SEHAT THIRD PARTY EVALUATION SERIES 2015-6

Ministry of Public Health of the Islamic Republic of Afghanistan

Drug Quality Assessment 2015

Royal Tropical Institute
December 2015

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LIST OF ABBREVIATIONS

BHC	Basic Health Center
BPHS	Basic Package of Health Services
CHC	Comprehensive Health Center
DH	District Hospital
DQA	Drug Quality Assessment
DT	Disintegration Test
EM	Essential Medicine
EPHS	Essential Package of Hospital Services
GPHF	Global Pharma Health Fund
HF	Health Facility
HFA	Health Facility Assessment
INN	International Nonproprietary Name
MOPH	Ministry of Public Health
PH	Provincial Hospital
RH	Regional Hospital
TLC	Thin-Layer Chromatography.
VI	Visual Inspection
WH	Warehouse
WHO	World Health Organization

EXECUTIVE SUMMARY

The Drug Quality Assessment 2015 provides information concerning drug quality of essential medicines (EM) in Afghan public healthcare facilities, run by MOPH-SM and NGOs under BPHS and EPHS contracts on behalf of the Ministry of Public Health.

Afghanistan's EM list 2015 includes approximately 500 items. An item should be included in this list in order to be legally imported. For this study we have analyzed a sample representing 5.0% of all possible pharmaceutical formulations that should, in theory, be present in the country's health system. This is, to the best of our knowledge, the first drug quality assessment to cover health facilities in all of Afghanistan's 34 provinces.

Methods. During the months of July to August 2015 a set of 25 EMs was collected from selected provincial warehouses, and a sample of EPHS and BPHS healthcare facilities. Each medicine was visually inspected, and subjected to disintegration and thin-layer chromatography tests using GPHF Minilabs®. Five drugs could not be included as they were only available as drug combinations and could not be tested due to limitations of the Minilab.

Relevant information on the storage conditions in which the EMs were kept at central warehouses was recorded using the WHO indicators for "Quality" ("Adequate conservation conditions and handing of medicines") [1].

All samples failing the GPHF Minilabs® tests, samples of two drugs that could not be tested using Minlabs, and a random selection of 10% of passed samples were sent outside the country to Stabicon, a WHO accredited quality control laboratory[2]. This was done for the purpose of quality control, in order to verify the validity of the Minilab testing.

Results. Of the 1,281 pharmaceutical products which were collected from across Afghanistan, 1188 were tested using the GPHF Minilabs® tests, from which 2.1% did not meet the requirements for visual inspection, identification, drug content, or disintegration. WHO Reference Laboratory tests, however, suggest that actual rates of substandard medications in Afghanistan are probably much higher. The quality control results yield an estimated failure rate of **15.1%** in the 10% sub-sample of all of the 1,281 pharmaceutical products tested.

The failed drugs were primarily analgesic tablets: ASA (Aspirin) and acetaminophen (Paracetamol). Of concern, however, is that 9% of tested Chloramphenicol 1gr powder for injection failed gold standard quality checks, as well as the majority of Aminophylline 100mg tablets.

[1] WHO (2007): "WHO operational package for assessing, monitoring and evaluating country pharmaceutical situation" – Survey form 17

[2] M/S Stabicon Life Sciences Pvt Ltd

Measuring true positives and true negatives for the Minilabs through comparison to a gold standard yields an overall sensitivity of 47.2% and a specificity of 93.2%. Investigation into the low sensitivity indicates that specifically the testing approach for Aspirin 500 mg and 100mg tablets, Salbutamol 4mg tablets and Aminophylline 100mg tablets may benefit from a review by the Minilab manufacturers. If these drugs are dropped from the calculations, the overall sensitivity for the Minilab increases to 77.8% with a specificity of 100%.

Stock-outs are also a concern. The mean number of EMs which could not be collected during the visits to the facilities is 11 out of 24 medications, or 46%.

Overall, the quality of storage conditions, which could indicate whether EMs found to be substandard were so due to degradation, were found to be high. Storage facilities in Afghanistan rank higher than expected when compared to other 'least developed countries'.

Study limitations. A significant amount of the targeted EMs was either found to be out of stock at the locations that were visited, or health facility staff refused to provide them to the data collection teams. This results in bias, therefore the results obtained must be interpreted with some caution, as the obtained results are not a truly representative picture of the quality of EMs found in the public pharmaceutical sector of Afghanistan.

As the assessment teams were unable to find many of the targeted products in the health facilities, it can be assumed that patients accessing health services would have similar difficulty. Replenishment systems need to be reviewed in order to ensure an unimpeded medical supply chain of EMs.

Some essential medicines, such as anti-tuberculosis drugs, could not be tested due to the unavailability of the testing solution for the Minilabs at time of testing. These pharmaceutical products play a crucial role in curbing global epidemics that are considered public health priorities, and it is good to know that solutions are now available and testing can be done in the following rounds.

Finally, the study has not targeted the private pharmaceutical market, where due to stock-outs the EPHS/BPHS clients would need to resort to in order to obtain the required medications. The influence of the private sector can weigh heavily on clinical outcomes and on recommendations for changes to current pharmaceutical policies. Details pertaining to the procurement strategies of the MoPH's healthcare implementing partners are also not available and limit a full quality assessment.

Conclusions and recommendations. Results indicate that substandard pharmaceutical products are present in the country's public medical supply chain, and could represent up to 15.1% of total essential medicines available through the BPHS and EPHS. Drug procurement staff is advised to be especially careful with the purchase of Aspirin, Paracetamol and Aminophylline tablets, as well as Chloramphenicol for injection.

Minilabs can be a reliable screening tool for testing for substandard medications, although further review is needed to improve the quality of testing for Aspirin, Aminophylline and Salbutamol.

The full extent of the problem of substandard medications requires further investigation as additional quality indicators, beyond those indicating whether an individual drug is counterfeit or not, were beyond the scope of this project. Further research is necessary in order to provide clear recommendations for pharmaceutical policy makers. Additional elements of Drug Quality need further investigation in order to provide evidence-based recommendations pertaining to Good Storage and Distribution Practices for EMs in the context of Afghanistan.

INTRODUCTION

Poor quality medicines have important consequences on the health of populations and the function of the health system. Poor quality drugs can affect the treatment of patients, increase antimicrobial drug resistance, and decrease trust in the health providers. Developing countries are largely affected by the challenge of counterfeit and substandard drugs in their markets due to low capacity in pharmaco- vigilance and weak drug regulatory systems. The World Health Organization (WHO) estimates that counterfeit pharmaceutical levels range from less than 1% in the developed world to more than 30% in less developed regions. In 2009, world leaders, predominantly from Africa, released the "Cotonou Declaration", recognizing counterfeit drugs as a key culprit preventing adequate access to quality medication, a key part of at least three of the Millennium Development Goals 2 proposed by the United Nations.

Annual drug quality assessments linked to the health facility assessment provide useful information to policy makers and BPHS/EPHS implementers on whether people have access to Essential Medicines (EMs), and that these medicines are safe, of good quality, and used rationally. This Drug Quality Assessment (DQA) 2015 will assess the availability and quality of Essential Medicines.

This report includes the findings, conclusions and recommendations of the First Round DQA conducted in EPHS and BPHS service delivery points and provincial warehouses, and highlights additional findings based upon our experience with the data collection and analysis.

OBJECTIVES

The **overall objective** of the Drug Quality Assessment is to provide the Ministry of Public Health (MOPH) with information concerning drug quality of EMs in warehouses and public Health facilities in Afghanistan.

