/vial	1	1	Tanzania (1)
Mekophar Chemical Pharmaceutical JS Co, 297/5 Ly Thuong Kiet Street, Ward 15, District 11, Ho Chi Minh City, Viet Nam	1g/vial	1	1	Viet Nam (1)
MinhDan Pharmaceutical JS Co, Lot N8-N5 Street-Hoa Xa Industrial Estate, Nam Dinh, Viet Nam	1g/vial	1	1	Viet Nam (1)
North China Pharmaceutical Co Ltd (NCPC), No. 388 East Heping Road, Shijiazhuang, Hebei, China	1g/vial	3	3	Burkina Faso (2), Madagascar (1)
Pharmax (UK) Ltd, Bristol, UK	1g/vial	1	1	Tajikistan (1)
Sanavita Pharmaceuticals GmbH, Lohstr. 2, 59368 Werne, Germany	1g/vial	1	1	Tajikistan (1)
Shandong Reyoung Pharmaceutical Co Ltd, No. 6 Erlangshan Road, Yiyuan County, Shandong Province, China	1g/vial	1	1	Burkina Faso (1)
Shandong (Yanzhou) Xier Kangtai Pharmaceutical Co Ltd, Private Economy Garden-Xinyan Town, Yanzhou City, Shandong, China	500mg/vial	1	1	Kenya (1)
Shanxi Shuguang, Pharmaceutical Co Ltd, No. 1 Kangle Street, Qi County, Jinzhong City, Shanxi Province, China	1g/vial	1	1	Madagascar (1)
Sinochem Ningbo Ltd, 21 Jiangxia st., Ningbo, Zhejiang, China	500mg/vial	1	1	Tajikistan (1)
Umedica Laboratories Pvt Ltd, Plot 221, GIDC, Vapi 396195, Gujarat, India	500mg/vial	1	1	Zimbabwe (1)
Viet Nam China Pharmaceutical JS Co (VCP), Thanh Xuan Commune, Soc Son District, Hanoi, Viet Nam	1g/vial	1	1	Viet Nam (1)
Ceftriaxone injection				
Aristo Pharmaceuticals Pvt Ltd, Plot No. 208, New Industrial Area No.2, Mandideep, District Raisen, Madhya Pradesh, India	1g/vial	1	1	Nepal (1)
Biosintez OAO, Penza, Russia	1g/vial	1	1	Tajikistan (1)
Borshchagovskiy khimiko-farmacevticheskiy zavod ZAO, str Mira 17, Kiev, Ukraine	1g/vial	1	1	Tajikistan (1)
CSPC OUYI (Shijiazhuang) Pharmaceuticals Co Ltd, No. 276 West Zhongshan Road, Shijiazhuang, China	1g/vial	1	1	Tajikistan (1)
CSPC Zhongnuo Pharmaceutical (Shijazhuang) Co Ltd, 47 Fengshou Road, Shijiazhuang, China	1g/vial	1	1	Nigeria (1)
CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co Ltd, No.188 Gongnong Road, Shijiazhuang, Hebei, China	1g/vial	2	2	Tanzania (1), Uganda (1)
Flamingo Pharmaceuticals Ltd, PO Box 27257 Mumbai 400071, India	500mg/vial	1	1	Kenya (1)

Manufacturer	Strength	No. of batches	No. of samples	Country of collection
Guilin Pharmaceutical (Shanghai) Co Ltd (GPSC), No.43 Qilidian Road, Guilin, Guangxi 541004, China	1g/vial	1	1	Uganda (1)
Hanmi Pharm Co Ltd, 395 Chupal Paengseong-eup, Pyeongtaek-si, Gyeonggi-do 451-805, Korea	1g/vial	1	1	Nigeria (1)
Karnataka Antibiotics and Pharmaceuticals Ltd, Plot No.14. II Phase, Peenya, Bangalore 560058, India	1g/vial	1	1	Zimbabwe (1)
Kopran Ltd, Village Savroli, Taluka: Khalapur, District: Raigad, Maharashtra, India	1g/vial	1	1	Kenya (1)
Lupin Ltd, Mumbai, India	1g/vial	1	1	Nepal (1)
M.J. Biopharm Pvt Ltd, L-7 M.I.D.C. Indl. Area, Dist. Raigad, Taloja, Navi Mumbai 410208, India	1g/vial	1	1	Uganda (1)
MinhDan Pharmaceutical JS Co, Lot N8-N5 street-Hoa Xa Industrial Estate, Nam Dinh, Viet Nam	1g/vial	1	1	Viet Nam (1)
North China Pharmaceutical Co Ltd (NCPC), No. 217-1 East Heping Road, Shijiazhuang, Hebei, China	1g/vial	1	1	Madagascar (1)
North China Pharmaceutical Co Ltd (NCPC), No. 388 East Heping Road, Shijiazhuang, Hebei, China	1g/vial	1	1	Burkina Faso (1)
	250mg/vial	1	1	Burkina Faso (1)
Okasa Pharma, L-2, additional MIDC, Satara 415 004, Maharashtra, India (for Cipla Ltd, Mumbai Central, India)	1g/vial	1	1	Madagascar (1)
Plethico Pharmaceuticals Ltd, A.B.Road, Manglia – 453 771, Indore (M.P.), India	1g/vial	1	1	Tanzania (1)
Popular Pharmaceuticals Ltd, 164 Tongi Industrial Area, Tongi, Gazipur-1711, Dhaka, Bangladesh	250mg/vial	1	1	Kenya (1)
Ranbaxy Laboratories Ltd, Industrial Area-3, Dewas 455003, India	1g/vial	2	2	Nepal (1), Nigeria (1)
Sance Laboratories Pvt Ltd, P.B. NO. 2, Kozhuvanal, Pala, Kottayam - 686523, Kerala, India	1g/vial	1	1	Tanzania (1)
Shandong (Yanzhou) Xier Kangtai Pharmaceutical Co Ltd, Private Economy Garden-Xinyan Town, Yanzhou, Shandong, China	1g/vial	2	2	Kenya (1), Madagascar (1)
Strides Arcolab Ltd, India	1g/vial	1	1	Burkina Faso (1)
Tarchomin Pharmaceutical Works “Polfa” S.A., A.Fleming str. 2, 03-176 Warsaw, Poland	1g/vial	1	1	Viet Nam (1)
Umedica Laboratories Pvt Ltd, Plot 221, GIDC, Vapi 396195, Gujarat, India	500mg/vial	1	1	Zimbabwe (1)
Viet Nam China Pharmaceutical JS Co (VCP), Thanh Xuan Commune, Soc Son District, Hanoi, Viet Nam	1g/vial	1	1	Viet Nam (1)
Dexamethasone injection				
Bryntsalov - A ZAO, Nagatinskaya str. 1, Moscow, Russia	4mg/mL	1	1	Tajikistan (1)
Cadila Healthcare Ltd, Sarkhej-Bavla N.H. No. 8A, Moraiya, Sanand, Ahmdabad 382 210, India	4mg/mL	3	3	Nepal (1), Uganda (2)
Celon Laboratories Ltd, No. 2 Aleap Industrial Estate, Gajularamaram, RR District, 500072 Andhra Pradesh, India	4mg/mL	1	1	Zimbabwe (1)
CSPC OUYI (Shijiazhuang) Pharmaceuticals Co Ltd, No. 276 West Zhongshan Road, Shijiazhuang, China	4mg/mL	1	1	Kenya (1)
Farmak PAO, str Frunze 63, 04080 Kiev, Ukraine	4mg/mL	1	1	Tajikistan (1)

Manufacturer	Strength	No. of batches	No. of samples	Country of collection
Fresenius Kabi Bidiphar JS Co, Zone 8, Nhon Phu Ward, Quy Nhon City, Binh Dinh Province, Viet Nam	4mg/mL	1	1	Viet Nam (1)
Hindustan Pharmaceuticals, Barauni - 851 112, India	4mg/mL	1	1	Nepal (1)
Jiangsu Pharma Corp., China	4mg/mL	1	1	Tajikistan (1)
Leshan Sanjiu-Longmarch Pharmaceuticals Co Ltd, No. 120, Baiyang Road, Leshan, Sichuan 614006, China	4mg/mL	2	2	Tanzania (2)
North China Pharmaceutical Co Ltd (NCPC), No 6 Heping East Road, Huayo East Street, Shijiazhuang, Hebei, China	4mg/mL	1	1	Madagascar (1)
Pharbaco Central Pharmaceutical JS Co No 1, Thanh Xuan, Soc Son, Hanoi, Viet Nam	4mg/mL	1	1	Viet Nam (1)
Pymepharco Co, 166-170 Nguyen Hue Street, Tuy Hoa City, Phu Yen Province (licence from Stada Pharm GmbH, Germany), Viet Nam	4mg/mL	1	1	Viet Nam (1)
Sanjvani Parenteral Ltd, R-40, TTC Rabale, Thane Belapur Road, Navi Mumbai - 400 701, India	4mg/mL	1	1	Nepal (1)
Shandong (Yanzhou) Xier Kangtai Pharmaceutical Co Ltd, Private Economy Garden-Xinyan Town, Yanzhou City, Shandong, China	4mg/mL	3	3	Madagascar (1), Nigeria (2)
Amoxicillin dispersible tablets				
Barnaulskiy zavod medicinskih preparatov OOO, Silikatnaya str. 16a, Barnaul, Russia	500mg	1	1	Tajikistan (1)
Biokhimik OAO, 4300030, Vasenko str. 15A, Saransk, Russia	250mg	1	1	Tajikistan (1)
Kampala Pharmaceutical Industries (1996) Ltd, Plot M444B Stretcher Road, Ntinda, Kampala, Uganda	125mg	1	1	Uganda (1)
Medicamen Biotech Ltd, SP-1192 A&B, Phase-IV, Industrial Area, Bhiwadi-301019, India	250mg	1	1	Tajikistan (1)
Medopharm Pvt Ltd, 50 Kayarambedu Village, Guduvanchery, India	125mg	3	3	Uganda (3)
Milan Laboratories Pvt Ltd, Plot No. 63/67/87, J.C.I.E Ltd, Kamothe, Panvel, Navi Mumbai, India	125mg	1	1	Uganda (1)
National Health Care Pvt Ltd, Chhatapipra, Birgunj, Nepal	250mg	1	1	Nepal (1)
S.R. Drug Laboratories Pvt Ltd, Satungal, Kathmandu, Nepal	250mg	1	1	Nepal (1)
Zinc sulfate/gluconate dispersible tablets/syrup				
Agog Pharma Ltd, Plot No. 33, Sector II, The Vasai Taluka, Indl. Co-op. Estate Ltd, Vasai (East), Thane, India	20mg	2	2	Uganda (2)
Bidiphar 1 Pharmaceutical JS Co, 498 NguyenThai Hoc Str., Quy Nhon City, Binh Dinh Province, Viet Nam	10mg/5mL syrup	2	2	Viet Nam (2)
Chi Pharmaceuticals Ltd, 14 Chivita Avenue, Ajao Estate, Isolo, Lagos, Nigeria	20mg	1	1	Nigeria (1)
Cosmos Ltd, Tangwe Rd, Off Lunga Lunga Rd, PO Box 41433-00100, Nairobi, Kenya	20mg	1	1	Kenya (1)
Divine Essential Formulations, Km 10, Lasu-Ojo Rd, Igando-Lagos, Nigeria	20mg conventional tablets	1	1	Nigeria (1)

Manufacturer	Strength	No. of batches	No. of samples	Country of collection
Laboratoires Pharmaceutiques Rodael, 1 route de Socx, 59380 Bierne, France	20mg	3	3	Tajikistan (1), Uganda (1), Zimbabwe (1)
Lomus Pharmaceuticals Pvt Ltd, Gothatar, Kathmandu, Nepal	10mg	1	1	Nepal (1)
Medicamen Biotech Ltd, SP-1192 A&B, Phase-IV, Industrial Area, Bhiwadi-301019, India	20mg	1	1	Tajikistan (1)
National Health Care Pvt Ltd, Chhatapipra, Birgunj, Nepal	20mg	1	1	Nepal (1)
S.R. Drug Laboratories Pvt Ltd, Satungal, Kathmandu, Nepal	zinc gluconate, 10mg dispersible tablets	1	1	Nepal (1)
Shelys Pharmaceuticals Ltd, Plot No. 696, New Bagamoyo Road, Mwenge, PO Box 3016, Dar es Salaam, Tanzania	20mg	2	2	Tanzania (2)
Square Pharmaceuticals Ltd, Dhaka Unit, Kaliakoir, Gazipur, Bangladesh	20mg	1	1	Kenya (1)
Universal Corporation Ltd, Club Road, Plot No. 13777, PO Box 1748-00902, Kikuyu, Kenya	20mg	1	1	Kenya (1)
Varichem Pharmaceutical, 194 Gleneagles Road, Willowvale, Harare, Zimbabwe	20mg dispersible tablets	1	1	Zimbabwe (1)
Zenufa Laboratories Ltd, PO Box 77914, Dar es Salaam, Tanzania	10mg/5mL syrup	2	2	Tanzania (2)
Levonorgestrel tablets				
BaDinh Pharmaceutical Biological JS Co, Que Vo Industrial, Bac Ninh Province, Viet Nam	0.75mg	1	1	Viet Nam (1)
Cipla Ltd, Plot No L-139 to L-146, Verna Industrial Estate, Verna-Goa 403722, India	0.75mg	1	1	Madagascar (1)
	1.5mg	1	1	Nepal (1)
Famy Care Ltd, 1608/1609, G.I.D.C, Sarigam, 396155 Valsad, Gujarat, India	0.75mg	2	3	Madagascar (1), Tanzania (1), Zimbabwe (1)
Gedeon Richter Plc, Gyömrői út 19-21, Budapest 1103, Hungary	0.75mg	3	3	Tajikistan (1), Uganda (2)
Glenmark Pharmaceuticals Ltd, B/2-2, Mahalaxmi Chambers, 22, Bhulabhai Desai Road, Mumbai - 400 026, India	0.75mg	1	1	Kenya (1)
HLL Life Care Ltd, India	0.75mg	1	1	Nepal (1)
Par Laboratories, India (for Simba Pharmaceuticals Ltd, Kenya)	0.75mg	1	1	Kenya (1)
Renata Ltd, Dhaka, Bangladesh	0.75mg	1	1	Kenya (1)

Manufacturer	Strength	No. of batches	No. of samples	Country of collection
Stada-VN JV Co Ltd, K63/1 Nhuyen Thi Soc Street, Xuan Thoi Dong Ward, Hoc Mon District, Ho Chi Minh City, Viet Nam	0.75mg	1	1	Viet Nam (1)
Mifepristone tablets				
BaDinh Pharmaceutical Biological JS Co, Que Vo Industrial, Bac Ninh Province, Viet Nam	10mg	1	1	Viet Nam (1)
Danapha Pharmaceutical JS Co, 253 Dung Si Thanh Khe Street, Thanh Khe District, Da Nang City, Viet Nam	10mg	2	2	Viet Nam (2)
Mediplantex National Pharmaceutical JS Co Ltd, 358 Duong Giai Phong, Thanh Xuan, Hanoi, Viet Nam	10mg	1	1	Viet Nam (1)
Namha Pharmaceutical JS Co, 415 Han Thuyen, Nam Dinh City, Viet Nam	10mg	2	2	Viet Nam (2)
Stada-VN JV Co Ltd, K63/1 Nhuyen Thi Soc Street, Xuan Thoi Dong Ward, Hoc Mon District, Ho Chi Minh City, Viet Nam	10mg	2	2	Viet Nam (2)

Assay: 90.0-110.0%; **Related substances**: NMT one peak >2%; no peak >5%; **pH**: 3.0 – 5.0
Appearance: clear colourless solution, free from visible particles