The **specific objectives** are as follows:

1. Assess the quality of pharmaceuticals in a sample of
   - Warehouses (WH),
   - Essential Package of Hospital Services (EPHS) facilities
   - Basic Package of Health Services (BPHS) facilities
2. To build local capacity in cost-effective and sustainable drug quality testing

METHODS

Overview

The Afghanistan Drug Quality Assessment 2015 is implemented as follows:

1. Identification of EMs to be sampled according to a set of pre-established criteria

2. Sample collection of EMs during data collection rounds for the Health Facility Assessment Survey (Balanced Scorecard) round 2015. In addition to the EMs, the information was collected including the following:

    a. Sample information on EMs, by International Nonproprietary Name (INN), dosage form and strength, route of administration, information related to the product's manufacturer and number of sample units taken (stock outs)
    b. Results of physical/visual inspection of packaging and description of dosage form of samples collected (tablets and vials).
    c. WHO Storage point checklist including temperature control, sunlight, moisture, storage procedures.
    d. Storage conditions during transport between health facility and KIT Kabul office.

3. Quality testing of EMs in the KIT/SRTRO office in Afghanistan using GPHF-Minilab® kits. Testing was done through Visual Inspection (VI), Disintegration (DT) and Thin Layer Chromatography (TLC) tests.

4. Confirmation of Minilab results: All failed samples plus a random sample of 10% of overall samples were sent to a WHO certified laboratory in India (M/S Stabicon Life Sciences Pvt Ltd) for verification and confirmation.

Sampling procedure for the selection of Essential Medicines

A set of **30 EMs** were selected to be collected from the central storage point of each implementing agency in each province and from selected EPHS/BPHS Health facilities and implementers' central storage points.

The EMs to be sampled were selected from a list of EMs which had to meet ALL of the following criteria:

- Each EM can be tested using the GPHF Minilabs®. This testing methodology was selected for reasons of cost-effectiveness and sustainability; it is the same method currently being rolled out by MoPH.
- Each EM is part of the "Essential Drug List of Hospital by Type of Hospital" of the Essential Package of Hospital Service (2005) and present in each of the three levels within the EPHS (DH, PH and RH)
- Each EM is part of the list of "regular supply of Essential Drugs" of the Basic Package of Health Services (2010) and present in both the BHC and CHC levels of the BPHS
- Each EM should be in instant soluble solid oral dosage form such as capsule/tablet or injectable (GPHF-Minilabs® only analyze these pharmaceutical dosage forms)[3]. Therefore children's formulations (syrup and suspension) are not included in the list.

As per the protocol submitted to the MoPH for the DQA study, there were 30 essential medicines randomly selected from among the EMs that met all the above criteria. Random selection was done using the final list of EMs arranged by type of medication (analgesics, antibiotics, etc), dropping every n^{th} drug on the list in order to meet the required sample size. The final list is outlined in Table 1.

Afghanistan's EM list 2015 includes approximately 500 items. An item should be included in this list in order to be legally imported. As five items out of thirty were excluded due to unavailability of standards, the current sample represents 5% of all possible pharmaceutical formulations that should, in theory, be present in the country's public health system.

[3] See https://www.gphf.org/images/downloads/current_gphf_minilab_method_inventory.pdf for detailed medicine listing for GPHF Minilab

Table 1: Name, dosage form and strength of drugs to be sampled.

	Essential Medicine name (INN), dosage form and strength
1	Amoxicillin tablet 500mg (anhydrous)
2	Amoxicillin tablet 250mg (anhydrous)
3	Ampicillin powder for injection 500mgs (as sodium salt) in vial
4	Chloramphenicol capsule 250mg
5	Chloramphenicol powder for injection 1 gram (sodium succinate) in vial
6	Metronidazole tablet 400mg
7	Metronidazole tablet 250mg
8	Phenoxy Methyl Penicillin tablet 500mg (as potassium salt)
9	Phenoxy Methyl Penicillin tablet 250mg (as potassium salt)
10	Co-Trimoxazole (Sulfamethoxazole+Trimethoprime) tablet 400mg + 80mg
11	Co-Trimoxazole(Sulfamethoxazole+Trimethoprime)tablet 100mg + 20mg
12	Artemether 80mg/ml 2ml Ampule (for IM only)
13	Chloroquine tablet, base 150mg (as phosphate or sulfate)
14	Pyrimethamine +Sulfadoxine tablet 25mg + 500mg
15	Quinine tablet 300mg (as bisulfate or sulfate)
16	*Isoniazid tablet 300mg**
17	*Isoniazid tablet 150mg**
18	*Ethambutol tablet 400mg**
19	*Pyrazinamide tablet 500mg**
20	Rifampicin capsule or tablet 300 mg
21	*Rifampicin capsule or tablet 150mg mg**
22	Streptomycin powder for injection 1g (as sulfate) in vial
23	Mebendazole chewable tablet 100mg
24	Acetylsalicylic acid 500 mg
25	Acetylsalicylic acid 100 mg
26	Aminophylline tablet 100mg
27	Aminophylline injection, 25mg/ml in 10-ml ampoule
28	Hydrochlorothiazide tablet 50mg
29	Acetaminophen (Paracetamol) tablet 500mg
30	Salbutamol tablet 4mg (as sulfate)

* EMs finally not collected

The **quantity of units/sample** collected for each EM was as follows:

- 80 units if tablets or capsules
- 20 units if injectables + 25 vials of 2ml or 5 vials of 10mls or 50 vials of 1ml.

These are the minimum quantity of tablets/vials required to perform the GPHF-Minilab® tests, plus the verification/confirmation tests by the WHO prequalification external laboratory, plus retention units of each sample for quality control purposes.

When fewer units were found, samples with under 80 units (capsules/tablets) or the required quantities of injectables were also collected according to the established protocols. For example, if there were only 30 capsules available, all of them were taken, even though fewer than the 80 units (capsules/tablets) were physically present.

Sampling procedure for selection of sample collection points

Afghanistan's Public Health services are provided through BPHS and EPHS health facilities covered by the *System Enhancement for Health Action in Transition* (SEHAT) project, including all health facilities managed by the implementing NGOs under EPHS and BPHS contracts. In addition to these facilities, the central storage points for drugs and medical supplies for each province were added to the data collection points, in line with WHO protocols. The sampled locations represent the medical supply chain of EMs in each province. Data collection was conducted as follows:

- NGO central storage point (warehouse) – A complete set of the selected 30 EMs, as well as relevant information about storage conditions, was collected from the central storage point for each NGO implementer in each province.
- EPHS facility – One EPHS FACILITY in each province (included in the sample of the Health Facility Assessment (HFA) was randomly selected for inclusion in the DQA. (See the EPHS Balanced Scorecard Report 2015 for more details on the sampling strategy for health facilities.) In each of these EPHS Health facilities a complete set of the 30 selected EMs was collected if available.
- BPHS facility – At BPHS health facilities (randomly selected from the BPHS Balanced Scorecard 2015 sampled facilities – see the BPHS BSC report 2015 for details), the data collectors compared batch numbers of the drugs already sampled at the warehouse or hospital in which it is housed. Any drugs with batch numbers different from those already sampled were collected.

In total, 97 Central Storage Points and Health Facilities were included in the sample, distributed across the all the 34 provinces.

Transport of samples

EM samples were collected by field staff participating in the 2015 National Health Facility Assessment (NHFA). These field staff were responsible for collecting EM samples during their visits and were trained on the proper collection of samples to minimize the possibility that drug quality would be affected during transport.

Each EM sample was placed in a container to protect it from light, air and moisture as required by the manufacturers' recommendations. The container was sealed and temperature-proof.

All the EM samples were transported to Kabul in these containers. After their arrival in the main office each sample was coded and stored in a storeroom that met the requirements for good storage conditions as defined by WHO. To ensure the conditions during transport and in the storeroom were in accordance with good practice, and complied with manufacturer's recommendations, specialized devices (Log-tag®) were also included in the transport containers. Log-tags are used to measure the temperature and humidity during transport.

Ethical consideration

The protocol of the drug quality assessment was shared with the MOPH IRB and an exemption was requested because the study did not involve human subjects.