✓= complies; ✖= does not comply

Appendix 3 Oxytocin injection – test results

Country of collection* / sample code	Strength IU/mL	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Storage conditions declared by the manufactu-rer	Registered	Appear-ance	Iden-tity	Assay %	Related substances	pH	Extract-able volume	Conclu sion	Information on preservatives
BF/OXT/ 130509/05-09-2013	5	100x1mL ampoules amber glass	130509	2013-05	2016-04	BP	Zhejiang Ruixin Pharmaceuticals Co Ltd, Zhejiang, China	Distributor, public / Ouagadougou	Controlled: 7°C	Secondary packaging not available	No - central supply based on global tender	✓	✓	✓ 98.9	✖ **11 peaks >2%; 3 peaks >5%**	✓ 4.1	✓	✖	Secondary packaging not available - smaller peak detected at Rt corresponding to chlorobutanol
BF/OXT/ 20199/05-09-2013	5	10x1mL ampoules, glass	20199	2012-02	2015-02	BP	Rotexmedica GmbH Arzneimittel-work, 22946 Trittau, Germany	Central medical store, public / Ouagadougou	Controlled: 5°C	2 - 8°C, do not freeze	No - central supply based on global tender	✓	✓	✓ 100.1	✓ no peaks detected	✓ 4.2	✓	✓	Preservatives not declared nor detected
KE/OXT/ 19/10-9-13	10	10x1mL ampoules, glass	JA302	2013-02	2016-01	BP	Umedica Laboratories Pvt Ltd, Plot 221, GIDC, Vapi 396195, Gujarat, India	Distributor, private / Nairobi	Controlled: 24°C, RH 55%	Not exceeding 30°C	Yes	✓	✓	✓ 95.5	✖ **3 peaks >2%;** no peak >5%	✓ 4.2	✓	✖	No preservatives declared - huge peak detected at Rt corresponding to chlorobutanol
MG/OXT/ 01/290813	10	100x1mL ampoules, glass	130414	2013-04	2016-04	BP	North China Pharmaceutical Co Ltd (NCPC), No. 217-1 East Heping Road, Shijiazhuang, Hebei, China	Central medical store, public / Antananarivo	Controlled: 17.6°C, RH 34.8%	Keep in cold, dry and dark place	Yes	✓	✓	✓ 97.1	✖ **12 peaks >2%; 3 peaks >5%**	✓ 4.1	✓	✖	Preservatives not declared nor detected
NP/OXT/ O1/27Aug2013	5	5x1mL ampoules, glass	TAC2U2	2012-12	2014-02	IP	Tablets India Ltd, 179 T.H.Road, Chennai 600081, India	Distributor, private / Kathmandu	Not controlled	Not exceeding 30°C, do not freeze	Yes	Clear colourless solution, **visible particles in 37 of 40 ampoules**	✓	✓ 91.9	✖ **3 peaks >2%;** no peak >5%	✓ 4.0	✓	✖	Chlorobutanol declared - corresponding peak detected

* BF=Burkina Faso, KE=Kenya, MG=Madagascar, NP=Nepal, NG=Nigeria=, TJ=Tajikistan, TZ=Tanzania, UG=Uganda, VN=Viet Nam, ZW=Zimbabwe

Assay: 90.0-110.0%; **Related substances**: NMT one peak >2%; no peak >5%; **pH**: 3.0 – 5.0 ✓= complies; ✖= does not comply
Appearance: clear colourless solution, free from visible particles

Country of collection* / sample code	Strength IU/mL	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Storage conditions declared by the manufactu-rer	Registered	Appear-ance	Iden-tity	Assay %	Related substances	pH	Extract-able volume	Conclu sion	Information on preservatives
NP/OXT/ O2/27Aug2 013	5	5x1mL ampoules, glass	404	2012-06	2014-06	IP	Hindustan Pharmaceuticals, Barauni - 851 112, India	Distributor, private / Kathmandu	Not controlled	Do not freeze	Yes	**5 different kinds of ampoules contained in the sample,** all contain clear colourless solution, **visible particles in 26 of 40 ampoules**	✖ **no oxytocin in one type of ampoules**	✖ **0 - 68.7% in individual ampoules**	✖ **Number of peaks varies in individual ampoules up to: 16 peaks >2%; 12 peaks >5%**	Not tested	Not tested	✖	Chlorobutanol declared - not clearly confirmed
NP/OXT/ O3/1Sep201 3	5	5x1mL ampoules, glass	12AE58	2012-11	2014-10	IP	Akums Drugs and Pharmaceuticals Ltd,India	Distributor, public / Kathmandu	Not controlled	Store in a cold&dark place, do not freeze	No - supply on global tender basis	✓	✓	✖ **87.2**	✖ **5 peaks >2%;** no peak >5%	✓ 4.3	✓	✖	Phenol declared - corresponding peak detected
NG/OXT/ 1/230913	10	10x1mL ampoules, glass	30528	2013-04	2016-04	BP	Rotexmedica GmbH Arzneimittelwork, 22946 Trittau, Germany	Importer-distributor, private / Lagos	Controlled: 5°C	2 - 8°C, do not freeze	Yes	✓	✓	✓ 98.0	✓ no peak >2%	✓ 4.2	✓	✔	Preservatives not declared nor detected
NG/OXT/ 2/260913	10	100x1mL ampoules, glass	N-2308	2012-07	2014-06	None	Kwality Pharmaceutical (P) Ltd, Nag kalan, Majitha Road, Amritsar, India	Importer-distributor, private / Lagos	Controlled: 5°C	2 - 8°C, protect from light & heat	Yes	Clear colourless solution, **visible particles in 27 of 60 ampoules**	✓	✖ **78.6**	✖ **9 peaks >2%; 4 peaks >5%**	✓ 4.4	✓	✖	No preservatives declared - smaller peak detected at Rt corresponding to chlorobutanol
NG/OXT/ 3/081013	10	10x1mL ampoules, glass	12G16	2012-07	2015-07	None	Zhejiang Tianfeng Pharmaceutical Factory, No. 518 Daxiang Road, Huzhou, Zhejiang (Jinling Pharmaceutical Co Ltd Group), China	Importer-distributor, private / Lagos	Controlled: 5°C	Store in cool & dark place	Yes	✓	✓	✖ **52.0**	✖ **14 peaks >2%; 6 peaks >5%**	✓ 3.4	✓	✖	No preservatives declared - huge peak detected at Rt corresponding to chlorobutanol

* BF=Burkina Faso, KE=Kenya, MG=Madagascar, NP=Nepal, NG=Nigeria=, TJ=Tajikistan, TZ=Tanzania, UG=Uganda, VN=Viet Nam, ZW=Zimbabwe

Appendix 3: Oxytocin injection – test results

Assay: 90.0-110.0%; **Related substances**: NMT one peak >2%; no peak >5%; **pH**: 3.0 – 5.0 ✓= complies; ✖= does not comply
Appearance: clear colourless solution, free from visible particles

Country of collection* / sample code	Strength IU/mL	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Storage conditions declared by the manufactu-rer	Registered	Appear-ance	Iden-tity	Assay %	Related substances	pH	Extract-able volume	Conclu sion	Information on preservatives
TJ/OXT/ 1/30082013	5	10x1mL ampoules, glass	ENL 05301	2013-02	2015-01	BP	Nitin Lifesciences Ltd, Rampur Road, Paonta Sahib, Sirmour - 173025, Himachal Pradesh, India	Importer-distributor, private / Dushanbe	Controlled	Below 25°C, do not freeze, protect from light	Re-registration pending	✓	✓	✓ 101.3	✖ **6 peaks >2%; 2 peaks >5%**	✓ 4.3	✓	✖	Chlorobutanol declared - only very small corresponding peak detected
TJ/OXT/ 2/30082013	5	10x1mL ampoules, glass	021012	2012-10	2015-10	None	Bryntsalov - A ZAO, Nagatinskaya str. 1, Moscow, Russia	Importer-distributor, private / Dushanbe	Controlled	8 - 20°C, protected from light	Yes	✓	✓	✓ 101.4	✓ 1 peak >2%; no peak >5%	✓ 3.9	✓	✔	Chlorobutanol declared - corresponding peak detected
TJ/OXT/ 3/30082013	5	5x1mL ampoules, glass	A34013 A	2013-04	2016-04	None	Gedeon Richter Plc, Gyömrői út 19-21, Budapest 1103, Hungary	Importer-distributor, private / Dushanbe	Controlled	2 - 15°C, protected from light	Yes	✓	✓	✓ 94.8	✓ 1 peak >2%; no peak >5%	✓ 4.1	✓	✔	Chlorobutanol declared - corresponding peak detected
TZ/OXT/ 04/090913	5	10x1mL ampoules, glass	V13210	2013-06	2015-05	BP	Vital Healthcare Pvt Ltd, Plot No. H-10, MIDC, Satpur Nashik-422007, India	Importer, private / Dar es Salaam	Controlled	8 - 25°C, do not freeze	Yes	✓	✓	✖ **88.9**	✖ **4 peaks >2%; 1 peak >5%**	✓ 4.6	✓	✖	Chlorobutanol declared - corresponding peak detected
TZ/OXT/ 13/120913	5	10x1mL ampoules, glass	20960	2012-12	2015-12	BP	Rotexmedica GmbH Arzneimittelwork, 22946 Trittau, Germany	Importer-central medical store, public / Dar es Salaam	Controlled	2 - 8°C, do not freeze	Yes	✓	✓	✓ 98.9	✓ no peaks detected	✓ 4.2	✓	✔	Preservatives not declared nor detected
TZ/OXT/ 16/130913	5	10x1mL ampoules, glass	V12480	2012-11	2014-10	BP	Vital Healthcare Pvt Ltd, Plot No. H-10, MIDC, Satpur Nashik-422007, India	Importer-distributor, private / Dar es Salaam	Controlled	8 - 25°C, do not freeze	Yes	✓	✓	✓ 94.0	✖ **3 peaks >2%; 1 peak >5%**	✓ 4.7	✓	✖	Chlorobutanol declared - corresponding peak detected
UG/OXT/ 07/06-09-2013	10	10x1mL ampoules, glass	120713	2012-07	2015-06	BP	Ningbo Dahongying Pharmaceutical Co Ltd, No.396 Mingzhu Road, Ningbo, Zhejiang, China	Wholesaler-importer, private / Kampala	Controlled: 25.6°C	Below 25°C, protect from light	Yes	✓	✓	✖ **86.1**	✖ **7 peaks >2%; 4 peaks >5%**	✓ 4.0	✓	✖	No preservatives declared - smaller peak detected at Rt corresponding to chlorobutanol

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Assay: 90.0-110.0%; **Related substances**: NMT one peak >2%; no peak >5%; **pH**: 3.0 – 5.0 ✓= complies; ✖= does not comply
Appearance: clear colourless solution, free from visible particles

Country of collection* / sample code	Strength IU/mL	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Storage conditions declared by the manufactu-rer	Registered	Appear-ance	Iden-tity	Assay %	Related substances	pH	Extract-able volume	Conclu sion	Information on preservatives
UG/OXT/ 15/09-09-2013	10	10x1mL ampoules, glass	130318	2013-03	2016-02	BP	Ningbo Dahongying Pharmaceutical Co Ltd, No.396 Mingzhu Road, Ningbo, Zhejiang, China	Central medical store, public / Entebbe	Controlled: 24°C, RH 65%	Below 25°C, protect from light	Yes	✓	✓	✖ **85.2**	✖ **8 peaks >2%; 5 peaks >5%**	✓ 3.9	✓	✖	No preservatives declared - smaller peak detected at Rt corresponding to chlorobutanol
UG/OXT/22/09-09-2013	10	100x1mL ampoules, glass	121237	2012-12	2015-12	None	Zhejiang Ruixin Pharmaceuticals Co Ltd, Kaifa Road, Lishui, Zhejiang, China	NGO store / Kampala	Controlled: 2°C	2 - 8°C, protect from light	Yes	✓	✓	✖ **89.8**	✖ **12 peaks >2%; 4 peaks >5%**	✓ 3.8	✓	✖	No preservatives declared - smaller peak detected at Rt corresponding to chlorobutanol
VN/OXT/ 01/240913	5	10x1mL ampoules, glass	30061	2013-04	2016-04	BP	Rotexmedica GmbH Arzneimittelwork, 22946 Trittau, Germany	Importer-distributor, public / Hanoi	Controlled: 6°C	2 - 8°C, do not freeze	Yes	✓	✓	✓ 102.4	✓ no peaks detected	✓ 4.2	✓	✓	Preservatives not declared nor detected
ZW/OXT/ 01/11/09/13	10	10x1mL ampoules, glass	UF30101	2013-03	2015-03	BP	Biologici Italia Laboratories, Via F.Serpero 2, 20060 Masate, Milano, Italy	Central medical store, public / Harare	Controlled: 6°C	Below 25°C, protect from light	No - donation	✓	✓	✓ 99.9	✓ no peak >2%	✓ 4.4	✓	✓	Chlorobutanol declared - corresponding peak detected
ZW/OXT/ 02/11/09/13	10	10x1mL ampoules, glass	30304	2013-01	2016-01	BP	Rotexmedica GmbH Arzneimittelwork, 22946 Trittau, Germany	Central medical store, public / Harare	Controlled: 6°C	2 - 8°C, do not freeze	Yes	✓	✓	✓ 100.6	✓ no peak >2%	✓ 4.2	✓	✓	Preservatives not declared nor detected

* BF=Burkina Faso, KE=Kenya, MG=Madagascar, NP=Nepal, NG=Nigeria=, TJ=Tajikistan, TZ=Tanzania, UG=Uganda, VN=Viet Nam, ZW=Zimbabwe

Assay: 90.0-110.0%; **pH**: 5.5 – 7.0; **Appearance**: clear colourless liquid, free from visible particles ✓= complies; ✖= does not comply

Appendix 4 Magnesium sulfate injection – test results

Country of collection* / sample code	Strength mg/mL	Pack size	Batch No.	Manu-facture date	Expiry date	Label claim	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Registered	Appear-ance	Iden-tity	Assay %	pH	Conclu-sion
BF/MS/ 200592/07-11-2013	500	10x10mL ampoules, glass	200592	Not stated	2015-09	Magnesium sulfate BP- USP 5g: 20.25mmol - 10mL	USP	Laboratoire Renaudin, Itxassou, France	Distributor, public / Ouagadougou	Not controlled, actual temperature 29°C	Yes	✓	✓	✓ 96.5	✖ **7.3**	✖
KE/MS/ 03/04-9-13	500	25x10mL ampoules, glass	I-12019	2012-08	2014-07	Each mL contains magnesium sulfate heptahydrate BP 500mg	BP	Harson Laboratories, 12 R.C.Patel Industrial Estate, Akota, Baroda-390020, India	Distributor, private / Nairobi	Controlled: 20°C, RH 60%	Yes	✓	✓	✓ 100.8	✓ 6.5	✓
KE/MS/ 13/07-09-13	500	10x10mL ampoules, glass	V13042	2013-02	2016-01	Each mL contains magnesium sulfate BP 500mg	BP	Vital Healthcare Pvt Ltd, Plot No. H-10, MIDC, Satpur Nashik-422007, India	Distributor, private / Nairobi	Controlled: 23°C, RH 60%	Yes	✓	✓	✓ 94.6	✓ 6.1	✓
NP/MS/ M1/1Sep2013	500	50x2mL ampoules, glass	128	2013-04	2015-03	Magnesium sulfate IP 50% w/v	USP	Hindustan Pharmaceuticals, Barauni - 851 112, India	Distributor, private / Kathmandu	Controlled	Yes	✓	✓	✓ 95.0	✓ 6.4	✓
NP/MS/ M2/30Aug2013	500	50x2mL ampoules, amber glass	124	2012-09	2014-08	Magnesium sulfate IP 50% w/v	USP	Hindustan Pharmaceuticals, Barauni - 851 112, India	Treatment centre directly purchasing medicines, public / Kathmandu	Not controlled	Yes	✓	✓	✓ 95.3	not tested	✓ (pH not tested)
NP/MS/ M3/1Sep2013	500	50x2mL ampoules, amber glass	126	2013-02	2015-01	Magnesium sulfate IP 50% w/v	USP	Hindustan Pharmaceuticals, Barauni - 851 112, India	Hospital directly purchasing medicines, public / Patan, Lalitpur	Not controlled	Yes	✓	✓	✓ 97.2	✓ 6.5	✓
NG/MS/ 4/230913	500	10x10mL ampoules, glass	0011912	2013-07	2016-07	Magnesium sulfate (heptahydrate) 50% w/v	None	Martindale Pharmaceuticals, Romford, Essex, Rm3 8UG, UK	Importer-distributor, private / Lagos	Controlled	Yes	✓	✓	✓ 99.8	✓ 6.2	✓
NG/MS/ 5/260913	500	5x10mL ampoules, glass	M130718	2013-07	2016-07	Magnesium sulfate heptahydrate BP 50% w/v	None	Furen Pharmaceutical Group Co Ltd, (Steyuan Group), XuanWu Economic Development Area, Luyi County, Henan Province, China	Importer-distributor, private / Lagos	Controlled	Yes	✓	✓	✓ 94.0	✓ 6.7	✓
NG/MS/ 6/300913	500	5x10mL ampoules, glass	EA-3561	2013-05	2015-04	Magnesium sulfate heptahydrate BP 50% w/v	None	Lincoln Pharmaceuticals Ltd, Trimul Estate, Khatraj Chokdi, Kalol, Gandhinagar, Gujarat, India	Importer-distributor, private / Lagos	Controlled	Yes	✓	✓	✓ 97.8	✓ 6.9	✓

* BF=Burkina Faso, KE=Kenya, MG=Madagascar, NP=Nepal, NG=Nigeria=, TJ=Tajikistan, TZ=Tanzania, UG=Uganda, VN=Viet Nam, ZW=Zimbabwe

Appendix 4: Magnesium sulfate injection – test results

Assay: 90.0-110.0%; **pH**: 5.5 – 7.0; **Appearance**: clear colourless liquid, free from visible particles ✓= complies; ✖= does not comply