Procedures for Drug Quality testing of Essential Medicines

The analysis of the EM samples was first performed using GPHF-Minilab®. The Minilab is a way of broadly verifying the quality of essential medicines[4] which involves a four-stage test as follows:

- A physical inspection scheme of dosage forms and associated packaging material for an early rejection of the more crudely presented counterfeits
- A simple tablet and capsule disintegration test in order to verify label claims on enteric-coating and other modified-release systems
- Simplified colour reaction tests for a quick check of any drug present, thus verifying label claims on identity
- Easy-to-use thin layer chromatographic tests for a quick check on drug content, thus verifying label claims on potency'

When a pharmaceutical sample is analyzed by means of quality control tests such as those outlined above, we can never fully ascertain its quality as not all aspects of quality are measurable. There is no way to ascertain whether there is enough stability present to support the product's shelf life. This means that we cannot know how long the physical and chemical characteristics measured in the laboratory tests will remain the same from the moment of testing. Further, useful bioavailability comparisons between pharmaceutical analogues are not considered with these methods.

[4] http://www.gphf.org/en/minilab/

We therefore caution that whenever the quality control results meet the product specification, we may be misled into believing that a pharmaceutical product's quality is adequate. This may actually not be the case as storage or other conditions can cause the quality of the product to deteriorate quite rapidly and quality may be impaired at moment of use. Nevertheless, the selection of GPHF-Minilab® follows the logic employed by pharmaceutical authorities and is not without value. Pharmaceutical products that fail GPHF-Minilab® tests (and where a sample of results are corroborated by double testing at WHO prequalification laboratories) are unequivocally substandard.

Storage conditions questionnaire

Degraded medicines may result from exposure of good-quality medicines to light, heat, and humidity. It can be difficult to distinguish degraded medicines from those that left the factory as substandard, but the distinction is important as the causes and remedies are different. In order to ascertain whether the quality of drugs, as tested by the Minilab procedures, could be considered as substandard due to storage conditions at the point of sample collection, a 10-point questionnaire, following WHO standards, was completed for each field site visited. The questionnaire was taken from Survey form 17 from the WHO (2007) Guideline "WHO operational package for assessing, monitoring and evaluating country pharmaceutical situation".

RESULTS

Overview of sampled locations

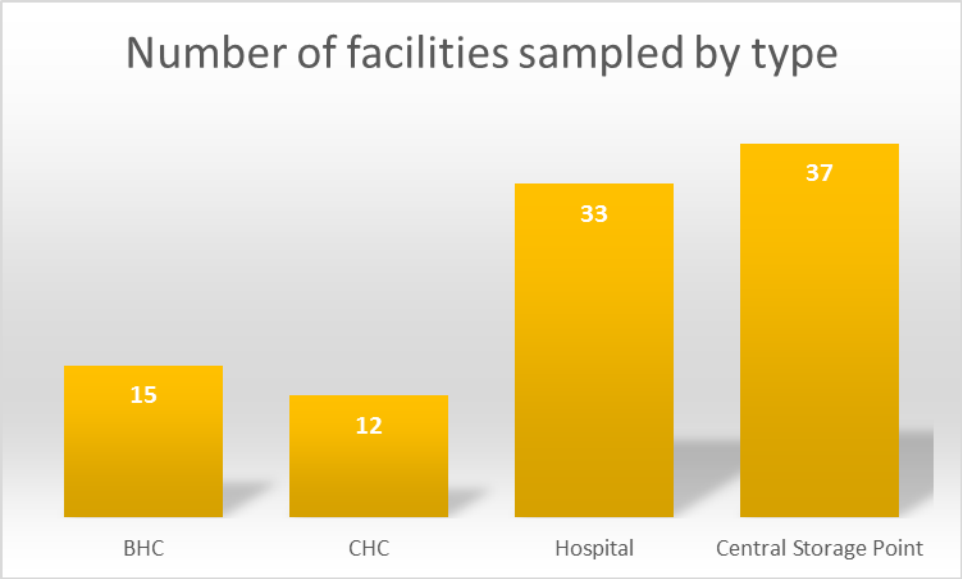
Table 2: Number of warehouses/facilities sampled per province.

Province		Number of sites	Percent of total sample
1	Badakhshan	3	3.1
2	Badghis	3	3.1
3	Baghlan	3	3.1
4	Balkh	3	3.1
5	Bamyan	3	3.1
6	Daykundi	4	4.1
7	Farah	2	2.1
8	Faryab	3	3.1
9	Ghazni	3	3.1
10	Ghor	3	3.1
11	Helmand	2	2.1
12	Herat	3	3.1
13	Jawzjan	3	3.1
14	Kabul	3	3.1
15	Kandahar	3	3.1
16	Kapisa	3	3.1
17	Khost	3	3.1
18	Kunar	2	2.1
19	Kunduz	3	3.1
20	Laghman	3	3.1
21	Logar	3	3.1
22	Nangarhar	2	2.1
23	Nimroz	3	3.1
24	Nuristan	3	3.1
25	Paktika	2	2.1
26	Paktya	2	2.1
27	Panjsher	3	3.1
28	Parwan	3	3.1
29	Samangan	3	3.1
30	Saripul	3	3.1
31	Takhar	3	3.1
32	Uruzgan	3	3.1
33	Wardak	3	3.1
34	Zabul	3	3.1
	Total	**97**	**100.0**

A frequency distribution of the sample by type of facility is shown in Table 3.

Table 3: Type of facility from which EM samples were collected

Facility type		Frequency	Percent	Cumulative Percent
1	BHC	15	15.5	15.5
2	CHC	12	12.4	27.8
3	Hospital	33	34.0	61.9
4	Central Storage Point	37	38.1	100.0
	Total	**97**	**100.0**	



The BPHS facilities included in the sample add up to 28% whilst EPHS covers 34% and the central storage points provide 38% of the facilities selected in the sample. A cross tabulation of the two variables, province and type of facility, is shown in Table 4. The Provinces of Kabul, Ghazni, Nangarhar, Kunar, Farah, Nimroz and Paktika have no BPHS facilities included because either the batch numbers of their samples were identical to the batch numbers of samples already collected or because no sample could be collected due unavailability of drugs or staff refusal. All the other provinces include one BPHS (CHC or BHC) and at least one other facility, either an EPHS facility, the provincial warehouse operated by the implementing NGO, or both.

Table 4: Type of facility surveyed per province

Province		Type of facility				Total
		BHC	CHC	Hospital	Central Storage Point	
1	Badakshan	1	0	1	1	3
2	Badghis	1	0	1	1	3
3	Baghlan	0	1	1	1	3
4	Balkh	1	0	1	1	3
5	Bamyan	1	0	1	1	3
6	Daykundi	0	1	1	2	4
7	Farah	0	0	1	1	2
8	Faryab	0	1	1	1	3
9	Ghazni	0	0	1	2	3
10	Ghor	0	1	1	1	3
11	Helmand	0	1	0	1	2
12	Herat	0	1	1	1	3
13	Jawzjan	1	0	1	1	3
14	Kabul	0	0	2	1	3
15	Kandahar	0	1	1	1	3
16	Kapisa	0	1	1	1	3
17	Khost	0	1	1	1	3
18	Kunar	0	0	1	1	2
19	Kunduz	1	0	1	1	3
20	Laghman	0	1	1	1	3
21	Logar	1	0	1	1	3
22	Nangarhar	0	0	0	2	2
23	Nimroz	0	0	1	2	3
24	Nuristan	1	0	1	1	3
25	Paktika	0	0	1	1	2
26	Paktya	1	0	1	0	2
27	Panjsher	1	0	1	1	3
28	Parwan	1	0	1	1	3
29	Samangan	1	0	1	1	3
30	Saripul	0	1	1	1	3
31	Takhar	1	0	1	1	3
32	Uruzgan	1	0	1	1	3
33	Wardak	0	1	1	1	3
34	Zabul	1	0	1	1	3
Total		**15**	**12**	**33**	**37**	**97**

The distribution of NGOs per province is given in the following table (Table 5). In 11 provinces in the medical supply chain sampled to represent local EM providers there is only one implementing

partner. In five provinces, three different implementers managed the supply. In the remaining 18 provinces, the facilities selected are implemented by two different NGOs. This category represents about half of all cases selected in the sample.

Table 5: Sampled facilities by NGO for each province

Province	NGO	No. of facilities	NGO	No. of facilities	NGO	No. of facilities	Total
Badakhshan	AKDN	1	CAF-BARAN	2			3
Badghis	MOVE	1	PU-AMI-MOVE	2			3
Baghlan	BDN	2	MOPH	1			3
Balkh	BDN	2	OHPM	1			3
Bamyan	AKDN	1	CAF-BARAN	1	BARAN		3
Daykundi	CAF	2	PU-AMI	1	PU-AMI /MOVE	1	4
Farah	CHA	1	MMRCA	1			2
Faryab	AADA	1	SAF	1	TTKA	1	3
Ghazni	BDN	1	ORCD	1	MMRCA	1	3
Ghor	ACTD	2	MOPH	1			3
Helmand	ACTD	2					2
Herat	BDN	3					3
Jawzjan	SAF	2	ICRC	1			3
Kabul	BRAC	2	MOPH	1			3
Kandahar	BARAN	1	AHDS	1	ICRC	1	3
Kapisa	SM	3					3
Khost	AADA	1	OHPM	2			3
Kunar	PU-AMI	2					2
Kunduz	MOPH	1	SCI	2			3
Laghman	SCA	3					3
Logar	CAF/SHDP	2	MRCA	1			3
Nangaraar	AADA	1	HN-TPO	1			2
Nimroz	MOVE	1	SAF	1		1	3
Nuristan	IMC	3	0	0			3
Paktika	IMC	2	0	0			2
Paktya	MRCA	1	MRCA/HN-TPO	1			2
Panjsher	SM	3	0	0			3
Parwan	SM	3					3
Samangan	AADA	2	MOPH	1			3
Saripul	BDN	2	MOPH	1			3
Takhar	AADA	3					3
Uruzgan	AHDS	2	AHDS	1			3
Wardak	SCA	3					3
Zabul	CORD/HADF	2	MOPH	1			3
Total		**59**		**35**		**3**	**97**

A complete overview of all the NGOs included in the sample of Facilities is given in Table 6. The NGOs named here were those in place at the time the data were collected, that is around the month of August 2015.

Table 6: Number of facilities sampled per NGO

NGO name		Frequency	Percent
1	AADA	8	8.2
2	ACTD	4	4.1
3	AHDS	4	4.1
4	AKDN	2	2.1
5	BARAN	2	2.1
6	BDN	10	10.3
7	BRAC	2	2.1
8	CAF	2	2.1
9	CAF/BARAN	3	3.1
10	CAF/SHDP	2	2.1
11	CHA	1	1.0
12	CordAid/HADAAF	2	2.1
13	HN-TPO	1	1.0
14	ICRC	2	2.1
15	IMC	5	5.2
16	MMRCA	2	2.1
17	MoPH	7	7.2
18	MOVE	3	3.1
19	MRCA	2	2.1
20	MRCA/ HN-TPO	1	1.0
21	OHPM	3	3.1
22	ORCD	1	1.0
23	PU-AMI	3	3.1
24	PU-AMI/MOVE	3	3.1
25	SAF	4	4.1
26	SCA	6	6.2
27	SCI	2	2.1
28	SM	9	9.3
29	TTKA	1	1.0
	Total	**97**	**100.0**

The most frequently sampled NGOs/implementers are BDN with 10%, MoPH-SM 9.3% and AADA with 8% of all Health facilities included in the sample.

An additional element in the Drug Quality Assessment is the inclusion of the warehouses (or central storage points) of the implementing NGOs, in addition to the health facilities. Since there is usually more than one implementing NGO per province, it is interesting to look at the distribution of warehouses selected by NGO. The frequency distribution is shown in Table 7. Furthermore, the protocol predicted that samples will be drawn from two central storage points in 7 provinces (Badghis, Badakhshan, Daykundi, Farah, Ghazni, Nangarhar and Nimroz). In Badghis, Badakhshan and Farah, however, samples could be collected from only one warehouse (see Table 4), although there were two NGOs working in the province. The implication is a few NGOs either do not have a provincial storage point or the storage point is run jointly by a consortium of NGOs. Out of 41 foreseen central storage points, 37 were actually visited.

Table 7: Frequency Distribution of Central Storage Points by NGO taken up in the sample

NGO		**Frequency**	**Percent**
1	AADA	4	10.8
2	ACTD	2	5.4
3	AHDS	1	2.7
4	BARAN	2	5.4
5	BDN	4	10.8
6	BRAC	1	2.7
7	CAF	1	2.7
8	CAF/BARAN	1	2.7
9	CAF/SHDP	1	2.7
10	CHA	1	2.7
11	CordAid/HADAAF	1	2.7
12	HN-TPO	1	2.7
13	IMC	2	5.4
14	MMRCA	1	2.7
15	MOVE	2	5.4
16	OHPM	1	2.7
17	ORCD	1	2.7
18	PU-AMI	2	5.4
19	SAF	2	5.4
20	SCA	2	5.4
21	SCI	1	2.7
22	SM	3	8.1
	Total	**37**	**100.0**

Overview of sampled Essential Medicines

From the locations described above, a total of **1,281** samples of EMs were collected from across all provinces in Afghanistan.

Five drug formulations (Isoniazid tablet 300 mg, Isoniazid tablet 150 mg, Ethambutol tablet 400 mg, Pyrazinamide tablet 500 mg and Rifampicin tablet 150 mg) were not collected because they are only available in fixed dose combination form at HFs. These are numbered equivalently in Table 1 as drugs number 16-19 and 21. It is also worth mentioning that we were only able to collect one sample of Rifampicin capsule 300 mg from the whole of Afghanistan. Other samples of Rifampicin were in combination forms and could not be tested by GPHF Minilabs at the time.

GPHF-Minilab® results

The list of essential drugs used in the DQA consists of 30 essential drugs, listed in Table 1. The essential medicines are referred to by their corresponding number in this Essential Drug List. The first variable to be analyzed from this point of view is the number of essential drugs that were collected, the number that passed the test and the number that failed, across all provinces.

Table 8: Essential medicines Collected from the collection sites sampled in the First Round of the DQA, August 2015.

Essential medicine ID and Name	No of units collected/Results		Grand total (per EM)
1. Amoxicillin tablet 500 mg	No. of units collected		6,280
	Results	Passed samples	79 (100%)
		Failed samples	0
		Samples not tested	0
2. Amoxicillin tablet 250 mg	No. of units collected		5,360
	Results	Passed samples	71 (100%)
		Failed samples	0
		Samples not tested	0
3. Ampicillin powder for injection 500 mg in vial	No. of units collected		1,555
	Results	Passed samples	57 (100%)
		Failed samples	0
		Samples not tested	0
4. Chloramphenicol capsule 250 mg	No. of units collected		4,585
	Results	Passed samples	60 (100%)
		Failed samples	0
		Samples not tested	0
5. Chloramphenicol powder for injection 1 gm in vial	No. of units collected		1,440
	Results	Passed samples	0
		Failed samples	0
		Samples not tested	57 (100%)