Country of collection* / sample code	Strength mg/mL	Pack size	Batch No.	Manu-facture date	Expiry date	Label claim	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Registered	Appear-ance	Iden-tity	Assay %	pH	Conclu-sion
TJ/MS/ 1/30082013	250	10x10mL ampoules, plastic	170513	Not stated	2015-06	Each mL contains magnesium sulfate heptahydrate 250mg	None	Nikopharm, str. Engels 1, Makeevka, Donetsk, Ukraine	Importer-distributor, private Dushanbe	Controlled	Yes	✓	✓	✓ 96.5	✓ 6.8	✓
TJ/MS/ 2/30082013	250	10x10mL ampoules, plastic	50113	Not stated	2016-02	Each mL contains magnesium sulfate 250mg	None	Moskhimfarmpreparaty OAO, Str. Kamenshiki 9, Semashko, 115172 Moscow, Russia	Importer-distributor, private Dushanbe	Controlled	Re-registration pending	✓	✓	✓ 98.6l	✓ 6.3	✓
TJ/MS/ 3/30082013	250	10x5mL ampoules, glass	711112	Not stated	2015-12	Each mL contains magnesium sulfate 250mg	None	Dalkhimfarm OAO, Str. Tashketskaya 22, Khabarovsk 680001, Russia	Importer-distributor, private Dushanbe	Controlled	Yes	✓	✓	✓ 98.3	✓ 6.2	✓
TZ/MS/ 17/130913	500	10mL ampoules, plastic	108966	Not stated	2015-03	Each mL contains magnesium sulfate heptahydrate 500mg	USP	Pharmaceutical Solution Industry (PSI), PO Box 17476, Jeddah 21484, Saudi Arabia	Importer-distributor, private / Dar es Salaam	Controlled	Yes	✓	✓	✓ 98.0	✓ 5.8	✓
TZ/MS/ 12/120913	500	25x10mL ampoules, plastic	108966	2012-04	2015-03	Each mL contains magnesium sulfate heptahydrate 500mg	USP	Pharmaceutical Solution Industry (PSI), PO Box 17476, Jeddah 21484, Saudi Arabia	Importer- central medical store, public / Dar es Salaam	Controlled	Yes	✓	✓	✓ 101.8	✓ 6.7	✓
UG/MS/ 14/07-09-2013	500	10x10mL ampoules, glass	V13042	2013-02	2016-01	Each mL contains magnesium sulfate BP 500mg	BP	Vital Healthcare Pvt Ltd, Plot No. H-10, MIDC, Satpur Nashik-422007, India	Retailer, private / Kampala	Air-conditioned	No - special import permit	✓	✓	✓ 92.3	✓ 6.6	✓
VN/MS/ 01/011013	150	10x10mL ampoules, glass	86GAA001	2013-01	2016-01	Each ampoule contains magnesium sulfate 1.5g	None	Fresenius Kabi Bidiphar JS Co, Zone 8, Nhon Phu Ward, Quy Nhon City, Binh Dinh Province, Viet Nam	Importer-distributor, public / Ho Chi Minh City	Controlled: 25°C, RH 50%	Yes	✓	✓	✓ 103.9	✖ **7.2**	✖
VN/MS/ 02/250913	150	10x10mL ampoules, glass	86GAA009	2013-01	2016-01	Each ampoule contains magnesium sulfate 1.5g	None	Fresenius Kabi Bidiphar JS Co, Zone 8, Nhon Phu Ward, Quy Nhon City, Binh Dinh Province, Viet Nam	Manufacturer-distributor, private / Quy Nhon City	Controlled: 22°C, RH 57%	Yes	✓	✓	✓ 104.0	✓ 6.5	✓
VN/MS/ 03/011013	150	50x10mL ampoules, plastic	1202869	2012-07	2014-07	Magnesium sulfate 0.15g/mL, Mg^{2+} 0.609mmol/mL	None	Laboratoire Aguettant, 1 rue A.Fleming, 69007 Lyon, France	Importer-distributor, public / Ho Chi Minh City	Controlled: 25°C, RH 60%	Yes	✓	✓	✓ 104.4	✓ 5.9	✓
ZW/MS/ 01/11/09/13	500	5x10mL ampoules, glass	3812mg-A	Not stated	2015-08	1 ampoule of 10mL contains Magnesium sulfate heptahydrate 5.0g	None	Inresa Arzneimittel GmbH, Obere Hardtstrasse 18, 79114 Freiburg, Germany	Central medical store, public / Harare	Controlled: 24°C	No - donation	✓	✓	✓ 96.3	✓ 6.8	✓

* BF=Burkina Faso, KE=Kenya, MG=Madagascar, NP=Nepal, NG=Nigeria=, TJ=Tajikistan, TZ=Tanzania, UG=Uganda, VN=Viet Nam, ZW=Zimbabwe

Assay: upper fiducial limit of error NLT 97.0%, lower fiducial limit of error NMT 110.0% of the stated content; ✓= complies; ✖= does not comply
Composition of gentamicin: C_1: 25.0 – 50.0%, C_{1a}: 10.0 – 35.0%, C_2 + C_{2a}: 25.0 – 55.0%; **pH**: 3.0 – 5.5
Appearance: clear colourless solution, free from visible particles

Appendix 5 Gentamicin injection

Country of collection* / sample code	Strength	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at samp-ling site	Registered	Appear-ance	Iden-tity	Assay	Composition of gentamicin			pH	Conclu sion
														C1 (%)	C1a (%)	C2+C2a (%)		
BF/GEN/ 30160/02-09-2013	80mg/2mL	10x2mL ampoules	30160	2013-01	2016-01	None	Rotexmedica GmbH, Group Panpharma, Germany	Importer, private / Ouagadougou	Controlled: 25°C	No - central supply based on global tender	✓	✓	✓ 98.2% FL: 95.3-101.2%	✓ 28.1	23.0	48.9	✓ 3.8	✓
BF/GEN/ 20429/04-09-2013	80mg/2mL	10x2mL ampoules	20429	2012-11	2015-11	None	Rotexmedica GmbH, Group Panpharma, Germany	Importer, public / Ouagadougou	Controlled: 23°C	No - central supply based on global tender	✓	✓	✓ 99.2% FL: 97.0-101.4%	✓ 28.1	21.1	50.8	✓ 3.9	✓
BF/GEN/ 12A0281/04-09-2013	80mg/2mL	5x2mL ampoules	12A0281	2012-10	2015-10	None	Medis - Les Laboratoires de Médicaments Stériles SA, Route de Tunis KM7, BP 206, Nabeul 8000, Tunisisa	Importer, public / Ouagadougou	Controlled: 23°C	Yes	✓	✓	✖ **92.6%** FL: 91.4-**94.0%** **86.4%** FL: 84.3-**88.5%** **84.6%** FL: 82.5-**86.8%** **(Ø: 87.9%)**	✓ 29.7	22.1	48.2	✓ 3.9	✖
KE/GEN/ 12/07-09-13	80mg/2mL	100x2mL ampoules, brown	130415	2013-04	2016-04	None	Shandong (Yanzhou) Xier Kangtai Pharmaceutical Co Ltd, Private Economy Garden-Xinyan Town, Yanzhou City, Shandong, China	Distributor, private / Nairobi	Controlled: 23°C, RH 60%	Yes	✓	✓	✓ 104.8% FL: 103.4-106.3%	✓ 29.6	31.4	39.0	✓ 3.0	✓
KE/GEN/ 16/09-09-13	80mg/2mL	100x2mL ampoules	120922	2012-09	2015-09	None	CSPC OUYI (Shijiazhuang) Pharmaceuticals Co Ltd, No. 276 West Zhongshan Road, Shijiazhuang, China	Wholesaler, private / Nairobi	Controlled: 23°C, RH 60%	Yes	✓	✓	✓ 105.9% FL: 104.4-107.4%	✓ 29.4	25.0	45.6	✓ 5.3	✓

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Assay: upper fiducial limit of error NLT 97.0%, lower fiducial limit of error NMT 110.0% of the stated content; ✓= complies; ✖= does not comply
Composition of gentamicin: C_1: 25.0 – 50.0%, C_{1a}: 10.0 – 35.0%, C_2 + C_{2a}: 25.0 – 55.0%; **pH**: 3.0 – 5.5
Appearance: clear colourless solution, free from visible particles

Country of collection* / sample code	Strength	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at samp-ling site	Registered	Appear-ance	Iden-tity	Assay	Composition of gentamicin			pH	Conclu sion
														C1 (%)	C1a (%)	C2+C2a (%)		
KE/GEN/ 04/05-09-13	20mg/2mL	5x2mL ampoules	206001	2012-06	2015-05	None	Square Pharmaceuticals Ltd, Pabna Unit, Pabna 6600, Bangladesh	NGO store, Nairobi	Controlled: 22°C, RH 63%	Yes	✓	✓	✓ 101.3% FL: 98.8-104.0%	✖ **23.0** **24.2** **24.1** **Ø: 23.8**	✖ **35.2** 33.2 33.9 Ø: 34.1	41.8 42.6 42.0 Ø: 42.1	✓ 3.8	✖
MG/GEN/ 02/110913	80mg/2mL	100x2mL ampoules	111298	2011-12	2014-11	None	CSPC OUYI (Shijiazhuang) Pharmaceuticals Co Ltd, No. 276 West Zhongshan Road, Shijiazhuang, China	Wholesaler, private / Antananarivo	Controlled: 18.6°C, RH 33.9%	Yes	✓	✓	✓ 106.0% FL: 103.3-108.8%	✖ **24.0** **24.9** **24.8** **Ø: 24.6**	✖ **36.2** 35.0 **35.3** **Ø: 35.5**	39.8 40.1 40.0 Ø: 40.0	✓ 4.1	✖
MG/GEN/ 03/300813	80mg/2mL	10x2mL ampoules	130408	2013-04	2016-04	None	North China Pharmaceutical Co Ltd (NCPC), No 6 Heping East Road, Huayo East Street, Shijiazhuang, Hebei, China	Wholesaler, private / Antananarivo	Controlled: 16.9°C, RH 35.2%	Yes	✓	✓	✓ 107.9% FL: 105.9-109.9%	✓ 27.6	✓ 30.5	41.9	✖ **5.6**	✖
NP/GEN/ G1/27Aug2013	20mg/2mL	10x2mL vials	PT0126	2012-06	2014-08	None	Abbott Healthcare Pvt Ltd, Plot No. 67-70, Sector II, Pithampur 454 775, Dhar, Madhay Pradesh, India	Distributor, private / Kathmandu	Not controlled	Yes	✓	✓	✓ 95.9% FL: 94.1-97.6%	✓ 26.3	✓ 29.1	44.6	✓ 4.7	✓
NP/GEN/ G2/27Aug2013	80mg/2mL	10x2mL vials	TVF 2D1	2012-11	2014-10	None	Tablets India Ltd, 179 T.H.Road, Chennai 600081, India	Distributor, private / Kathmandu	Not controlled	Yes	✓	✓	✖ **91.4%** FL: 89.6-**93.2%** **94.0%** FL: 91.4-**96.7%** **92.6%** FL: 90.0-**95.3%** **(Ø: 92.7%)**	✓ 25.1	✓ 32.3	42.6	✓ 4.2	✖
NP/GEN/ G3/3Sep2013	80mg/2mL	2mL vial	KA8133017	2013-05	2015-04	None	Biochem Pharmaceutical Industries Ltd, Survey No.48, Ringanwada Village, Daman (U.T.) 396 210, India	Hospital directly purchasing medicines, public / Patan, Lalitpur	Not controlled	Yes	✓	✓	**93.8%** FL: 92.0-**95.6%** 97.1% FL: 95.6-98.6% 95.1% FL: 93.7-**96.6%** (Ø: 95.3%)	✓ 26.1	✓ 33.2	40.8	✓ 4.5	**Border-line**

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Appendix 5: Gentamicin injection – test results

Assay: upper fiducial limit of error NLT 97.0%, lower fiducial limit of error NMT 110.0% of the stated content; ✓= complies; ✖= does not comply
Composition of gentamicin: C_1: 25.0 – 50.0%, C_{1a}: 10.0 – 35.0%, C_2 + C_{2a}: 25.0 – 55.0%; **pH**: 3.0 – 5.5
Appearance: clear colourless solution, free from visible particles

Country of collection* / sample code	Strength	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at samp-ling site	Registered	Appear-ance	Iden-tity	Assay	Composition of gentamicin			pH	Conclu sion
														C1 (%)	C1a (%)	C2+C2a (%)		
NG/GEN/ 7/270913	80mg/2mL	50x2mL ampoules	DJ3252	2013-01	2018-01	None	Lek Pharmaceutical and Chemical Co d.d. Verovskova 57, 1526 Ljubljana, Slovenia	Importer-distributor, private / Lagos	Controlled	Yes	✓	✓	✓ 99.8% FL: 96.6-103.1%	✓ 27.3	22.9	49.8	✓ 4.0	✓
NG/GEN/ 8/081013	80mg/2mL	10x2mL ampoules, brown	130510	2013-05	2016-05	None	Greenfield Pharmaceutical (Jiang su) Co Ltd, No 38, Tai Jiu Road Taizhou, Jiangsu Province, China	Importer-distributor, private / Lagos	Controlled	Yes	✓	✓	✖ **90.5%** FL: 87.4-**93.6%** **86.8%** FL: 84.7-**89.1%** **86.1%** FL: 83.9-**88.3%** **(Ø: 87.8%)**	✓ 25.2	25.6	49.2	✓ 4.9	✖
NG/GEN/ 9/260913	80mg/2mL	100x2mL ampoules, brown	130511	2013-05	2016-04	None	Hubei Tianyao Pharmaceutical Co Ltd, No 7 Dufu block, Jianshe Road, Xiangfan, China	Importer-distributor, private / Lagos	Controlled	Yes	✓	✓	✓ 97.3% FL: 94.9-99.8%	✓ 29.8	32.0	38.2	✓ 5.4	✓
TJ/GEN/ 1/30082013	40mg/1mL	10x1mL ampoules	A53540	2012-07	2017-07	None	Krka d.d., Shmarjeshka cesta 6, 8000 Novo Město, Slovenia	Importer-distributor, private / Dushanbe	Controlled	Yes	✓	✓	✓ 105.4% FL: 102.8-108.1%	✓ 37.4	26.1	46.6	✓ 3.8	✓
TJ/GEN/ 2/30082013	80mg/2mL	10x2mL ampoules, brown	120022	2012-04	2015-04	None	Sanavita Pharmaceuticals GmbH, Lohstr. 2, 59368 Werne, Germany	Importer-distributor, private / Dushanbe	Controlled: 15-20°C	Re-registration pending	✓	✓	✓ 95.6% FL: 93.8-97.3%	✓ 30.6	26.3	43.1	✓ 5.1	✓
TJ/GEN/ 3/30082013	80mg/2mL	30x2mL ampoules	120413	2012-04	2015-04	None	CSPC OUYI (Shijiazhuang) Pharmaceuticals Co Ltd, No. 276 West Zhongshan Road, Shijiazhuang, China	Importer-distributor, private / Dushanbe	Controlled: 15-20°C	Re-registration pending	✓	✓	✓ 100.0% FL: 98.2-101.8%	✓ 25.4	29.4	45.2	✓ 3.6	✓
TZ/GEN/ 01/060913	80mg/2mL	2mL ampoule	EA-3110	2013-01	2015-12	None	Lincoln Pharmaceuticals Ltd, Trimul Estate, Khatraj Chokdi, Kalol, Gandhinagar, Gujarat, India	Importer, private / Dar es Salaam	Controlled	Yes	✓	✓	✖ **93.3%** FL: 92.4-**94.1%** **92.5%** FL: 91.1-**93.9%** **93.8%** FL: 92.4-**95.2%** **(Ø: 93.2%)**	✓ 25.4	30.6	44.1	✓ 3.2	✖

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Appendix 5: Gentamicin injection – test results

Assay: upper fiducial limit of error NLT 97.0%, lower fiducial limit of error NMT 110.0% of the stated content; ✓= complies; ✖= does not comply
Composition of gentamicin: C_1: 25.0 – 50.0%, C_{1a}: 10.0 – 35.0%, C_2 + C_{2a}: 25.0 – 55.0%; **pH**: 3.0 – 5.5
Appearance: clear colourless solution, free from visible particles