Essential medicine ID and Name	No of units collected/Results		Grand total (per EM)
6. Metronidazol tablet 400 mg	No. of units collected		3,440
	Results	Passed samples	43 (100%)
		Failed samples	0
		Samples not tested	0
7. Metronidazol tablet 250 mg	No. of units collected		2,647
	Results	Passed samples	34 (100%)
		Failed samples	0
		Samples not tested	0
8. Penicillin V tablet 500 mg	No. of units collected		2,800
	Results	Passed samples	35 (100%)
		Failed samples	0
		Samples not tested	0
9. Penicillin V tablet 250 mg	No. of units collected		4,160
	Results	Passed samples	52 (100%)
		Failed samples	0
		Samples not tested	0
10. Cotrimoxazol tablet 400 mg + 80 mg	No. of units collected		6,640
	Results	Passed samples	84 (100%)
		Failed samples	0
		Samples not tested	0
11. Cotrimoxazol tablet 100 mg + 20 mg	No. of units collected		5,129
	Results	Passed samples	65 (100%)
		Failed samples	0
		Samples not tested	0
12. Artemether 80 mg/ml ampoule	No. of units collected		796
	Results	Passed samples	0
		Failed samples	0
		Samples not tested	36 (100%)
13. Chloroquine tablet 150 mg	No. of units collected		1,840
	Results	Passed samples	24 (100%)
		Failed samples	0
		Samples not tested	0
14. Pyrimethine + Sulfadoxine tablet 25 mg + 500 mg	No. of units collected		2922
	Results	Passed samples	40 (100%)
		Failed samples	0
		Samples not tested	0

Essential medicine ID and Name	No of units collected/Results		Grand total (per EM)
15. Quinine tablet 300 mg	No. of units collected		2270
	Results	Passed samples	30 (100%)
		Failed samples	0
		Samples not tested	0
20. Rifampicin cap/tab 300 mg	No. of units collected		80
	Results	Passed samples	1 (100%)
		Failed samples	0
		Samples not tested	0
22. Streptomycin powder for injection 1 gm in vial	No. of units collected		749
	Results	Passed samples	33 (100%
		Failed samples	0
		Samples not tested	0
23. Mebendazol chewable tablet 100 mg	No. of units collected		4,668
	Results	Passed samples	60 (100%)
		Failed samples	0
		Samples not tested	0
24. Acetylesalicylic acid (Aspirin) 500 mg	No. of units collected		4,560
	Results	Passed samples	46 (81%)
		Failed samples	**11 (19%)**
		Samples not tested	0
25. Acetylesalicylic acid (Aspirin) 100 mg	No. of units collected		3,280
	Results	Passed samples	42 (100%)
		Failed samples	0
		Samples not tested	0
26. Aminophylline tablet 100 mg	No. of units collected		4430
	Results	Passed samples	59 (100%)
		Failed samples	0
		Samples not tested	0
27. Aminophylline injection 25 mg/ml in 10 ml ampoule	No. of units collected		1,289
	Results	Passed samples	58 (100%)
		Failed samples	0
		Samples not tested	0
28. Hydrochlorothiazide tablet 50 mg	No. of units collected		4,700
	Results	Passed samples	63 (100%)
		Failed samples	0
		Samples not tested	0

Essential medicine ID and Name	No of units collected/Results		Grand total (per EM)
29. Acetaminophen (paracetamol) tablet 500 mg	No. of units collected		6,280
	Results	Passed samples	73 (92%)
		Failed samples	**6 (8%)**
		Samples not tested	0
30. Salbutamol tablet 4 mg	No. of units collected		4,850
	Results	Passed samples	54 (87%)
		Failed samples	**8 (13%)**
		Samples not tested	0

Total No. of samples collected			1,281
Number of samples tested with Minilab			1188
Total No. of passed samples			1,163 (91%)
Total No. of failed samples			**25 (2.1 % of tested samples)**
Total No. of samples not tested			93 (7%)

Out of 1281 samples of EMs collected from all over Afghanistan, 1,188 (93%) samples could be tested with Minilab. A total of 25 EMs (2.1 %) failed the MiniLab tests.

Essential Medicines availability in Health Facilities and Storage Central Points (Stock Out)
EMs numbered 16 to 21 (Isoniazid tablet 300 mg, Isoniazid tablet 150 mg, Ethambutol tablet 400 mg, Pyrazinamide tablet 500 mg and Rifampicin tablet 150 mg) are not included in the current discussion because 5 EMs were not collected in the course of the DQA survey, and the inclusion of Rifampicin tablet 150mg, of which only a single sample was obtained, would bias results too much. The remaining 24 drugs, however, were expected to be present at the 97 central storage points and health facilities visited.

The mean number of EMs which could NOT be collected during the visits to the facilities because they were out of stock, is 11 out of 24 or 46%. Anywhere from 3 to 24 EMs out of the total sample of 24 EMs were unavailable in the 97 health facilities/warehouses visited. This not only indicates that access to EMs may be a significant problem across the health facilities and warehouses, but it also signifies that we were unable to collect 45.5% of the EMs that should have been included in the sample due to either stock-outs or due to the refusal of the health facility staff to provide the study teams with the EMs requested.

Table 9: Total sample collection points per number of EMs out of stock

No. of EMs out of stock	No. of sample collection points	Percent
3	5	5.2
4	5	5.2
5	5	5.2
6	13	13.4
7	8	8.2
8	3	3.1
9	9	9.3
10	3	3.1
11	3	3.1
12	8	8.2
13	3	3.1
14	3	3.1
15	4	4.1
16	6	6.2
17	4	4.1
18	6	6.2
19	3	3.1
21	3	3.1
22	1	1.0
23	1	1.0
24	1	1.0
Total	**97**	**100.0**

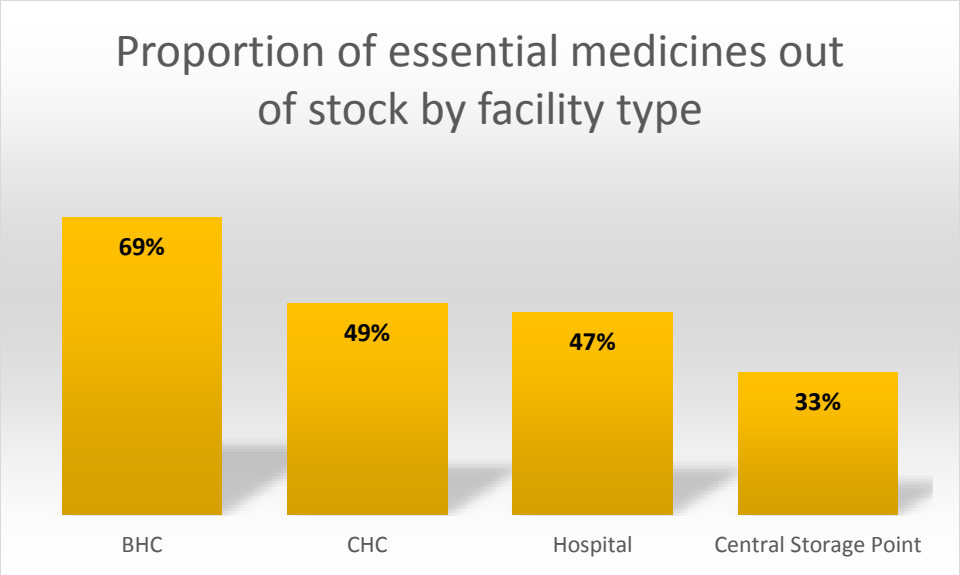
The province with the lowest proportion of out of stock EMs across the sampled facilities is Ghazni, with about one fifth (18%) of drugs out of stock, while Parwan has the highest proportion at four fifths (81%) (Table 10). Although zero reporting is assumed to indicate “out of stock”, there may be other reasons for not being able to retrieve any specimens. For example, there may be unwillingness to give the drugs to the teams if they are the last batch in stock and may be needed for a patient. Another reason may be unwillingness to participate in the investigation at all, as was the case in one of the locations where the number registered with 0 drugs collected was 100%. For these reasons the ‘out of stock’ figures are possibly biased upwards. They are maximum estimates. Therefore, in next DQA round the instruments should include a question that clarifies why the EM was not collected.

Table 10: Proportion of Sampled Essential Medicines out of stock per province

Province		Proportion of Sampled Essential Medicines out of stock
1	Parwan	81%
2	Kapisa	67%
3	Kunar	63%
4	Badakshan	63%
5	Uruzgan	61%
6	Balkh	58%
7	Panjsher	58%
8	Helmand	56%
9	Kandahar	56%
10	Takhar	54%
11	Saripul	54%
12	Kabul	53%
13	Kunduz	53%
14	Jawzjan	53%
15	Zabul	53%
16	Wardak	43%
17	Nuristan	43%
18	Nangarhar	42%
19	Ghor	42%
20	Samangan	40%
21	Bamyan	40%
22	Daykundi	39%
23	Logar	38%
24	Nimroz	38%
25	Khost	38%
26	Laghman	36%
27	Faryab	36%
28	Heart	32%
29	Paktya	31%
30	Badghis	29%
31	Paktika	29%
32	Farah	27%
33	Baghlan	21%
34	Ghazni	18%

Table 11: Proportion of Essential Medicines out-of-stock by type of facility

Type of facility		Proportion of Essential medicines out of stock
1	BHC	69%
2	CHC	49%
3	Hospital	47%
4	Central Storage Point	33%



The proportion of EMs which are out of stock is lowest at the central storage points, intermediate at the hospitals and CHCs (49 and 47% respectively), but high at BHCs (69%).

Sample Information per Essential Medicine

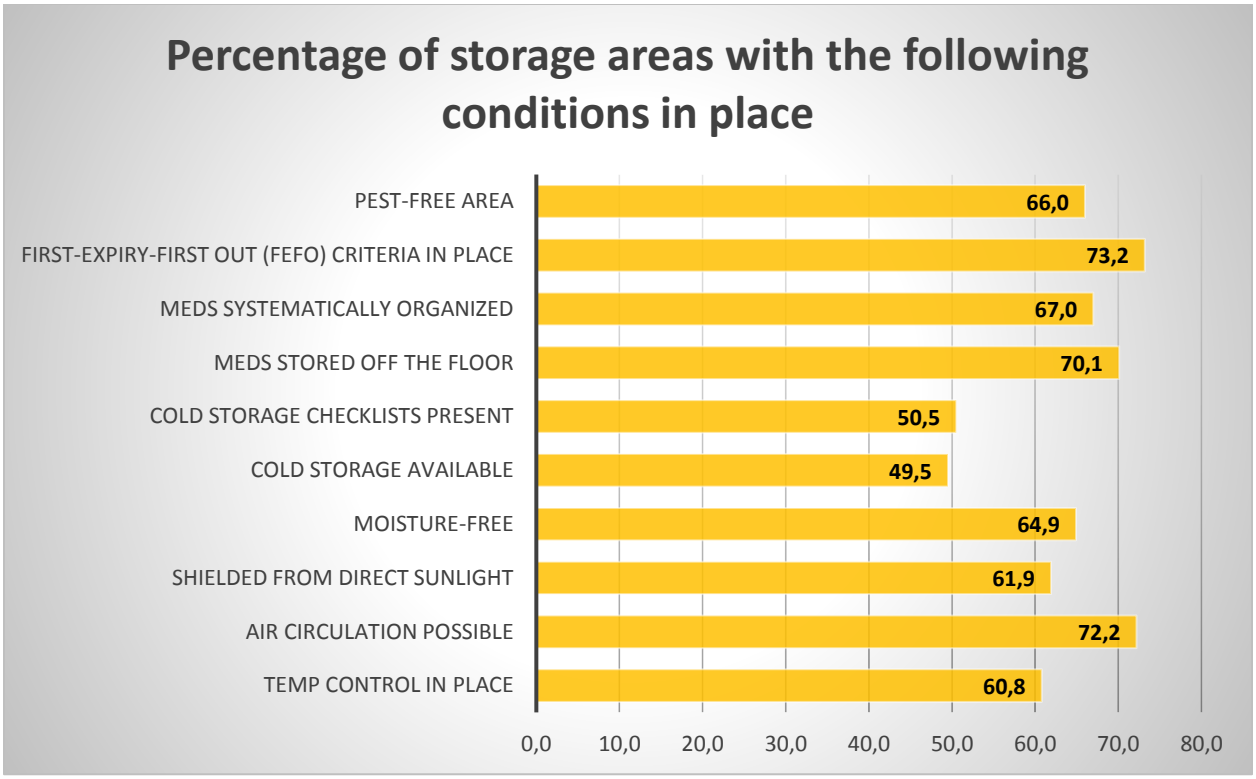
Sample information per Essential Medicine include generic names, route of administration (Oral, IV, IM), trade or brand name, manufacturer name, and name of reference standard used. Three questions are also asked on the quality of the drugs as observed by visual inspection. These question are whether the shape was uniform, whether the color was uniform and whether there were any signs of physical damage.

Storage conditions

The current section presents the findings from the storage conditions questionnaire. These data apply to the locations sampled, and not to the individual EMs.

Table 12: Indicators of storage procedures conform to recommended practice

1. Method in place to control temperature (e.g. roof and ceiling)	**Frequency**	**Percent**
No	22	22.7
Yes	59	60.8
No Response/Blank	16	16.5
2. Windows that can be opened or air vents in place	**Frequency**	**Percent**
No	11	11.3
Yes	70	72.2
No Response/Blank	16	16.5
3. No direct sunlight can enter the area (e.g. window panes painted)	**Frequency**	**Percent**
No	21	21.6
Yes	60	61.9
No Response/Blank	16	16.5
4. Area is moisture-free (e.g. no leaking ceiling, roof, drains, taps)	**Frequency**	**Percent**
No	18	18.6
Yes	63	64.9
No Response/Blank	16	16.5
5. Availability of cold storage	**Frequency**	**Percent**
No	33	34.0
Yes	48	49.5
No Response/Blank	16	16.5
6. Availability of a regularly filled temperature chart for cold storage	**Frequency**	**Percent**
No	30	30.9
Yes	49	50.5
No Response/Blank	18	18.6
7. Medicines stored off the floor	**Frequency**	**Percent**
No	13	13.4
Yes	68	70.1
No Response/Blank	16	16.5
8. Medicines stored in a systematic way (e.g. alphabetical, pharmacological)	**Frequency**	**Percent**
No	16	16.5
Yes	65	67.0
No Response/Blank	16	16.5
9. Medicines storage according to first-expiry-first out (FEFO)	**Frequency**	**Percent**
No	10	10.3
Yes	71	73.2
No Response/Blank	16	16.5
10. Evidence of pest-free area	**Frequency**	**Percent**
No	17	17.5
Yes	64	66.0
No Response/Blank	16	16.5



Based on the above summary graph, it is evident that overall, the main weaknesses in achieving optimal storage conditions in health faciltities and warehouses in Afghanistan are related to temperature control. The weakest areas are the availability of cold storage and cold storage checklists, accompanied by a lack of temperature control means (i.e. fans, airconditioning) and shielding from direct sunlight.