Country of collection* / sample code	Strength	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at samp-ling site	Registered	Appear-ance	Iden-tity	Assay	Composition of gentamicin			pH	Conclu sion
														C1 (%)	C1a (%)	C2+C2a (%)		
TZ/GEN/ 14/130913	80mg/2mL	2mL ampoule	EA-2C14	2012-12	2015-11	None	Lincoln Pharmaceuticals Ltd, Trimul Estate, Khatraj Chokdi, Kalol, Gandhinagar, Gujarat, India	Importer-distributor, private / Dar es Salaam	Controlled	Yes	✓	✓	✓ 97.2% FL: 96.4-98.1%	✓ 25.4	29.0	45.7	✓ 3.5	✓
TZ/GEN/ 08/090913	80mg/2mL	2mL ampoule	P03299	2013-03	2016-02	None	Intas Pharmaceuticals Ltd, Matoda-382210, Ahmedabad, India	Importer-central medical store, public / Dar Es Salaam	Controlled	Yes	✓	✓	✓ 95.9% FL: 93.8-98.1%	✓ 25.3	32.3	42.4	✓ 3.3	✓
TZ/GEN/ 03/090913	80mg/2mL	2mL ampoule	V13080	2013-02	2016-01	BP	Vital Healthcare Pvt Ltd, Plot No. H-10, MIDC, Satpur Nashik-422007, India	Importer, private / Dar es Salaam	Controlled	Yes	✓	✓	✓ 96.6% FL: 95.0-98.2%	✓ 25.3	33.3	41.4	✓ 3.3	✓
UG/GEN/ 25/12-09-2013	80mg/2mL	10x2mL ampoules, brown	130113	2013-01	2016-01	BP	CSPC OUYI (Shijiazhuang) Pharmaceuticals Co Ltd, No. 276 West Zhongshan Road, Shijiazhuang, China	Wholesaler-importer, private / Kampala	Not controlled - actual temperature 25°C, protected from sunlight	Yes	✓	✓	✖ **113.5%** FL: **111.4**-115.6% **114.1%** FL: **111**.0-117.4% **114.7%** FL: **111.5%**-118.0% **(Ø: 114.1%)**	✓ 28.9	30.9	40.2	✓ 5.1	✖
UG/GEN/ 09/06-09-2013	80mg/2mL	2mL ampoule	130215	2013-02	2016-01	None	Ningbo Dahongying Pharmaceutical Co Ltd, No.396 Mingzhu Road, Ningbo, Zhejiang, China	Wholesaler-importer, private / Kampala	Controlled	Yes	✓	✓	✓ 106.3% FL: 105.2-107.4%	✓ 27.8	30.1	42.1	✓ 3.6	✓
UG/GEN/ 16/09-09-2013	80mg/2mL	10x2mL ampoules, brown	130202	2013-02	2016-02	None	Zhejiang Tianfeng Pharmaceutical Factory No. 518 Daxiang Road, Huzhou, Zhejiang, China	Central medical store, public / Entebbe	Controlled: 24°C, RH 65%	Yes	✓	✓	✓ 103.1% FL: 102.1-104.2%	✓ 28.3	30.3	41.5	✓ 3.0	✓

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Assay: upper fiducial limit of error NLT 97.0%, lower fiducial limit of error NMT 110.0% of the stated content; ✓= complies; ✖= does not comply
Composition of gentamicin: C_1: 25.0 – 50.0%, C_{1a}: 10.0 – 35.0%, C_2 + C_{2a}: 25.0 – 55.0%; **pH**: 3.0 – 5.5
Appearance: clear colourless solution, free from visible particles

Country of collection* / sample code	Strength	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at samp-ling site	Registered	Appear-ance	Iden-tity	Assay	Composition of gentamicin			pH	Conclu sion
														C1 (%)	C1a (%)	C2+C2a (%)		
VN/GEN/ 01/240913	80mg/2mL	20x2mL ampoules	86FHA01 1	2012-08	2015-08	None	Fresenius Kabi Bidiphar JS Co, Zone 8, Nhon Phu Ward, Quy Nhon City, Binh Dinh Province, Viet Nam	Importer-distributor, public / Hanoi	Controlled: 23°C, RH 59%	Yes	✓	✓	✓ 108.7% FL: 106.7-110.7%	✖ **24.5** **24.9** **24.9** **Ø: 24.8**	34.6 34.1 34.3 Ø: 34.3	40.9 41.0 40.8 Ø: 40.9	✓ 4.9	✖
VN/GEN/02/011013	80mg/2mL	50x2mL ampoules	30713	2013-07	2015-07	None	Pymepharco Co, 166-170 Nguyen Hue Street, Tuy Hoa City, Phu Yen Province, Viet Nam	Manufacturer-distributor, private / Ho Chi Minh City	Controlled: 24°C, RH 61%	Yes	✓	✓	✓ 108.6% FL: 107.6-109.7%	✖ **24.1** **24.6** **24.6** **Ø: 24.4**	31.0 30.7 30.8 Ø: 30.8	44.9 44.7 44.7 Ø: 44.8	✓ 4.8	✖
VN/GEN/ 03/011013	80mg/2mL	10x2mL ampoules, brown	120904	2012-09	2015-09	None	Shandong Reyoung Pharmaceutical Co Ltd, No. 6 Erlangshan Road, Yiyuan County, Shandong Province, China	Importer-distributor, public / Ho Chi Minh City	Controlled: 25°C, RH 50%	Yes	✓	✓	✓ 99.7% FL: 98.7-100.6%	✓ 28.1	30.2	41.7	✖ **5.6**	✖
ZW/GEN/ 01/10/09/13	80mg/2mL	5x2mL ampoules	P04358	2013-04	2016-03	None	Intas Pharmaceuticals Ltd, Matoda-382210, Ahmedabad, India	Importer, private / Harare	Controlled: 25°C, RH 21%	Yes	✓	✓	✖ **94.7%** FL: 93.5-**95.9%** **92.3%** FL: 90.9-**93.8%** **91.7%** FL: 90.2-**93.2%** **(Ø: 92.9%)**	✓ 25.2	31.1	43.7	✓ 3.1	✖
ZW/GEN/ 02/11/09/13	80mg/2mL	2mL ampoule	019UF12/ 3	2012-05	2017-05	USP	Biologici Italia Laboratories, Via F.Serpero 2, 20060 Masate, Milano, Italy	Central medical store, public / Harare	Controlled: 24°C	No - donation	✓	✓	✓ 102.6% FL: 101.3-103.9%	✓ 30.1	25.4	44.5	✓ 3.6	✓

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Assay: 90.0 – 110.0% total penicillins calculated as procaine benzylpenicillin; **Procaine**: 36.0 – 44.0% of stated amount of procaine benzylpenicillin; ✓= complies; ✖= does not comply

Related substances: 4-aminobenzoic acid ≤ 0.5%, any other secondary peak ≤ 1%; **pH**: 5.0 – 7.5; **Water**: 2.8 – 4.2%
Appearance: white powder

Appendix 6 Procaine benzylpenicillin injection – test results

Country of collection* / sample code	Strength	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Procaine %	Related substances	pH	Water %	Uniform ity of mass	Conclu-sion
MG/PBP/ 04/300813	1 MIU	50 vials	120901	2012-09	2015-09	BP	North China Pharmaceutical Co Ltd (NCPC), No. 217-1 East Heping Road, Shijiazhuang, Hebei, China	Wholesaler-importer, private / Antananarivo	Controlled: 16.9°C, RH 35.2%	Yes	✓	✓	✓ 0.979 MIU = 97.9%	✓ 42.4	✓ 4-aminobenzoic acid: 0.02%; max other: 0.3%	✓ 6.5	✓ 3.2	✓	✓
MG/PBP/ 05/110913	1 MIU	10 vials	130317	2013-03	2016-03	None	CSPC Zhongnuo Pharmaceutical (Shijazhuang) Co Ltd, 47 Fengshou Road, Shijiazhuang city, China	Wholesaler-importer, private / Antananarivo	Controlled: 19.1°C, RH 33.6%	Yes	✓	✓	✓ 0.967 MIU = 96.7%	✓ 39.0	✓ 4-aminobenzoic acid: 0.02%; max other: 0.3%	✓ 5.8	✓ 3.2	✓	✓
ZW/PBP/ 01/11/09/13	3 MIU	50 vials	300240	2012-06	2015-06	None	Panpharma SA, France	Central medical store, public / Harare	Controlled: 24°C	No - donation	✓	✓	✓ 3.15 MIU = 104.9%	✓ 42.4	✓ 4-aminobenzoic acid: 0.02%; max other: 0.3%	✓ 5.3	✓ 3.2	✓	✓

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Assay: 90.0 – 110.0% total penicillins calculated as procaine benzylpenicillin; **Procaine**: 36.0 – 44.0% of stated amount of procaine benzylpenicillin; ✓= complies; ✖= does not comply
Related substances: 4-aminobenzoic acid ≤ 0.5%, any other secondary peak ≤ 1%; **pH**: 5.0 – 7.5; **Water**: 2.8 – 4.2%
Appearance: white powder

Procaine benzylpenicillin + benzylpenicillin injection – test results

Country of collection* / sample code	Strength	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Procaine %	Related substances	pH	Water %	Uniformity of mass	Conclu-sion
BF/PBP/ 120916/05-09-2013	3 MIU + 1 MIU	100 vials	120916	2012-09	2015-08	None	North China Pharmaceutical Co Ltd (NCPC), No. 388 East Heping Road, Shijiazhuang, Hebei, China	Distributor, public / Ouagadougou	Not controlled, not air-conditioned	Yes	✓	✓	✓ 3.96 MIU = 98.9%	✓ 33.2	✓ 4-aminobenzoic acid: 0.03%; max other: 0.3%	✓ 6.7	✓ 2.6	✓	✓
TZ/PBP/ 06/090913	3 MIU + 1 MIU	50 vials	619130405	2013-04	2016-04	None	CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co Ltd, No.188 Gongnong Road, Shijiazhuang, Hebei, China	Importer-central medical store, public / Dar es Salaam	Controlled	Yes	✓	✓	✓ 3.94 MIU = 98.6%	✓ 33.2	✓ 4-aminobenzoic acid: 0.03%; max other: 0.4%	✓ 6.6	✓ 2.7	✓	✓
UG/PBP/ 13/07-09-2013	3 MIU + 1 MIU	10 vials	619130103	2013-01	2016-01	None	CSPC Zhongnuo Pharmaceutical (Shijazhuang) Co Ltd, 47 Fengshou Road, Shijiazhuang city, China	Wholesaler-importer, private / Kampala	Not controlled - actual temperature 25°C, protected from sunlight	Yes	✓	✓	✓ 3.93 MIU = 98.3%	✓ 33.4	✓ 4-aminobenzoic acid: 0.03%; max other: 0.3%	✓ 6.6	✓ 2.7	✓	✓

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Assay: 95.0-105.0%; **Related substances**: ampicillin dimer ≤ 4.5%, any other secondary peak ≤ 2%; **pH**: 8.0 – 10.0; **Water**: NMT 2.0% ✓= complies; ✖= does not comply
Uniformity of mass: NMT two of the individual masses outside the limits of ± 10% of the average mass and none outside the limits of ± 20%

Appendix 7 Ampicillin injection – test results

Country of collection* / sample code	Strength mg/vial	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Related substances	pH	Water %	Uniformity of mass	Conclusion
BF/AMP/ 130321/04-09-2013	1000	50 vials, glass	130321	2013-03	2016-02	BP	North China Pharmaceutical Co Ltd (NCPC), No. 388 East Heping Road, Shijiazhuang, Hebei, China	Importer, public / Ouagadougou	Not con-trolled, not air-condi-tioned - actual temperature 29°C	Yes	Fine, light yellowish powder	✓	✓ 99.7	✓ dimer: 3.6% max other: 2.0%	✓ 8.9	✓ 0.7	✓	✓
BF/AMP/ 120854/04-09-2013	1000	50 vials, glass	120854	2012-08	2015-07	BP	North China Pharmaceutical Co Ltd (NCPC), No. 388 East Heping Road, Shijiazhuang, Hebei, China	Importer, public / Ouagadougou	Not con-trolled, not air-condi-tioned - actual temperature 29°C	Yes	Fine, light yellowish powder	✓	✓ 96.3	✖ **dimer: 4.8% max other: 5.3%**	✓ 8.8	✓ 1.2	✓	✖
BF/AMP/ 110408/04-09-2013	1000	50 vials, glass	110408	2011-04	2014-04	None	Shandong Reyoung Pharmaceutical Co Ltd, No. 6 Erlangshan Road, Yiyuan County, Shandong Province, China	Importer, private / Ouagadougou	Not con-trolled, not air-condi-tioned - actual temperature 28°C	Yes	Fine, off-white powder	✓	✓ 100.7	✓ dimer: 0.4% max other: 0.6%	✓ 9.6	✓ 0.2	✓	✓
KE/AMP/ 20/10-09-13	500	50 vials, glass	120657	2012-06	2015-06	None	Shandong (Yanzhou) Xier Kangtai Pharmaceutical Co Ltd, Private Economy Garden-Xinyan Town, Yanzhou City, Shandong, China	Distributor, private / Nairobi	Controlled: 24°C, RH 55%	Yes	Fine, off-white powder	✓	✓ 95.3	✖ dimer: 3.1% **max other: 4.0%**	✓ 8.8	✓ 1.9	✓	✖
KE/AMP/ 04/04-09-13	500	50 vials, glass	672130413	2013-04	2016-04	BP	CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co Ltd, No.188 Gongnong Road, Shijiazhuang, Hebei, China	NGO store, Nairobi	Controlled: 22°C, RH 63%	Yes	Fine, light yellowish powder	✓	✓ 98.1	✓ dimer: 3.5% max other: 1.5%	✓ 9.1	✓ 1.1	Inconclusive n=18 Ø: 565.3mg min:-2.2%, max:+2.2%	✓ Uniformity of mass inconclusive due to insufficient number of vials
MG/AMP/ 06/110913	1000	10 vials, glass	130112	2013-01	2016-01	None	CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co Ltd, No.188 Gongnong Road, Shijiazhuang, Hebei, China	Wholesaler, private / Antananarivo	Controlled: 19.1°C, RH 33.6%	Yes	Fine, light yellowish powder	✓	✓ 96.8	✓ dimer: 3.0% max other: 1.6%	✓ 9.1	✓ 1.1	✓	✓

* BF=Burkina Faso, KE=Kenya, MG=Madagascar, NP=Nepal, NG=Nigeria=, TJ=Tajikistan, TZ=Tanzania, UG=Uganda, VN=Viet Nam, ZW=Zimbabwe

Assay: 95.0-105.0%; **Related substances**: ampicillin dimer ≤ 4.5%, any other secondary peak ≤ 2%; **pH**: 8.0 – 10.0; **Water**: NMT 2.0% ✓= complies; ✖= does not comply
Uniformity of mass: NMT two of the individual masses outside the limits of ± 10% of the average mass and none outside the limits of ± 20%

Country of collection* / sample code	Strength mg/vial	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Related substances	pH	Water %	Uniformity of mass	Conclusion
MG/AMP/07/300813	1000	50 vials, glass	120963	2012-09	2015-09	None	North China Pharmaceutical Co Ltd (NCPC), No. 388 East Heping Road, Shijiazhuang, Hebei, China	Central medical store, public / Antananarivo	Controlled: 17.6°C, RH 34.8%	Yes	Fine, light yellowish powder	✓	✖ **94.3**	✖ dimer: 2.5% **max other: 3.1%**	✓ 9.0	✓ 1.7	✓	✖
MG/AMP/08/110913	1000	50 vials, glass	130123	2013-01	2015-12	None	Shanxi Shuguang, Pharmaceutical Co Ltd, No. 1 Kangle Street, Qi County, Jinzhong City, Shanxi Province, China	Wholesaler, private / Antananarivo	Controlled:18.6°C, RH 33.9%	Yes	Fine, off-white powder	✓	✓ 95.7	✓ dimer: 4.1% max other: 2.0%	✓ 8.9	✓ 1.2	✓	✓
NP/AMP/AMP1/27Aug2013	250	1 vial, glass	M06J012	2012-09	2014-08	None	Aristo Pharmaceuticals Pvt Ltd, Plot No. 208, New Industrial Area No.2, Mandideep, District Raisen, Madhya Pradesh, India	Distributor, private / Kathmandu	Not controlled	Yes	Fine, off-white powder	✓	✓ 96.6	✓ dimer: 0.5% max other: 0.4%	✓ 9.1	✓ 1.0	✓	✓
NP/AMP/AMP2/27Aug2013	500	1 vial, glass + 1 ampoule water, plastic	M05A013	2013-01	2014-12	None	Aristo Pharmaceuticals Pvt Ltd, Plot No. 208, New Industrial Area No.2, Mandideep, District Raisen, Madhya Pradesh, India	Distributor, private / Kathmandu	Not controlled	Yes	Fine, off-white powder	✓	✓ 98.5	✓ dimer: 0.9% max other: 0.6%	✓ 9.1	✓ 1.0	Inconclusive n=18 Ø: 551.7mg min:-1.9%, max:+2.0%	✓ Uniformity of mass inconclusive due to insufficient number of vials
NP/AMP/AMP3/1Sep2013	250	1 vial, glass + 1 ampoule water, plastic	M06M022	2012-12	2014-11	None	Aristo Pharmaceuticals Pvt Ltd, Plot No. 208, New Industrial Area No.2, Mandideep, District Raisen, Madhya Pradesh, India	Hospital directly purchasing medicines, public / Patan, Lalitpur	Not controlled	Yes	Fine, off-white powder	✓	✓ 97.1	✓ dimer: 0.3% max other: 0.5%	✓ 9.2	✓ 1.3	Inconclusive n=19 Ø: 280.4mg min:-3.6%, max:+4.8%	✓ Uniformity of mass inconclusive due to insufficient number of vials
NG/AMP/15/260913	1000	50 vials, glass	674130307	2013-03	2016-03	None	CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co Ltd, No.188 Gongnong Road, Shijiazhuang, Hebei, China	Importer-distributor, private / Lagos	Controlled	Yes	Fine, off-white powder	✓	✓ 97.5	✖ dimer: 3.7% **max other: 2.2%**	✓ 9.0	✓ 1.2	✓	✖
TJ/AMP/1/30082013	500	10 vials, glass	130220	2013-02	2016-02	None	Sinochem Ningbo Ltd, 21 Jiangxia st., Ningbo, Zhejiang, China	Importer-distributor, private / Dushanbe	Controlled	Re-registrat-ion pending	Fine, off-white crystalline powder	✓	✓ 96.9	✖ **dimer: 4.7% max other: 2.6%**	✓ 8.8	✓ 1.2	✖ **1 vial >20%**	✖