Table 13: Score of locations on storage procedures questionnaire

Score on storage procedures questionnaire, out of 10 points		Number of locations with this score	Percent
	1	4	4.1
	2	1	1.0
	3	1	1.0
	4	1	1.0
	5	5	5.2
	6	12	12.4
	7	7	7.2
	8	12	12.4
	9	14	14.4
	10	23	23.7
	No Response/Blank	17	17.5
	Total	**97**	**100.0**

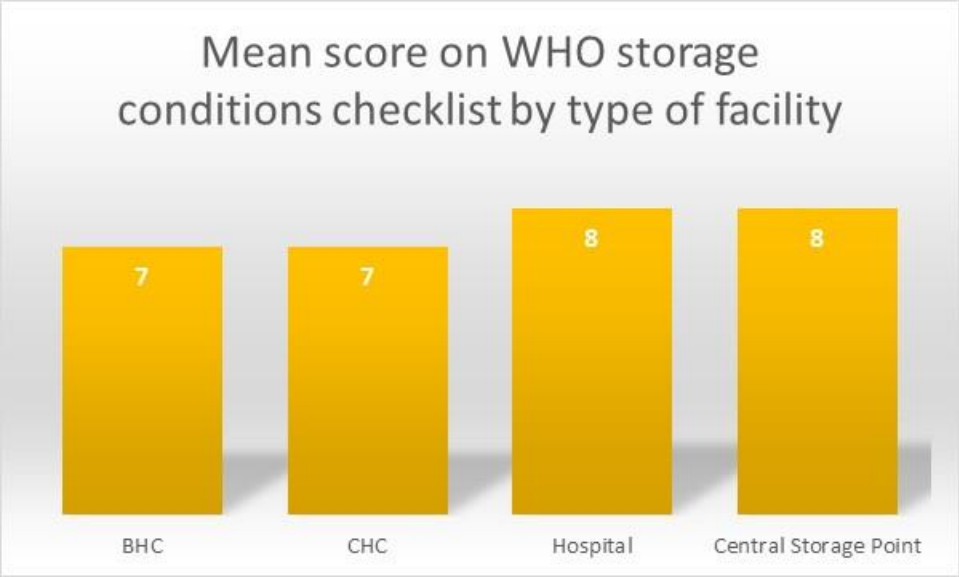
This variable was computed by summing up all positive responses to the questions asked on the storage procedures questionnaire. Scores should be interpreted to represent 'number of responses which indicate that the storage procedures are conform to recommended practice'. Its distribution by implementing NGO is shown in table 14. Table 15 shows that there are few differences per type of sample collection point.

Table 14: Scores on storage conditions questionnaire by implementing NGO

NGO/institution	Mean score out of a possible 10 points on storage conditions questionnaire
AADA	7
ACTD	9
AHDS	8
AKDN	10
BARAN	8
BDN	8
BRAC	8
CAF	10
CAF/BARAN	8
CAF/SHDP	6
CHA	9
CordAid/HADAAF	10
HN-TPO (only one facility in sample)	1
ICRC	8
IMC	9
MMRCA	10
MoPH	5
MOVE	7
MRCA	9
MRCA/HN	6
OHPM	6
ORCD	10
PU-AMI	4
PU-AMI/MOVE	7
SAF	7
SCA	8
SCI	6
MOPH-SM	8
TTKA	6

Table 15: Average storage conditions score per facility type

Type of facility	Mean score /10
BHC	7
CHC	7
Hospital	8
Central Storage Point	8



Results from cross-checks by WHO certified laboratory (Stabicon)

Three different sets of EMs were sent to the WHO certified laboratory in India (Stabicon) for testing:

1. All samples of the two EMs that could not be evaluated by the GPHF-Minilab® (Artemether Injections and Chloramphenicol Powder)
2. All samples of EMs that failed GPHF-Minilab quality checks
3. A random sample of 10% of all EMs that passed GPHF-Minilab quality checks

Table 16 summarizes the drugs that failed the verification tests as conducted by the WHO reference laboratory.

Table 16: Summary of samples which failed the verification tests in WHO prequalified laboratory.

No.	Drug Name	Number of samples tested	No. of samples that failed the tests
1	Chloramphenicol capsule 250 mg	6	1
2	Quninine tablet 300 mg	6	1
3	Mebendazol chewable tablet 100 mg	6	1
4	Acetylsalicylic acid (aspirin) 500 mg	17 total (11 'failed' samples plus 6 'randomly selected)	16 (11 failed both Minilab and Stabicon tests)
5	Acetylsalicylic acid (aspirin) 100 mg	6	5
6	Aminophylline tablet 100 mg	6	6
7	Acetaminophen (paracetamol) tablet 500 mg	11 total (6 'failed' plus 5 'random')	6 (failed both Minilab and Stabicon tests)
8	Chloramphenicol powder for injection 1 gm in vial	56	5 (Not tested with Minilab)
	Total		**41**

Some drugs especially stand out: ASA (Aspirin) 500 mg and Acetaminophen (Paracetamol) 500mg. The quality checked results suggest that a significant proportion of the aspirin provided through the EPHS/BPHS facilities is substandard, while over half of the paracetamol may be of poor quality.

Of primary concern is that 9% of the lifesaving drug Chloramphenicol 1gr injectable samples as well as all of the Aminophylline 100mg tablets failed the quality tests at the Stabicon laboratory.

Based on the results from the randomly selected sample of 10% of the EMs collected which were sent to Stabicon for quality checks (14.7% failed, representing 90.8% of total sample), plus the results of the drugs that could not be tested by the minilab (5.4% failed, representing 7.3% of samile), and the EMs that failed the initial Minilab tests (68% failed, representing 2% of sample), the overall weighted proportion of substandard drugs is estimated to be **15.1%**.

Results of tests by province and provider

When the results of the 41 failed drug samples are broken down by province and provider, it is evident that substandard drugs can be found across the country and across the implementing agencies. Although the sample is too small to be conclusive, when taking into account facilities sampled and number of substandard drugs identified, it appears that a slightly higher proportion of substandard drugs can be found in Daykundi and Nuristan, two of the most inaccessible provinces of Afghanistan.

Table 17: Failed samples by province and by provider

Province	NGO	Names of Failed Samples	No of Failed Samples
Badakhshan	AKDN		
	CAF-BARAN		
Badghis	MOVE		
	PU-AMI-MOVE	Acetylsalicylic acid (Aspirin) 500 mg	2
Baghlan	BDN		
	MOPH		
Balkh	BDN	Quinine tablet 300 mg	1
	OHPM		
Bamyan	AKDN		
	CAF-BARAN		
	BARAN		
Daykundi	CAF	Acetylsalicylic acid (Aspirin) 500 mg	2
		Acetaminophen (paracetamol) tablet 500 mg	2
	PU-AMI	Aminophylline tablet 100 mg	1
	PU-AMI /MOVE		
Farah	CHA	Acetylsalicylic acid (Aspirin) 500 mg	1
		Acetaminophen (paracetamol) tablet 500 mg	1
	MMRCA	Acetylsalicylic acid (Aspirin) 500 mg	1
Faryab	AADA		
	SAF		
	TTKA		
Ghazni	BDN		
	ORCD		
	MMRCA		
Ghor	ACTD		
	MOPH		
Helmand	ACTD	Chloramphenicol powder for injection 1 gm. in vial	1
Herat	BDN		
Jawzjan	SAF	Acetylsalicylic acid (Aspirin) 100 mg	1
	ICRC		
Kabul	BRAC	Aminophylline tablet 100 mg	1
	MOPH		

Province	NGO	Names of Failed Samples	No of Failed Samples
Kandahar	BARAN	Acetylsalicylic acid (Aspirin) 500 mg	1
		Acetylsalicylic acid (Aspirin) 100 mg	1
	AHDS		
	ICRC		
Kapisa	SM	Chloramphenicol powder for injection 1 gm. in vial	1
		Mebendazole chewable tablet 100 mg	1
		Acetylsalicylic acid (Aspirin) 500 mg	1
Khost	AADA		
	OHPM		
Kunar	PU-AMI	Acetaminophen (paracetamol) tablet 500 mg	1
Kunduz	MOPH	Acetylsalicylic acid (Aspirin) 500 mg	1
	SCI	Aminophylline tablet 100 mg	1
Laghman	SCA	Acetylesalicylic acid (Aspirin) 100 mg	1
Logar	CAF/SHDP		
	MRCA	Acetylsalicylic acid (Aspirin) 500 mg	1
Nangarhar	AADA		
	HN-TPO	Acetylsalicylic acid (Aspirin) 500 mg	1
		Acetylsalicylic acid (Aspirin) 100 mg	1
Nimroz	MOVE		
	SAF		
Nuristan	IMC	Acetylsalicylic acid (Aspirin) 500 mg	2
		Acetaminophen (paracetamol) tablet 500 mg	1
		Aminophylline tablet 100 mg	1
Paktika	IMC	Aminophylline tablet 100 mg	1
Paktya	MRCA	Aminophylline tablet 100 mg	1
	MRCA/HN-TPO		
Panjsher	SM	Acetylsalicylic acid (Aspirin) 500 mg	1
		Acetylsalicylic acid (Aspirin) 100 mg	1
Parwan	SM		
Samangan	AADA	Acetylsalicylic acid (Aspirin) 500 mg	2
		Acetaminophen (paracetamol) tablet 500 mg	1
	MOPH	Chloramphenicol powder for injection 1 gm in vial	1
Saripul	BDN	Chloramphenicol powder for injection 1 gm in vial	1
	MOPH		
Takhar	AADA		
Uruzgan	AHDS	Chloramphenicol powder for injection 1 gm in vial	1
Wardak	SCA	Chloramphenicol capsule 250 mg	1
Zabul	CORDAID-HADAAF		
	MOPH		
Total			**41**