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Assay: 95.0-105.0%; **Related substances**: ampicillin dimer ≤ 4.5%, any other secondary peak ≤ 2%; **pH**: 8.0 – 10.0; **Water**: NMT 2.0% ✓= complies; ✖= does not comply
Uniformity of mass: NMT two of the individual masses outside the limits of ± 10% of the average mass and none outside the limits of ± 20%

Country of collection* / sample code	Strength mg/vial	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Related substances	pH	Water %	Uniformity of mass	Conclusion
TJ/AMP/ 2/30082013	1000	50 vials, glass	120116	2012-10	2015-10	None	Sanavita Pharmaceuticals GmbH, Lohstr. 2, 59368 Werne, Germany	Importer-distributor, private / Dushanbe	Controlled	Re-registra-tion pending	Fine, white powder	✓	✓ 97.6	✓ dimer: 3.4% max other: 1.8%	✓ 9.1	✓ 0.7	✓	✓
TJ/AMP/ 3/30082013	1000	25 vials, glass	674121010	2012-10	2015-10	BP	Pharmax (UK) Ltd, Bristol, UK	Importer-distributor, private / Dushanbe	Controlled	Yes	Fine, white powder	✓	✓ 98.4	✖ dimer: 3.7% **max other: 2.8%**	✓ 8.7	✓ 2.0	✓	✖
TZ/AMP/ 02/060913	500	20 vials, glass	20130351	2013-03	2015-03	None	Harbin General Pharmaceutical Factory, No. 109 Yuefu Road, Nangang District, Harbin, China	Importer, private / Dar es Salaam	Controlled	Yes	Fine, off-white powder	✓	✓ 98.8	✓ dimer: 0.8% max other: 0.4%	✓ 9.7	✓ 0.2	✓	✓
TZ/AMP/ 07/090913	500	50 vials, glass	MDE-3306	2013-03	2016-02	BP	Lincoln Pharmaceuticals Ltd, Trimul Estate, Khatraj Chokdi, Kalol, Gandhinagar, Gujarat, India (Manufactured by) Manufactured at: Makcur Laboratories Ltd, 46/5-6-7, Village Zak, Tal. Dehgam, 382330 Gandhinagar, Gujarat, India	Importer-central medical store, public / Dar es Salaam	Controlled	Yes	Fine, off-white powder	✓	✓ 97.8	✓ dimer: 0.7% max other: 0.4%	✓ 9.4	✓ 0.5	✓	✓
UG/AMP/ 20/09-09-2013	500	50 vials, glass	BQ5012002-A	2012-03	2015-02	USP	Aurobindo Pharma Ltd, Unit XII, Survey No. 314, Bachupally Village, Quthubullapur Mandal, Ranga Reddy District, Andhra Pradesh, India	NGO store, Kampala	Controlled: 24°C, RH 65%	Yes	Fine, off-white crystalline powder	✓	✓ 98.2	✓ dimer: 0.8% max other: 1.0%	✓ 8.9	✓ 1.2	✓	✓
UG/AMP/ 17/09-09-2013	500	10 vials, glass	672121250	2012-12	2015-12	BP	CSPC Zhongnuo Pharmaceutical (Shijazhuang) Co Ltd, 47 Fengshou Road, Shijiazhuang city, China	Central medical store, public / Entebbe	Controlled: 24°C, RH 65%	Yes	Fine, off-white powder	✓	✓ 98.7	✖ dimer: 3.5% **max other: 3.8%**	✓ 9.0	✓ 0.9	✓	✖

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Assay: 95.0-105.0%; **Related substances**: ampicillin dimer ≤ 4.5%, any other secondary peak ≤ 2%; **pH**: 8.0 – 10.0; **Water**: NMT 2.0% ✓= complies; ✖= does not comply
Uniformity of mass: NMT two of the individual masses outside the limits of ± 10% of the average mass and none outside the limits of ± 20%

Country of collection* / sample code	Strength mg/vial	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Related substances	pH	Water %	Uniformity of mass	Conclusion
UG/AMP/ 24/12-09-2013	500	10 vials, glass	0204611	2011-09	2014-08	BP	Karnataka Antibiotics and Pharmaceuticals Ltd, Plot No.14. II Phase, Peenya, Bangalore 560058, India	Wholesaler-importer, private / Kampala	Not controlled - actual temperature 25°C	Yes	Fine, off-white powder	✓	✓ 96.0	✓ dimer: 1.3% max other: 0.9%	✓ 8.9	✓ 1.3	✓	✓
VN/AMP/ 01/250913	1000	50 vials, glass	010813	2013-08	2016-08	None	MinhDan Pharmaceutical JS Co, Lot N8-N5 Street-Hoa Xa Industrial Estate, Nam Dinh, Viet Nam	Manufacturer-distributor, private / Nam Dinh City	Controlled: 22°C, RH 57%	Yes	Fine, light yellowish powder	✓	✖ **93.3**	✓ dimer: 1.6% max other: 1.0%	✓ 9.0	✓ 1.3	✓	✖
VN/AMP/ 02/250913	1000	50 vials, glass	060713	2013-07	2017-07	None	Viet Nam China Pharmaceutical JS Co (VCP), Thanh Xuan Commune, Soc Son District, Hanoi, Viet Nam	Manufacturer-distributor, private / Hanoi	Controlled: 24°C, RH 55%	Yes	Fine, light yellowish powder	✓	✓ 96.3	✓ dimer: 3.4% max other: 1.9%	✓ 8.9	✓ 1.0	✓	✓
VN/AMP/ 03/021013	1000	20 vials, glass	13005TN	not stated	2016-07	None	Mekophar Chemical Pharmaceutical JS Co, 297/5 Ly Thuong Kiet Street, Ward 15, District 11, Ho Chi Minh City, Viet Nam	Manufacturer-distributor, private / Ho Chi Minh City	Controlled: 23°C, RH 62%	Yes	Fine, light yellowish powder	✓	✖ **93.9**	✖ dimer: 3.9% **max other: 3.6%**	✓ 8.9	✓ 1.3	✓	✖
ZW/AMP/ 01/10/09/13	500	10 vials, glass	V32014	2012-02	2015-01	BP	Umedica Laboratories Pvt Ltd, Plot 221, GIDC, Vapi 396195, Gujarat, India	Importer, private / Harare	Controlled: 25°C, RH 21%	Yes	Fine, off-white powder	✓	✓ 95.8	✓ dimer: 1.5% max other: 0.6%	✓ 9.1	✓ 0.8	✓	✓
ZW/AMP/ 02/11/09/13	500	25 vials, glass	BP5011004-A	2011-05	2014-04	USP	Aurobindo Pharma Ltd, Unit XII, Survey No. 314, Bachupally Village, Quthubullapur Mandal, Ranga Reddy District, Andhra Pradesh, India	Central medical store, public / Harare	Controlled: 24°C	No - donation	Fine, off-white crystalline powder	✓	✓ 99.0	✓ dimer: 0.6% max other: 0.6%	✓ 9.0	✓ 0.9	✓	✓
ZW/AMP/ 03/12/09/13	500	10 vials, glass	0202312	2012-08	2015-07	BP	Karnataka Antibiotics and Pharmaceuticals Ltd, Plot No.14. II Phase, Peenya, Bangalore 560058, India	Importer, private / Harare	Controlled: 22°C	Yes	Fine, off-white powder	✓	✓ 100.1	✓ dimer: 1.4% max other: 0.6%	✓ 9.0	✓ 1.0	✓	✓

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Assay: 92.0-108.0%; **Related substances**: any secondary peak ≤ 1%, sum of secondary peaks ≤ 5%; **pH**: 6.0 – 8.0; **Water**: NMT 11.0% ✓= complies; ✖= does not comply
Appearance: White powder

Appendix 8 Ceftriaxone injection - test results

Country of collection* / sample code	Strength mg/vial	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Related substances	pH	Water %	Uniform ity of mass	Conclu-sion
BF/CEF/ S121202/30 -08-2013	1000	1 vial, glass + 1 plastic ampoule with 10mL water for injection	S121202	2012-12	2014-11	USP	Strides Arcolab Ltd, Bangalore, India	Importer, private / Ouagadougou	Not controlled, not air-conditioned - actual temperature 30°C	Yes	✓	✓	✓ 98.0	✓ max sec.peak: 0.7% sum: 0.7%	✓ 6.3	✓ 9.5	✓	✓
BF/CEF/ 130226/05-09-2013	1000	1 vial, glass + 1 glass ampoule with 5mL water for injection	130226/ 121255	2013-02	2015-11	BP	North China Pharmaceutical Co Ltd (NCPC), No. 388 East Heping Road, Shijiazhuang, Hebei, China	Distributor, public / Ouagadougou	Not controlled, not air-conditioned - actual temperature 30°C	Yes	✓	✓	✓ 98.9	✓ max sec.peak: 0.2% sum: 0.2%	✓ 6.7	✓ 9.3	✓	✓
BF/CEF/ 111019/04-09-2013	250	1 vial, glass + 1 glass ampoule with 3mL water for injection	111019	2011-10	2014-09	BP	North China Pharmaceutical Co Ltd (NCPC), No. 388 East Heping Road, Shijiazhuang, Hebei, China	Importer, public / Ouagadougou	Not controlled, not air-conditioned - actual temperature 29°C	Yes	✓	✓	✓ 100.4	✓ max sec.peak: 0.6% sum: 0.5%	✓ 6.3	✓ 9.1	✓	✓
KE/CEF/ 07/05-09-13	250	1 vial	CLH07	2012-12	2015-07	None	Popular Pharmaceuticals Ltd, 164 Tongi Industrial Area, Tongi, Gazipur-1711, Dhaka, Bangladesh	NGO store / Nairobi	Controlled: 22°C, RH 63%	Yes	✓	✓	✓ 96.3	✓ max sec.peak: 0.6% sum: 0.6%	✓ 6.3	✓ 10.0	✓	✓
KE/CEF/ 01/04-09-13	1000	1 vial, glass + 1 plastic ampoule with 10mL water for injection	LA87012 002	2012-01	2014-10	None	Kopran Ltd, Village Savroli, Taluka: Khalapur, District: Raigad, Maharashtra, India	Distributor, private / Nairobi	Controlled: 20°C, RH 60%	Yes	✓	✓	✓ 98.4	✓ max sec.peak: 0.4% sum: 0.5%	✓ 6.6	✓ 9.8	✓	✓
KE/CEF/ 09/06-09-13	500	1 vial, glass + 1 plastic ampoule with 5mL water for injection	9658	2013-02	2016-01	None	Flamingo Pharmaceuticals Ltd, PO Box 27257 Mumbai 400071, India	Distributor, private / Nairobi	Controlled: 23°C, RH 60%	Yes	✓	✓	✓ 92.3	✓ max sec.peak: 0.3% sum: 0.4%	✓ 6.7	✓ 9.2	✓	✓
KE/CEF/ 08/06-09-13	1000	1 vial, glass + 1 glass ampoule with 10mL water for injection	130610	2013-06	2016-06	None	Shandong (Yanzhou) Xier Kangtai Pharmaceutical Co Ltd, Private Economy Garden-Xinyan Town, Yanzhou City, Shandong, China	Distributor, private / Nairobi	Controlled: 23°C, RH 60%	Yes	✓	✓	✖ **90.7**	✓ max sec.peak: 0.1% sum: 0.1%	✓ 6.6	✓ 8.7	✓	✖

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Assay: 92.0-108.0%; **Related substances**: any secondary peak ≤ 1%, sum of secondary peaks ≤ 5%; **pH**: 6.0 – 8.0; **Water**: NMT 11.0% ✓= complies; ✖= does not comply
Appearance: white powder

Country of collection* / sample code	Strength mg/vial	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Related substances	pH	Water %	Uniform ity of mass	Conclu-sion
MG/CEF/ 09/110913	1000	1 vial, glass + 1 glass ampoule with 10mL water for injection	130643	2013-06	2016-05	USP	Shandong (Yanzhou) Xier Kangtai Pharmaceutical Co Ltd, Private Economy Garden-Xinyan Town, Yanzhou City, Shandong, China	Wholesaler, private / Antananarivo	Controlled: 18.6°C, RH 33.9%	Yes	✓	✓	✓ 92.0	✓ max sec.peak: 0.2% sum: 0.2%	✓ 6.5	✓ 9.2	✓	✓
MG/CEF/ 10/300813	1000	10 vials, glass	120902	2012-09	2015-09	None	North China Pharmaceutical Co Ltd (NCPC), No. 217-1 East Heping Road, Shijiazhuang, Hebei, China	Wholesaler, private / Antananarivo	Controlled: 16.9°C, RH 35.2%	Yes	✓	✓	✓ 97.6	✓ max sec.peak: 0.2% sum: 0.2%	✓ 6.3	✓ 9.4	✓	✓
MG/CEF/ 11/110913	1000	1 vial, glass + 1 plastic ampoule with 10mL water for injection	ADH2005	2012-06	2014-11	USP	Okasa Pharma, L-2, additional MIDC, Satara 415 004, Maharashtra, India For: Cipla Ltd, Mumbai Central, India	Wholesaler, private / Antananarivo	Controlled: 19.1°C, RH 33.6%	Yes	✓	✓	✓ 102.7	✓ max sec.peak: 0.4% sum: 0.4%	✓ 6.5	✓ 9.0	✓	✓
NP/CEF/ C1/27Aug2013	1000	1 vial, glass + 1 plastic ampoule with 10mL water for injection	A2050ZP	2012-11	2014-10	None	Lupin Ltd, Mumbai, India	Distributor, private / Kathmandu	Not controlled	Yes	✓	✓	✓ 97.9	✓ max sec.peak: 0.6% sum: 0.6%	✓ 6.4	✓ 9.4	✓	✓
NP/CEF/ C2/27Aug2013	1000	1 vial, glass + 1 plastic ampoule with 10mL water for injection	2371387	2012-02	2014-01	None	Ranbaxy Laboratories Ltd, Industrial Area-3, Dewas 455003, India	Distributor, private / Kathmandu	Not controlled	Yes	✓	✓	✓ 98.5	✓ max sec.peak: 0.3% sum: 0.3%	✓ 6.6	✓ 8.5	✓	✓
NP/CEF/C3/27Aug2013	1000	1 vial, glass + 1 plastic ampoule with 10mL water for injection	M16G022	2012-07	2014-12	None	Aristo Pharmaceuticals Pvt Ltd, Plot No. 208, New Industrial Area No.2, Mandideep, District Raisen, Madhya Pradesh, India	Distributor, private / Kathmandu	Not controlled	Yes	✓	✓	✓ 97.1	✓ max sec.peak: 0.4% sum: 0.4%	✓ 6.4	✓ 9.1	✓	✓
NG/CEF/ 10/260913	1000	1 vial, glass + 1 glass ampoule with 10mL water for injection	2523307	2013-06	2016-05	None	Ranbaxy Laboratories Ltd, Industrial Area-3, Dewas 455003, India	Importer-distributor, private / Lagos	Controlled	Yes	✓	✓	✓ 99.7	✓ max sec.peak: 0.3% sum: 0.4%	✓ 6.5	✓ 9.2	✓	✓
NG/CEF/ 11/300913	1000	1 vial, glass + 1 glass ampoule with 3.5mL lidocaine (1%)	B12004	2012-11	2015-11	None	Hanmi Pharm Co Ltd, 395 Chupal Paengseong-eup, Pyeongtaek-si, Gyeonggi-do 451-805, Korea	Importer-distributor, private / Lagos	Controlled	Yes	✓	✓	✓ 98.0	✓ max sec.peak: 0.4% sum: 0.4%	✓ 6.6	✓ 9.2	✓	✓

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Appendix 8: Ceftriaxone injection - test results

Assay: 92.0-108.0%; **Related substances**: any secondary peak ≤ 1%, sum of secondary peaks ≤ 5%; **pH**: 6.0 – 8.0; **Water**: NMT 11.0% ✓= complies; ✖= does not comply
Appearance: White powder

Country of collection* / sample code	Strength mg/vial	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Related substances	pH	Water %	Uniform ity of mass	Conclu-sion
NG/CEF/ 12/260913	1000	1 vial, glass + 1 glass ampoule with 5mL lidocaine (1%) + 1 glass ampoule with 10mL water for injection	659130365	2013-03	2016-03	None	CSPC Zhongnuo Pharmaceutical (Shijazhuang) Co Ltd, 47 Fengshou Road, Shijiazhuang city, China	Importer-distributor, private / Lagos	Controlled	Yes	✓	✓	✖ **91.2**	✓ max sec.peak: 0.4% sum: 0.5%	✓ 6.7	✓ 9.0	✓	✖
TJ/CEF/ 1/30082013	1000	1 vial, glass + 1 glass ampoule with 5mL lidocaine (1%)	120503	2012-05	2015-05	None	CSPC OUYI (Shijiazhuang) Pharmaceuticals Co Ltd, No. 276 West Zhongshan Road, Shijiazhuang, China	Importer-distributor, private / Dushanbe	Controlled	Re-registration pending	✓	✓	✓ 96.2	✓ max sec.peak: 0.4% sum: 0.4%	✓ 6.6	✓ 9.0	✓	✔
TJ/CEF/ 2/30082013	1000	5 vials	010113	2012-05	2016-02	None	Borshchagovskiy khimiko-farmacevticheskiy zavod ZAO, str Mira 17, Kiev, Ukraine	Importer-distributor, private / Dushanbe	Controlled	Yes	✓	✓	✓ 99.3	✓ max sec.peak: 0.3% sum: 0.3%	✓ 6.5	✓ 9.2	✓	✔
TJ/CEF/ 3/30082013	1000	1 vial	940513	2012-05	2015-06	None	Biosintez OAO, Penza, Russia	Importer-distributor, private / Dushanbe	Controlled	Yes	✓	✓	✓ 96.8	✓ max sec.peak: 0.5% sum: 0.5%	✓ 6.6	✓ 9.4	✓	✔
TZ/CEF/ 05/090913	1000	10 vials	1205002	2012-05	2015-05	None	CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co Ltd, No.188 Gongnong Road, Shijiazhuang, Hebei, China	Importer-central medical store, public / Dar es Salaam	Controlled	Yes	✓	✓	✓ 97.5	✓ max sec.peak: 0.5% sum: 0.5%	✓ 6.7	✓ 9.2	✓	✔
TZ/CEF/ 19/130913	1000	1 vial, glass + 1 plastic ampoule with 10mL water for injection	18901387 050420	2013-04	2015-03	None	Plethico Pharmaceuticals Ltd, A.B.Road, Manglia – 453 771 Indore (M.P.), India	Importer-distributor, private / Dar es Salaam	Controlled	Yes	✓	✓	✓ 99.0	✓ max sec.peak: 0.4% sum: 0.4%	✓ 6.4	✓ 9.0	✓	✔
TZ/CEF/ 20/130913	1000	1 vial, glass + 1 plastic ampoule with 10mL water for injection	007413024	2013-06	2015-05	None	Sance Laboratories Pvt Ltd, P.B. NO. 2, Kozhuvanal, Pala, Kottayam - 686523, Kerala, India	Importer-distributor, private / Dar es Salaam	Controlled	Yes	✓	✓	✓ 99.3	✓ max sec.peak: 0.3% sum: 0.3%	✓ 6.4	✓ 9.3	✓	✔
UG/CEF/ 08/06-09-2013	1000	1 vial, glass	659130289	2013-02	2016-02	BP	CSPC Zhongnuo Pharmaceutical (Shijiazhuang) Co Ltd, No.188 Gongnong Road, Shijiazhuang, Hebei, China	Wholesaler-importer, private / Kampala	Controlled	Yes	✓	✓	✓ 98.2	✓ max sec.peak: 0.1% sum: 0.1%	✓ 6.5	✓ 8.5	✓	✔

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Appendix 8: Ceftriaxone injection - test results

Assay: 92.0-108.0%; **Related substances**: any secondary peak ≤ 1%, sum of secondary peaks ≤ 5%; **pH**: 6.0 – 8.0; **Water**: NMT 11.0% ✓= complies; ✖= does not comply
Appearance: white powder

Country of collection* / sample code	Strength mg/vial	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Related substances	pH	Water %	Uniform-ity of mass	Conclu-sion
UG/CEF/ 03/02-09-2013	1000	1 vial, glass + 1 glass ampoule with 10mL water for injection	LT130401	2013-01	2015-07	None	Guilin Pharmaceutical (Shanghai) Co Ltd (GPSC), No.43 Qilidian Road, Guilin, Guangxi 541004, China	Wholesaler-importer, private / Kampala	Controlled: 20°C	Yes	✓	✓	✓ 96.6	✓ max sec.peak: 0.3% sum: 0.4%	✓ 6.4	✓ 9.6	✓	✔
UG/CEF/ 18/09-09-2013	1000	1 vial, glass	T3C070613	2013-06	2015-05	USP	M.J. Biopharm Pvt Ltd, L-7 M.I.D.C. Indl. Area, Dist. Raigad, Taloja, Navi Mumbai 410208, India	Central medical store, public / Kampala	Controlled: 24°C, RH 65%	Yes	✓	✓	✓ 97.1	✓ max sec.peak: 0.7% sum: 0.8%	✓ 6.6	✓ 9.5	✓	✔
VN/CEF/ 01/240913	1000	1 vial	1070313	2013-03	2015-03	None	Tarchomin Pharmaceutical Works "Polfa" S.A., A.Fleming str. 2, 03-176 Warsaw, Poland	Importer-distributor, public / Hanoi	Controlled: 23°C, RH 59%	Yes	✓	✓	✓ 103.9	✓ max sec.peak: 0.2% sum: 0.2%	✓ 6.6	✓ 8.7	✓	✔
VN/CEF/ 02/250913	1000	10 vials	010413	2013-04	2016-04	None	MinhDan Pharmaceutical JS Co, Lot N8-N5 street-Hoa Xa Industrial Estate, Nam Dinh, Viet Nam	Manufacturer-distributor, private / Nam Dinh City	Controlled: 22°C, RH 57%	Yes	✓	✓	✓ 106.7	✓ max sec.peak: 0.2% sum: 0.2%	✓ 6.5	✓ 9.4	✓	✔
VN/CEF/ 03/250913	1000	10 vials	600913	2013-09	2016-09	None	Viet Nam China Pharmaceutical JS Co (VCP), Thanh Xuan Commune, Soc Son District, Hanoi, Viet Nam	Manufacturer-distributor, private / Hanoi	Controlled: 24°C, RH 55%	Yes	✓	✓	✓ 97.9	✓ max sec.peak: 0.2% sum: 0.2%	✓ 6.6	✓ 9.2	✓	✔
ZW/CEF/ 01/10/09/13	500	10 vials, glass	V32147	2012-11	2015-10	USP	Umedica Laboratories Pvt Ltd, Plot 221, GIDC, Vapi 396195, Gujarat, India	Importer, private / Harare	Controlled: 25°C, RH 21%	Yes	✓	✓	✓ 96.1	✓ max sec.peak: 0.6% sum: 0.6%	✓ 6.8	✓ 10.2	✓	✔
ZW/CEF/ 02/12/09/13	1000	1 vial, glass + 1 plastic ampoule with 10mL water for injection	4400313	2013-01	2015-12	USP	Karnataka Antibiotics and Pharmaceuticals Ltd, Plot No.14. II Phase, Peenya, Bangalore 560058, India	Importer, private / Harare	Controlled: 22°C	Yes	✓	✓	✓ 99.1	✓ max sec.peak: 0.3% sum: 0.4%	✓ 6.3	✓ 8.6	✓	✔

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Assay: 95.0-105.0%; **Free dexamethasone**: ≤ 0.5%; **pH**: 7.0 – 8.5
Appearance: clear colourless solution, free from visible particles

✓= complies; ✖= does not comply

Appendix 9 Dexamethasone injection - test results

Country of collection* / sample code	Strength mg/mL	Pack size	Batch No.	Manu-facture date	Expiry date	Label claim	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Free dexa-methasone	pH	Extract-able volume	Conclu-sion
KE/DEX/ 17/09-09-13	4	10x1mL ampoules, glass	130404	2013-04	2016-03	Each 1 mL contains Dexamethasone Sodium Phosphate equivalent to Dexamethasone 4mg (ref to USP)	CSPC OUYI (Shijiazhuang) Pharmaceuticals Co Ltd, No. 276 West Zhongshan Road, Shijiazhuang, China	Wholesaler, private / Nairobi	Controlled: 23°C, RH 60%	Yes	✓	✓	✖ **64.4**	✓ not detected	✓ 7.9	✓	✖
MG/DEX/ 12/300813	4	10x1mL ampoules, glass	120704	2012-07	2015-07	Each ampoule contains Dexamethasone Sodium Phosphate BP equivalent to Dexamethasone Phosphate 4mg	North China Pharmaceutical Co Ltd (NCPC), No 6 Heping East Road, Huayo East Street, Shijiazhuang, Hebei, China	Wholesaler, private / Antananarivo	Controlled: 16.9°C, RH 35.2%	Yes	✓	✓	✓ 99.6	✓ not detected	✓ 8.0	✓	✓
MG/DEX/ A1013/110913	4	5x10x1mL ampoules, glass amber	1303119	2013-03	2016-03	Each ampoule contains Dexamethasone 4mg	Shandong (Yanzhou) Xier Kangtai Pharmaceutical Co Ltd, Private Economy Garden-Xinyan Town, Yanzhou City, Shandong, China	Wholesaler, private / Antananarivo	Controlled: 19.1°C, RH 33.6%	Yes	✓	✓	✖ **84.6**	✓ not detected	✓ 8.0	✓	✖
NP/DEX/ D1/27Aug2013	4	6x2mL vials, glass	HM3187	2012-12	2014-05	Each 1 mL contains Dexamethasone Sodium Phosphate USP equivalent to Dexamethasone Phosphate 4mg	Cadila Healthcare Ltd, Sarkhej-Bavla N.H. No. 8A, Moraiya, Sanand, Ahmedabad 382 210, Manufactured at: 10-13, Sarkhej-Bavla Road, Changodar, Agmedabad 382 213, India	Distributor, private / Kathmandu	Not controlled	Yes	✓	✓	✓ 102.9	✓ not detected	✓ 7.9	✓	✓
NP/DEX/ D2/27Aug2013	4	100x2mL vials, glass	SDT 304	2013-04	2014-09	Each 1 mL contains Dexamethasone Sodium Phosphate IP equivalent to Dexamethasone Phosphate 4mg	Sanjvani Parenteral Ltd, R-40, TTC Rabale, Thane Belapur Road, Navi Mumbai - 400 701, India	Treatment centre directly purchasing medicines, public / Kathmandu	Not controlled	Yes	✓	✓	✓ 101.9	✓ not detected	✓ 7.5	✓	✓
NP/DEX/ D3/30Aug2013	4	10x2mL vials, glass	277	2013-03	2015-02	Each 1 mL contains Dexamethasone Sodium Phosphate IP equivalent to Dexamethasone Phosphate 4mg	Hindustan Pharmaceuticals, Barauni - 851 112, India	Hospital directly purchasing medicines, public / Kathmandu	Not controlled	Yes	✓	✓	✖ **82.1**	✖ **1.2%**	✓ 7.8	✓	✖

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Assay: 95.0-105.0%; **Free dexamethasone**: ≤ 0.5%; **pH**: 7.0 – 8.5
Appearance: clear colourless solution, free from visible particles

✓= complies; ✖= does not comply

Country of collection* / sample code	Strength mg/mL	Pack size	Batch No.	Manu-facture date	Expiry date	Label claim	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Free dexa-methasone	pH	Extract-able volume	Conclu-sion
NG/DEX/ 13/081013	4	10x1mL ampoules, glass amber	120365	2012-03	2015-03	Each 1 mL contains 4mg Dexamethasone Phosphate as a disodium salt	Shandong (Yanzhou) Xier Kangtai Pharmaceutical Co Ltd, Private Economy Garden-Xinyan Town, Yanzhou City, Shandong, China	Importer-distributor, private / Lagos	Controlled	Yes	✓	✓	✖ **88.8**	✓ not detected	✓ 7.2	✓	✖
NG/DEX/ 14/081013	4	10x1mL ampoules, glass	120620	2012-06	2015-06	Each ampoule contains Dexamethasone Sodium Phosphate 4mg	Shandong (Yanzhou) Xier Kangtai Pharmaceutical Co Ltd, Private Economy Garden-Xinyan Town, Yanzhou City, Shandong, China	Importer-distributor, private / Onitsha	Controlled	Yes	✓	✓	✓ 97.4	✓ not detected	✓ 7.8	✓	✓
TJ/DEX/ 1/300813	4	2x5x1mL ampoules, glass	110413	2012-05	2015-05	Each ampoule contains Dexamethasone Sodium Phosphate BP equivalent to Dexamethasone Phosphate 4mg	Farmak PAO, str Frunze 63, 04080 Kiev, Ukraine	Importer-distributor, private / Dushanbe	Controlled	Yes	✓	✓	✓ 102.6	✓ not detected	✓ 8.1	✓	✓
TJ/DEX/ 2/300813	4	25x1mL ampoules, glass	120720	2012-07	2015-07	Each 1mL contains Dexamethasone Phosphate 4mg as Dexamethasone Sodium Phosphate	Jiangsu Pharma Corp., China	Importer-distributor, private / Dushanbe	Controlled	Re-registration pending	✓	✓	✖ **92.8**	✖ **0.7%**	✓ 7.0	✓	✖
TJ/DEX/ 3/300813	4	5x5x1mL ampoules, amber	020213	2012-07	2016-02	Each 1mL contains Dexamethasone Phosphate 4mg as Dexamethasone Sodium Phosphate	Bryntsalov - A ZAO, Nagatinskaya str. 1, Moscow, Russia	Importer-distributor, private / Dushanbe	Controlled	Yes	✓	✓	✓ 100.6	✓ not detected	✓ 7.9	✓	✓
TZ/DEX/ 15/130913	4	10x2mL ampoules, glass amber	120812	2012-08	2015-08	Each 2 mL contain Dexamethasone Sodium Phosphate 8mg	Leshan Sanjiu-Longmarch Pharmaceuticals Co Ltd, No. 120, Baiyang Road, Leshan, Sichuan 614006, China	Importer-distributor, private / Dar es Salaam	Controlled	Yes	✓	✓	✓ 101.4	✓ not detected	✓ 8.0	✓	✓
TZ/DEX/ 09/090913	4	10x2mL ampoules, glass amber	130502	2013-05	2016-05	Each 2 mL contain Dexamethasone Sodium Phosphate 8mg	Leshan Sanjiu-Longmarch Pharmaceuticals Co Ltd, No. 120, Baiyang Road, Leshan, Sichuan 614006, China	Importer-central medical store, public / Dar es Salaam	Controlled	Yes	✓	✓	✓ 102.1	✓ not detected	✓ 8.1	✓	✓

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Assay: 95.0-105.0%; **Free dexamethasone**: ≤ 0.5%; **pH**: 7.0 – 8.5
Appearance: clear colourless solution, free from visible particles

✓= complies; ✖= does not comply

Country of collection* / sample code	Strength mg/mL	Pack size	Batch No.	Manu-facture date	Expiry date	Label claim	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Regis-tered	Appear-ance	Iden-tity	Assay %	Free dexa-methasone	pH	Extract-able volume	Conclu-sion
UG/DEX/ 21/09-09-2013	4	6x2mL vials, glass	MM9243	2012-11	2015-10	Each 1 mL contains Dexamethasone Sodium Phosphate USP equivalent to Dexamethasone Phosphate 4mg	Cadila Healthcare Ltd, Sarkhej-Bavla N.H. No. 8A, Moraiya, Sanand, Ahmdabad 382 210, India	NGO store, Kampala	Controlled: 24°C, RH 65%	Yes	✓	✓	✓ 104.9	✓ not detected	✓ 7.7	✓	✔
UG/DEX/ 12/07-09-2013	4	6x2mL vials, glass	MM9863	2012-12	2015-11	Each 1 mL contains Dexamethasone Sodium Phosphate USP equivalent to Dexamethasone Phosphate 4mg	Cadila Healthcare Ltd, Sarkhej-Bavla N.H. No. 8A, Moraiya, Sanand, Ahmdabad 382 210, India	Wholesaler-importer, private / Kampala	Controlled: 24°C, RH 65%	Yes	✓	✓	✓ 101.9	✓ not detected	✓ 7.0	✓	✔
VN/DEX/ 01/240913	4	10x1mL ampoules, glass	86GDA017	2013-04	2016-04	Each ampoule contains 4.4mg Dexamethasone Sodium Phosphate equivalent to 4.0mg Dexamethasone Phosphate	Fresenius Kabi Bidiphar JS Co, Zone 8, Nhon Phu Ward, Quy Nhon City, Binh Dinh Province, Viet Nam	Importer-distributor, public / Hanoi	Controlled: 23°C, RH 59%	Yes	✓	✓	**105.1** 104.9 **105.2 Ø: 105.1**	✓ not detected	✓ 7.8	✓	**Border-line**
VN/DEX/ 02/011013	4	10x1mL ampoules, glass	040713	2013-07	2016-07	Each ampoule of 1mL contains Dexamethasone Phosphate 4mg	Pymepharco Co, 166-170 Nguyen Hue Street, Tuy Hoa City, Phu Yen Province (licence from Stada Pharm GmbH, Germany), Viet Nam	Manufacturer-distributor, private / Ho Chi Minh City	Controlled: 24°C, RH 61%	Yes	✓	✓	✓ 104.3	✓ not detected	✓ 7.4	✓	✔
VN/DEX/ 03/2409013	4	10x1mL ampoules, glass	613005	2013-06	2016-06	Each 1 mL contains Dexamethasone Phosphate equivalent to 4mg as Dexamethasone Sodium Phosphate	Pharbaco Central Pharmaceutical JS Co No 1, Thanh Xuan, Soc Son, Hanoi, Viet Nam	Manufacturer-distributor, private / Hanoi	Controlled: 22°C, RH 54%	Yes	✓	✓	✓ 104.8	✖ **0.8%**	✓ 8.1	✓	✖
ZW/DEX/ 01/11/09/13	4	25x1mL vials, glass amber	DEI1302AC	2013-02	2015-01	Each 1 mL vial contains Dexamethasone Sodium Phosphate IP equivalent to Dexamethasone Phosphate 4mg	Celon Laboratories Ltd, Unit-I, Plot No. 2 Aleap Industrial Estate, Gajularamaram, RR District, 500072 Andhra Pradesh, India	Importer, private / Harare	Controlled: 28°C	No - special import permit	✓	✓	✓ 95.8	✓ not detected	✓ 7.6	✓	✔

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Assay: 90.0-110.0%; **Disintegration**: within 3 minutes; **Dissolution**: NLT 80% (Q) in 30 minutes ✓= complies; ✖= does not comply

Appendix 10 Amoxicillin dispersible tablets - test results

Country of collection* / sample code	Strength mg	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Registered	Appearance	Iden-tity	Assay %	Weight variat-ion	Disinteg ration	Dissolution	Dispers-ion finenness	Conclu-sion
NP/AMX/ AM1/27Aug2013	250	10x10 tablets in strips	TP-13/01	2013-03	2015-02	None	S.R. Drug Laboratories Pvt Ltd, Satungal, Kathmandu, Nepal	Distributor, private / Kathmandu	Not controlled	Yes	Off white, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 98.1	✓	✓	✓ at S1 Ø (n=6): 94%	✓	✓
NP/AMX/ AM2/27Aug2013	250	10x10 tablets in strips	NMTF-13084	2013-06	2014-11	None	National Health Care Pvt Ltd, Chhatapipra, Birgunj, Nepal	Distributor, private / Kathmandu	Not controlled	Yes	Off white, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 95.8	✓	✓	✓ at S1 Ø (n=6): 101%	✓	✓
TJ/AMX/ 1/30082013	250	2x10 tablets in blisters	120113	2012-07	2015-02	None	Biokhimik OAO, 4300030, Vasenko str. 15A, Saransk, Russia	Importer-distributor, private / Dushanbe	Controlled	Yes	White, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 102.3	✓	✓	✓ at S1 Ø (n=6): 97%	✓	✓
TJ/AMX/ 2/30082013	250	2x10 tablets in blisters	EBT12002	2012-07	2015-06	USP	Medicamen Biotech Ltd, SP-1192 A&B, Phase-IV, Industrial Area, Bhiwadi-301019, India	Importer-distributor, private / Dushanbe	Controlled: 20°C	Re-registration pending	Off white, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 101.4	✓	✓	✓ S2 Ø (n=12): 88%	✓	✓
TJ/AMX/ 3/30082013	500	2x10 tablets in blisters	610413	2012-04	2015-05	None	Barnaulskiy zavod medicinskih preparatov OOO, Silikatnaya str. 16a, Barnaul, Russia	Importer-distributor, private / Dushanbe	Controlled: 20°C	Re-registration pending	White, circular, flat faced tablets, single scored on one side and plain on the other	✓	✓ 104.5	✓	✓	✓ at S1 Ø (n=6): 96%	✓	✓
UG/AMX/ 10/06-09-2013	125	10x10 tablets in blisters	AMT12007	2012-06	2015-05	None	Milan Laboratories Pvt Ltd, Plot No. 63/67/87, J.C.I.E Ltd, Kamothe, Panvel, Navi Mumbai, India	Wholesaler-importer, private / Kampala	Controlled	Yes	Off white, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 105.7	✓	✓	✓ at S2 Ø (n=12): 88%	✓	✓
UG/AMX/ 02/02-09-2013	125	10x10 tablets in blisters	0112	2012-07	2014-06	None	Kampala Pharmaceutical Industries (1996) Ltd, Plot M444B Stretcher Road, Ntinda, Kampala, Uganda	Manufacturer, private / Kampala	Controlled: 24°C, RH 65%	Yes	White, circular, flat faced bevel edged tablets, single scored on one side, embossed "KPI" on one segment of the score and plain on the other	✓	✓ 106.6	✓	✓	✓ at S2 Ø (n=12): 108%	✓	✓

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Appendix 10: Amoxicillin dispersible tablets - test results

Assay: 90.0-110.0%; **Disintegration**: within 3 minutes; **Dissolution**: NLT 80% (Q) in 30 minutes ✓= complies; ✖= does not comply

Country of collection* / sample code	Strength mg	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Registered	Appearance	Iden-tity	Assay %	Weight variat-ion	Disinteg ration	Dissolution	Dispers-ion finenness	Conclu-sion
UG/AMX/ 23/12-09-2013	125	3x10 tablets in blisters	13178005	2013-06	2016-05	USP	Medopharm Pvt Ltd, 50 Kayarambedu Village, Guduvanchery 603 203, India	NGO store / Kampala	Controlled: 24°C, RH 65%	Yes	Off white, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 104.8	✓	✓	✓ at S1 Ø (n=6): 102%	✓	✓
UG/AMX/ 05/02-09-2013	125	10x20 tablets in blisters	ZRF1209	2012-08	2015-01	None	Medopharm Pvt Ltd, 50 Kayarambedu Village, Guduvanchery, India (for Blue Cross Laboratories Ltd, India)	Wholesaler-importer, private / Kampala	Controlled: 20°C	Yes	Pink, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 105.0	✓	✓	✓ at S2 Ø (n=12): 108%	✓	✓
UG/AMX/ 04/02-09-2013	125	10x20 tablets in blisters	ZRF1210	2012-09	2015-02	None	Medopharm Pvt Ltd, 50 Kayarambedu Village, Guduvanchery, India (for Blue Cross Laboratories Ltd, India)	Wholesaler-importer, private / Kampala	Controlled: 20°C	Yes	Pink, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 104.6	✓	✓	✓ at S1 Ø (n=6): 106%	✓	✓

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Assay: 95.0-105.0%; **Disintegration**: dispersible tablets within 60 seconds, conventional tablets within 15 minutes ✓= complies; ✖= does not comply

Appendix 11 Zinc tablets - test results

Country of collection* / sample code	INN	Dosage form	Strength mg	Label claim	Pack size	Batch No.	Manu-facture date	Expiry date	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Registered	Appearance	Iden-tity	Assay %	Content uniformity	Disintegration	Disper-sion finenness	Conclu-sion
KE/ZS/ 06/04-09-13	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate USP 54.89mg eq. to elemental zinc 20mg	10x10 tablets in blisters	20957	2012-07	2015-06	Cosmos Ltd, Tangwe Rd, Off Lunga Lunga Rd, PO Box 41433-00100, Nairobi, Kenya	NGO store / Nairobi	Controlled: 22°C, RH 63%	Yes	White, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 100.8	✓	✓	✓	✓
KE/ZS/ 10/06-09-13	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate BP 56.17mg eq. to elemental zinc 20mg	10x10 tablets in blisters	320238	2013-03	2015-02	Universal Corporation Ltd, Club Road, Plot No. 13777, PO Box 1748-00902, Kikuyu, Kenya	Distributor, private / Nairobi	Controlled: 23°C, RH 60%	Yes	Off white, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 101.2	✓	✓	✓	✓
KE/ZS/ 15/09-09-13	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate USP eq. to elemental zinc 20mg	10x10 tablets in blisters	303001	2013-03	2015-02	Square Pharmaceuticals Ltd, Dhaka Unit, Kaliakoir, Gazipur, Bangladesh	Wholesaler, private / Nairobi	Controlled: 23°C, RH 60%	Yes	Off white, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 98.0	✓	✓	✓	✓
NP/ZS/ Z1/27Aug2013	zinc gluconate	Dispersible tablets	10	Zinc Gluconate USP eq. to elemental zinc 10mg	10 tablets in strip	223012	2012-07	2014-06	S.R. Drug Laboratories Pvt Ltd, Satungal, Kathmandu, Nepal	Distributor, private / Kathmandu	Not controlled	Yes	Off white, circular, biconvex faced tablets, single scored on one side and embossed “SR” on the other	✓	✓ 102.8	✓	✓	✓	✓
NP/ZS/ Z2/1Sep2013	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate eq. to elemental zinc 20mg	10 tablets in strip	ZNTF 12055	2012-11	2014-10	National Health Care Pvt Ltd, Chhatapipra, Birgunj, Nepal	Hospital directly purchasing medicines, public / Patan, Lalitpur	Not controlled	Yes	Off white, circular, biconvex faced tablets, embossed “ZINC” on one side and plain on the other	✓	✓ 98.3	✓	✓	✓	✓
NP/ZS/ Z3/8Sep2013	zinc sulfate	Dispersible tablets	10	Zinc sulfate monohydrate USP eq. to elemental zinc 10mg	10 tablets in blister	ZN10212	2012-07	2014-06	Lomus Pharmaceuticals Pvt Ltd, Gothatar, Kathmandu, Nepal	Hospital directly purchasing medicines, public / Kathmandu	Controlled	Yes	Light pink, circular, convex tablets, single scored on one side and plain on the other	✓	✓ 102.8	✓	✓	✓	✓

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Assay: 95.0-105.0%; **Disintegration**: dispersible tablets within 60 seconds, conventional tablets within 15 minutes ✓= complies; ✖= does not comply

Country of collection* / sample code	INN	Dosage form	Strength mg	Label claim	Pack size	Batch No.	Manu-facture date	Expiry date	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Registered	Appearance	Iden-tity	Assay %	Content uniformity	Disinte gration	Disper-sion finenness	Conclu-sion
NG/ZS/ 16/240913	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate USP 54.9mg eq. to elemental zinc 20mg	1x10 tablets in blister	171A	2013-06	2016-05	Chi Pharmaceuticals Ltd, 14 Chivita Avenue, Ajao Estate, Isolo, Lagos, Nigeria	Manufacturer-importer-distributor, private / Lagos	No information	Yes	Off white, circular, flat faced bevel edged tablets, single scored on one side, embossed “Zn” and “20” on either side of the score, and embossed “CHI” on the other side	✓	✓ 103.0	✓	✓	✓	✓
NG/ZS/ 17/260913	zinc sulfate	Conventional tablets	20	Zinc sulfate monohydrate 20mg (on secondary packaging) Zinc sulfate 20mg (on primary packaging)	10x12 tablets in blisters	004ZS	2013-04	2016-03	Divine Essential Formulations, Km 10, Lasu-Ojo Rd, Igando-Lagos, Nigeria	Importer-distributor, private / Lagos	Controlled	Yes	Off white, circular, flat faced bevel edged tablets, single scored on one side and embossed “Tyonex” on the other	✓	✓ 102.3	✓	✓	Not requested for conventional tablets	✓
TJ/ZS/ 1/30082013	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate USP 54.89mg eq. to elemental zinc 20mg	1x25 tablets in blister	ET120205	2012-05	2015-04	Medicamen Biotech Ltd, SP-1192 A&B, Phase-IV, Industrial Area, Bhiwadi-301019, India	Importer-distributor, private / Dushanbe	Controlled	Yes	Off white, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 96.1	✓	✓	✓	✓
TJ/ZS/ 3/30082013	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate 54.90mg eq. to elemental zinc 20mg	10x10 tablets in blisters	F11	2011-09	2014-09	Laboratoires Pharmaceutiques Rodael, 1 route de Socx, 59380 Bierne, France	Hospital, public / Dushanbe	Controlled	No-donation (WHO-prequalified)	White, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 97.0	✓	✓	✓	✓
TZ/ZS/ 21/130913	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate USP 54.9mg eq. to elemental zinc 20mg	1x10 tablets in blister	130007	2013-04	2015-03	Shelys Pharmaceuticals Ltd, Plot No. 696, New Bagamoyo Road, Mwenge, PO Box 3016, Dar es Salaam, Tanzania	Manufacturer, private / Dar es Salaam	Controlled	Yes	White, circular, flat faced bevel edged tablets, single scored on one side, embossed “S” and “L” on either side of the score, and plain on the other side	✓	✓ 103.4	✓	✓	✓	✓

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Assay: 95.0-105.0%; **Disintegration**: dispersible tablets within 60 seconds, conventional tablets within 15 minutes ✓= complies; ✖= does not comply

Country of collection* / sample code	INN	Dosage form	Strength mg	Label claim	Pack size	Batch No.	Manu-facture date	Expiry date	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Registered	Appearance	Iden-tity	Assay %	Content uniformity	Disinte gration	Disper-sion finenness	Conclu-sion
TZ/ZS/ 22/130913	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate USP 54.9mg eq. to elemental zinc 20mg	1x10 tablets in blister	130012	2013-07	2015-06	Shelys Pharmaceuticals Ltd, Plot No. 696, New Bagamoyo Road, Mwenge, PO Box 3016, Dar es Salaam, Tanzania	Manufacturer, private / Dar es Salaam	Controlled	Yes	White, circular, flat faced bevel edged tablets, single scored on one side, embossed "S" and "L" on either segment, and plain on the other side	✓	✓ 97.4	✓	✓	✓	✓
UG/ZS/ 26/09-09-2013	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate BP eq. to elemental zinc 20mg	1x10 tablets in blister, co-packed with 2 sachets of 20.5g ORS	T34055	2013-07	2016-06	Agog Pharma Ltd, Plot No. 33, Sector II, The Vasai Taluka, Indl. Co-op. Estate Ltd, Vasai (East), Thane, India	Central medical store, public / Entebbe	Controlled: 25°C	Yes	Off white, circular, flat faced bevel edged tablets, single scored on one side and embossed "UG" on the other	✓	✓ 100.9	✓	✓	✓	✓
UG/ZS/ 11/06-09-2013	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate BP eq. to elemental zinc 20mg	1x10 tablets in blister	T34125	2013-08	2016-07	Agog Pharma Ltd, Plot No. 33, Sector II, The Vasai Taluka, Indl. Co-op. Estate Ltd, Vasai (East), Thane, India	Wholesaler-importer, private / Kampala	Controlled	Yes	Off white, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 104.5	✓	✓	✓	✓
UG/ZS/ 06/04-09-2013	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate 54.90mg eq. to elemental zinc 20mg	10x10 tablets in blister	1E6	2011-09	2014-09	Laboratoires Pharmaceutiques Rodael, 1 route de Socx, 59380 Bierne, France	NGO store / Kampala	No information	Yes (WHO-prequalified)	Off white, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 101.6	✓	✓	✓	✓
ZW/ZS/ 01/06/09/13	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate 54.88mg eq. to elemental zinc 20mg	10x10 tablets in blisters	230255	2013-08	2015-08	Varichem Pharmaceutical, 194 Gleneagles Road, Willowvale, Harare, Zimbabwe	Manufacturer, private / Harare	Controlled: 25°C, RH 36%	Yes	Off white, circular, flat faced bevel edged tablets, single scored on one side and embossed "V-Zn" on the other	✓	✓ 100.9	✓	✓	✓	✓
ZW/ZS/ 02/11/09/13	zinc sulfate	Dispersible tablets	20	Zinc sulfate monohydrate 54.90mg eq. to elemental zinc 20mg	10x10 tablets in blisters	G27	2012-10	2015-10	Laboratoires Pharmaceutiques Rodael, 1 route de Socx, 59380 Bierne, France	Central medical store, public / Harare	Controlled: 24°C	No - donation (WHO-prequalified)	White, circular, flat faced bevel edged tablets, single scored on one side and plain on the other	✓	✓ 101.7	✓	✓	✓	✓

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Assay: 90.0-110.0%; **pH**: 2.5 – 4.5; **Specific gravity**: 1.18 – 1.24 ✓= complies; ✖= does not comply

Zinc sulfate syrup - test results

Country of collection* / sample code	Strength	Label claim	Pack size	Batch No.	Manu-facture date	Expiry date	Manufacturer	Type of sampling site	Storage conditions at sampling site	Registered	Appear-ance	Identity	Assay %	pH	Specific gravity	Conclusion
TZ/ZS /11/100913	10mg/ 5mL	Each 5mL contain Zinc sulfate monohydrate USP 27.5mg eq. To elemental zinc 10.0mg	1x100mL bottle, amber	LF3006	2013-09	2015-08	Zenufa Laboratories Ltd, PO Box 77914, Dar es Salaam, Tanzania	Manufacturer, private / Dar es Salaam	Controlled	Yes - provisional	Clear straw coloured solution	✓	✓ 107.4	✓ 3.6	✓ 1.23	✓
TZ/ZS /10/100913	10mg/ 5mL	Each 5mL contain Zinc sulfate monohydrate USP 27.5mg eq. To elemental zinc 10.0mg	1x100mL bottle, amber	LF3003	2013-03	2015-02	Zenufa Laboratories Ltd, PO Box 77914, Dar es Salaam, Tanzania	Manufacturer, private / Dar es Salaam	Controlled	Yes - provisional	Clear straw coloured solution	✓	✓ 106.4	✓ 3.4	✓ 1.23	✓
VN/ZS /01/250913	10mg/ 5mL	Each 5mL contain 10mg Zinc (as Zinc sulfate monohydrate)	1x100mL bottle, amber	00113	2013-08	2016-08	Bidiphar 1 Pharmaceutical JS Co, 498 NguyenThai Hoc Str., Quy Nhon City, Binh Dinh Province, Viet Nam	Manufacturer-distributor, private / Quy Nhon City	Controlled: 23°C, RH 56%	Yes	Clear colourless solution	✓	✓ 104.9	✓ 3.7	✓ 1.18	✓
VN/ZS /02/250913	10mg/ 5mL	Each 5mL contain 10mg Zinc (as Zinc sulfate monohydrate)	1x100mL bottle, amber	00112	2012-08	2015-08	Bidiphar 1 Pharmaceutical JS Co, 498 NguyenThai Hoc Str., Quy Nhon City, Binh Dinh Province, Viet Nam	Manufacturer-distributor, private / Quy Nhon City	Controlled: 23°C, RH 56%	Yes	Clear colourless solution	✓	✓ 98.9	✓ 3.2	✓ 1.18	✓

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Assay: 90.0-110.0%; **Related substances**: any secondary peak ≤ 1%, sum of secondary peaks ≤ 2%; **Disintegration**: 15 minutes ✓= complies; ✖= does not comply

Appendix 12 Levonorgestrel tablets - test results

Country of collection* / sample code	Strength mg	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Registered	Appearance	Iden-tity	Assay %	Related substances	Content uniformity	Dissolution	Conclu sion
KE/LNG/ 11/06-09-13	0.75	1x2 tablets in blister	10113009	2013-02	2015-02	None	Renata Ltd, Dhaka, Bangladesh	Distributor, private / Nairobi	Controlled: 23°C, RH 60%	Yes	White, round tablets, embossed "R" on one side	✓	✓ 103.4	✓ max sec.peak: 0.1% sum: 0.1%	✓	✓ at S1 Ø (n=6): 98%	✓
KE/LNG/ 02/04-09-13	0.75	1x2 tablets in blister	E084110 01	2011-08	2014-07	BP	Glenmark Pharmaceuticals Ltd, B/2-2, Mahalaxmi Chambers, 22, Bhulabhai Desai Road, Mumbai - 400 026, India	Distributor, private / Nairobi	Controlled: 20°C, RH 60%	Yes	White, round tablets, single scored on one side	✓	✓ 101.0	✓ max sec.peak: 1.0% sum: 1.2%	✓	✓ at S2 Ø (n=12): 81%	✓
KE/LNG/ 14/09-09-13	0.75	1x2 tablets in blister	PT12044	2013-02	2016-01	None	Par Laboratories (for Simba Pharmaceuticals Ltd, Kenya), India	Wholesaler, private / Nairobi	Controlled: 23°C, RH 60%	Yes	White, round tablets, single scored on one side	✓	✓ 98.0	✓ no peaks detected	✖ **3 of 10 tablets out of 85-115%; 1 of them out of 75-125%;** (min: 81.1%, max: 135.2%)	✖ **at S1 to S3 criteria Ø (n=6): 10% min: 9%; max: 11%**	✖
MG/LNG/ 14/110913	0.75	1x2 tablets in blister	PR209	2012-08	2017-07	BP	Famy Care Ltd, 1608/1609, G.I.D.C, Sarigam, 396155 Valsad, Gujarat, India	Wholesaler, private / Antananarivo	Controlled: 19.1°C, RH 33.6%	Yes (WHO-prequalified)	White, round tablets, embossed "PN" on one side	✓	✓ 101.2	✓ max sec.peak: 0.2% sum: 0.4%	✓	✓ at S1 Ø (n=6): 99%	✓
MG/LNG/ 15/110913	0.75	1x2 tablets in blister	X35312	2013-04	2015-09	BP	Cipla Ltd, Plot No L-139 to L-146, Verna Industrial Estate, Verna-Goa 403722, India	Wholesaler, private / Antananarivo	Controlled: 19.1°C, RH 33.6%	Yes (WHO-prequalified)	White, round tablets	✓	✓ 100.5	✓ max sec.peak: 0.3% sum: 1.2%)	✓	✓ at S1 Ø (n=6): 103%	✓
NP/LNG/ L1/27Aug2013	1.5	1x1 tablet in blister	X25962	2012-10	2014-09	None	Cipla Ltd, Verna Industrial Estate, Verna-Goa 403722, India	Distributor, private / Kathmandu	Not controlled	Yes (WHO-prequalified)	Pink, round tablets, embossed white butterfly on both sides	✓	✓ 101.1	✓ max sec.peak: 0.2% sum: 0.4%	✓	✓ at S1 Ø (n=6): 98%	✓
NP/LNG/ L2/27Aug2013	0.75	1x2 tablets in blister	PR-12-001	2012-08	2017-07	None	HLL Life Care Ltd, India	Distributor, private / Kathmandu	Not controlled	Yes	White, round tablets	✓	✓ 97.5	✓ max sec.peak: 0.2% sum: 1.0%	✓	✓ at S2 Ø (n=12): 76%	✓

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Assay: 95.0-105.0%; **Related substances**: any secondary peak ≤ 1%, sum of secondary peaks ≤ 2%; **Dissolution**: NLT 75% (Q) in 30 minutes ✓= complies; ✖= does not comply
Content uniformity: NMT one individual content outside the limits of 85-105% of the average content and none outside the limits of 75-125%

Country of collection* / sample code	Strength mg	Pack size	Batch No.	Manu-facture date	Expiry date	Refer-ence on the label	Manufacturer	Type of sampling site / city	Storage conditions at the sampling site	Registered	Appearance	Iden-tity	Assay %	Related substances	Content uniformity	Dissolution	Conclu sion
TJ/LNG/ 1/30082013	0.75	1x2 tablets in blister	T19521N	2011-09	2016-09	None	Gedeon Richter Plc, Gyömrői út 19-21, Budapest 1103, Hungary	Importer-distributor-pharmacy, private / Dushanbe	Controlled: 20°C	Yes (WHO-prequalified)	White, round tablets, embossed "INOR" in circle on one side	✓	✓ 100.7	✓ max sec.peak: 0.2% sum: 0.4%)	✓	✓ at S1 Ø (n=6): 88%	✓
TZ/LNG/ 18/130913	0.75	1x2 tablets in blister	P2201	2012-02	2016-01	BP	Famy Care Ltd, 1608/1609, G.I.D.C, Sarigam, 396155 Valsad, Gujarat, India	Importer-distributor, private / Dar es Salaam	Controlled	Yes (WHO-prequalified)	White, round tablets	✓	✓ 98.9	✓ max sec.peak: 0.3% sum: 1.0%	✓	✓ at S1 Ø (n=6): 93%	✓
UG/LNG/ 01/31-08-2013	0.75	1x2 tablets in blister	T2B828V	2012-11	2017-11	None	Gedeon Richter Plc, Gyömrői út 19-21, Budapest 1103, Hungary	Wholesaler-importer, private / Kampala	Controlled: 26°C	Yes (WHO-prequalified)	White, round tablets, embossed "INOR" in circle on one side	✓	✓ 102.6	✓ max sec.peak: 0.2% sum: 0.5%	✓	✓ at S1 Ø (n=6): 91%	✓
UG/LNG/ 19/09-09-2013	0.75	1x2 tablets in blister	T070016	2010-07	2015-07	None	Gedeon Richter Plc, Gyömrői út 19-21, Budapest 1103, Hungary	Central medical store, public / Entebbe	Controlled: 24°C, RH 65%	No – donation (WHO-prequalified)	White, round tablets, embossed "INOR" in circle on one side	✓	✓ 100.3	✓ max sec.peak: 0.6% sum: 0.8%	✓	✓ at S1 Ø (n=6): 86%	✓
VN/LNG/ 01/240913	0.75	1x2 tablets in blister	03	2013-07	2016-07	None	BaDinh Pharmaceutical Biological JS Co, Que Vo Industrial, Bac Ninh Province, Viet Nam	Manufacturer-distributor, private / Bac Ninh province	Controlled: 24°C, RH 55%	Yes	White, round tablets, embossed "BD" on one side	✓	✓ 102.6	✓ max sec.peak: 0.3% sum: 0.7%)	✓	**✖ at S1 to S3 criteria Ø (n=6): 50% min: 43%; max: 56%**	**✖**
VN/LNG/ 02/011013	0.75	1x2 tablets in blister	020313	2013-03	2015-03	None	Stada-VN JV Co Ltd, K63/1 Nhuyen Thi Soc Street, Xuan Thoi Dong Ward, Hoc Mon District, Ho Chi Minh City, Viet Nam	Manufacturer-distributor, private / Ho Chi Minh City	Controlled: 23°C, RH 60%	Yes	White, round tablets, single scored on one side	✓	✓ 102.0	✓ max sec.peak: 0.3% sum: 0.5%)	✓	✓ at S1 Ø (n=6): 93%	✓
ZW/LNG/ 01/10/09/13	0.75	1x2 tablets in blister	PR209	2012-08	2017-07	BP	Famy Care Ltd, 1608/1609, G.I.D.C, Sarigam, 396155 Valsad, Gujarat, India	Importer, private / Harare	Controlled: 24°C	Yes (WHO-prequalified)	White, round tablets, embossed "PN" on one side	✓	✓ 100.5	✓ max sec.peak: 0.2% sum: 0.6%)	✓	✓ at S1 Ø (n=6): 100%	✓

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Assay: 90.0-110.0%; **Related substances**: any secondary peak ≤ 1%, sum of secondary peaks ≤ 2%; **Disintegration**: 15 minutes ✓= complies; ✖= does not comply

Appendix 13 Mifepristone tablets - test results

Country of collection* / sample code	Strength mg	Pack size	Batch No.	Manu-facture date	Expiry date	Manufacturer	Type of sampling site	Storage conditions at the sampling site	Registered	Appearance	Iden-tity	Assay %	Related substances	Uniformity of mass	Disinteg-ration	Conclu sion
VN/MIF 01/240913	10	1 tablet in blister	12101	2012-12	2015-12	Namha Pharmaceutical JS Co, 415 Han Thuyen, Nam Dinh City, Viet Nam	Manufacturer-distributor, private / Nam Dinh City	Controlled: 23°C, RH 57%	Yes	Yellow, round, biplanar tablets, embossed "10" on one side	✓	✓ 102.4	✓ max sec.peak: 0.3% sum: 0.3%	✓	✓	✓
VN/MIF/ 02/240913	10	1 tablet in blister	13101	2013-05	2016-05	Namha Pharmaceutical JS Co, 415 Han Thuyen, Nam Dinh City, Viet Nam	Manufacturer-distributor, private / Nam Dinh City	Controlled: 23°C, RH 57%	Yes	Yellow, round, biplanar tablets, embossed "10" on one side	✓	✓ 100.0	✓ max sec.peak: 0.2% sum: 0.3%	✓	✓	✓
VN/MIF/ 03/240913	10	1 tablet in blister	266412	2012-07	2015-07	Mediplantex National Pharmaceutical JS Co Ltd, 358 Duong Giai Phong, Thanh Xuan, Hanoi, Viet Nam	Manufacturer-distributor, private / Hanoi	Controlled: 25°C, RH 40%	Yes	Yellow, round, biplanar tablets, embossed "10" on one side	✓	✓ 98.4	✓ max sec.peak: 0.3% sum: 0.4%	✓	✓	✓
VN/MIF/ 04/240913	10	1 tablet in blister	010413	2013-05	2016-05	Danapha Pharmaceutical JS Co, 253 Dung Si Thanh Khe Street, Thanh Khe District, Da Nang City, Viet Nam	Manufacturer-distributor, private / Da Nang City	Controlled: 24°C, RH 62%	Yes	Yellow, round, biplanar tablets	✓	✓ 96.0	✓ max sec.peak: 0.4% sum: 0.8%	✓	✓	✓
VN/MIF/ 05/240913	10	1 tablet in blister	020713	2013-07	2016-07	Danapha Pharmaceutical JS Co, 253 Dung Si Thanh Khe Street, Thanh Khe District, Da Nang City, Viet Nam	Manufacturer-distributor, private / Da Nang City	Controlled: 26°C, RH 58%	Yes	Yellow, round, biplanar tablets	✓	✓ 97.1	✓ max sec.peak: 0.4% sum: 0.8%	✓	✓	✓
VN/MIF/ 06/011013	10	1 tablet in blister	080713	2013-07	2017-07	Stada-VN JV Co Ltd, K63/1 Nhuyen Thi Soc Street, Xuan Thoi Dong Ward, Hoc Mon District, Ho Chi Minh City, Viet Nam	Manufacturer-distributor, private / Ho Chi Minh City	Controlled: 23°C, RH 60%	Yes	Yellow, round, biplanar tablets, embossed "10" on one side	✓	✓ 98.7	✓ max sec.peak: 0.3% sum: 0.3%	✓	✓	✓
VN/MIF/ 07/011013	10	1 tablet in blister	090713	2013-07	2017-07	Stada-VN JV Co Ltd, K63/1 Nhuyen Thi Soc Street, Xuan Thoi Dong Ward, Hoc Mon District, Ho Chi Minh City, Viet Nam	Manufacturer-distributor, private / Ho Chi Minh City	Controlled: 23°C, RH 60%	Yes	Yellow, round, biplanar tablets, embossed "10" on one side	✓	✓ 98.6	✓ max sec.peak: 0.2% sum: 0.3%	✓	✓	✓
VN/MIF/ 08/240913	10	1 tablet in blister	02	2013-05	2016-05	BaDinh Pharmaceutical Biological JS Co, Que Vo Industrial, Bac Ninh Province, Viet Nam	Manufacturer-distributor, private / Bac Ninh province	Controlled: 24°C, RH 55%	Yes	Yellow, round, biplanar tablets, embossed "10" on one side	✓	✓ 98.3	✓ max sec.peak: 0.3% sum: 0.3%	✓	✓	✓

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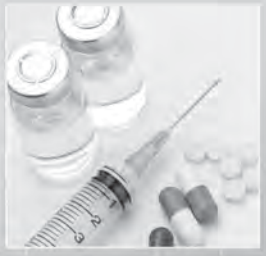

The United Nations Commission on Life-Saving Commodities for Women and Children (UNCoLSC) was established in March 2012 in response to the call in the UN Secretary-General's Global Strategy for Women's and Children's Health for increasing access to and appropriate use of medicines, medical devices and health supplies that effectively address leading avoidable causes of death during pregnancy, childbirth and childhood.

With a strong focus on the reproductive, maternal, newborn and child health the Commission identified 13 essential but overlooked life-saving commodities that, if more widely accessed and properly used, could save the lives of more than 6 million women and children.

This survey reported here is an initial quality survey targeting some life-saving medicines available on the markets of selected Every Woman Every Child (EWEC) countries by determining the most common safety and quality risks and to identify the most promising manufacturers. The manufacturers identified may then be supported in developing and marketing a product of assured quality with a focus on good manufacturing practices, quality production, bioequivalence, stability and competitive pricing such that low- and middle-income countries can afford these commodities.

The overall proportion of samples that did not comply with the testing specifications was relatively high (23%, 47 of 204 samples) indicating that international quality and GMP standards are not yet fully adopted by the respective manufacturers nor consistently implemented by national regulatory bodies. The number of sampled WHO-prequalified medicines was small (11 samples of 4 products), but with zero failure rates suggest that the WHO prequalification reliably assures uniform quality standards.

A meeting held with regulators from participating countries to discuss and analyse the outcomes of the survey agreed on conclusions and recommendations which should be implemented in practice and could contribute to achieving the UNCoLSC goals and to strengthening regulatory systems in the surveyed countries as well as being informative for the authorities of other EWEC countries.

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