Table 18: Details of failed EMs

#	Medication	Distributor/Manufacturer	BATCH NO	Province	NGO
1	Acetylsalicylic acid 100mg Tablets	Mission Pharma Denmark	In product pouch no label	Jawzjan	SAF
2	Acetylsalicylic acid 100mg Tablets	Mission pharma Denmark	In product pouch no label	Kandahar	BARAN
3	Acetylsalicylic acid 100mg Tablets	No Response/Blank	9201	Nangrahar	HN-TPO
4	Acetylsalicylic acid 100mg Tablets	PARS DAROU Iran	65042	Laghman	SCA
5	Acetylsalicylic acid 100mg Tablets	PARS DAROU Iran	6781	Panjsher	MoPH
6	Acetylsalicylic acid 500mg Tablets	ATABAY Pharma Turkey	8982	Kunduz	MoPH
7	Acetylsalicylic acid 500mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	AP5-06	Farah	MMRCA
8	Acetylsalicylic acid 500mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	AP5-07	Nangrahar	HN-TPO
9	Acetylsalicylic acid 500mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	AP5-10	Daykundi	CAF
10	Acetylsalicylic acid 500mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	AP5-12	Samangan	AADA
11	Acetylsalicylic acid 500mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	AP5-13	Daykundi	CAF
12	Acetylsalicylic acid 500mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	AP5-13	Logar	MRCA
13	Acetylsalicylic acid 500mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	AP5-16	Samangan	AADA
14	Acetylsalicylic acid 500mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	AP5-17	Badghis	PU-AMI/MOVE
15	Acetylsalicylic acid 500mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	AP5-17	Nuristan	IMC
16	Acetylsalicylic acid 500mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	AP5-17	Nuristan	IMC
17	Acetylsalicylic acid 500mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	NR	Badghis	PU-AMI/MOVE
18	Acetylsalicylic acid 500mg Tablets	Jiangsu Pengyao Pharma Co.ltd China	130108	Farah	CHA
19	Acetylsalicylic acid 500mg Tablets	Jiangsu Pengyao Pharma Co.ltd China	130108	Kapisa	MoPH
20	Acetylsalicylic acid 500mg Tablets	Jiangsu Pengyao Pharma Co.ltd China	1401210	Panjsher	MoPH
21	Acetylsalicylic acid 500mg Tablets	Mission pharma Denmark	In product pouch no label	Kandahar	BARAN
22	Aminophylline 100mg Tablets	Cimoerres? (simcere pharma china?)	In product pouch no label	Kunduz	SCI
23	Aminophylline 100mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	AM-12	Kunar	PU-AMI
24	Aminophylline 100mg Tablets	Lisko Pakistan PVT	AB02	Nuristan	IMC
25	Aminophylline 100mg Tablets	Mission Pharma	In product pouch no label	Paktika	IMC
26	Aminophylline 100mg Tablets	Mission Pharma	In product pouch no label	Paktya	MRCA

#	Medication	Distributor/Manufacturer	BATCH NO	Province	NGO
27	Aminophylline 100mg Tablets	Mission Pharma Denmark	In product pouch no label	Kabul	BRAC
28	Chloramphenicol 250mg Capsules	Pliva Pakistan	204	Wardak	SCA
29	Chloramphenicol Powder for Injection 1gm	Pliva Pakistan	036	Kapisa	MoPH
30	Chloramphenicol Powder for Injection 1gm	Pliva Pakistan	036	Uruzgan	AHDS
31	Chloramphenicol Powder for Injection 1gm	Pliva Pakistan	037	Samangan	MoPH
32	Chloramphenicol Powder for Injection 1gm	Pliva Pakistan	038	Helmand	ACTD
33	Chloramphenicol Powder for Injection 1gm	Pliva Pakistan	038	Saripul	BDN
34	Mebendazole 100mg chewable Tablets	Industria farmaceutica NOVA-ARGENTIA-ITALY	In product pouch no label	Kapisa	MoPH
35	Paracetamol 500mg Tablets	COMBITIC GLOBAICAPLET PVT LTD INDIA	140445 (PML-132)	Farah	CHA
36	Paracetamol 500mg Tablets	GlaxoSmithKline, karachi-Pakistan	1844	Kunar	PU-AMI
37	Paracetamol 500mg Tablets	JAWA pharma Pakistan	9701	Nuristan	IMC
38	Paracetamol 500mg Tablets	JAWA pharma Pakistan	9701	Samangan	AADA
39	Paracetamol 500mg Tablets	QHSK Yanzhon-China?	140445 (does not look like a batch)	Daykundi	CAF
40	Paracetamol 500mg Tablets	QHSK Yanzhon-China?	NR	Daykundi	CAF
41	Quinine 300mg Tablets	Lahor Chemical Pharma Works PVT.LTD	In product pouch no label	Balkh	BDN

Table 18 outlines the data we were able to collect on the distributors/manufacturers of the EMs tested. There are unmistakably errors in this dataset as the field workers failed to differentiate between distributors and manufacturers at times. This is an issue that will be addressed by more detailed training and adaptation of the data collection tool for the following round. From this data it is evident that the source of substandard aspirin and chloramphenicol is a common one that is used by multiple implementing agencies.

Sensitivity and Specificity of Minilab results

Sensitivity and specificity are statistical measures of the performance of a binary classification test, comparing (a sample of) the conducted tests against a gold standard. In the case of the DQA, the GPHF-Minilab results are compared against the WHO certified lab in India, with the latter being considered the gold standard. The results of the cross-checks done for both the failed EMs as well as those for the randomly sampled "passed" EMs are used to calculate the sensitivity and specificity of the GPHF-Minilab results, in order to validate the findings reported in Table 8.

Sensitivity (also called the true positive rate) measures the proportion of correctly identified instances of the condition which is being measured (or "failed" quality tests for EM using Minilabs). Specificity (also called the true negative rate) measures the proportion of negatives (in this case, "passed" quality tests for EM using Minilabs) that are correctly identified as such.

Understanding true positives and true negatives for the MiniLab tests can be confusing, given that a "failed" test is considered "positive", while a "passed" drug quality test is defined as "negative" in the definitions used. The definitions can therefore seem counterintuitive to many..

A perfect test has both 100% sensitivity and 100% specificity but this is seldom found. In reality, there is normally a trade-off between the two, with tests with high sensitivity often being less specific and vice versa.

Overall results for sensitivity and specificity for the GPHF Minilab

154 samples were sent to India for comparison against the Gold Standard. The results were as follows:

- Of 25 "failed" samples, 17 were correctly identified as such
- Of 129 "passed" samples, 111 samples were correctly identified as such

	Reference Lab + ("Fail")	Reference Lab – ("Pass")	Total
Minilab + ("Fail")	17 (True Positives - TP)	8 (False Positives – FP)	**25**
Minilab – ("Pass")	18 (False Negatives - FN)	111 (True Negatives - TN)	**129**
Total	**35**	**119**	**154**

Sensitivity= TP/(TP+FN)
Specificity= TN/ (FP+ TN)

Using these standard formulas for calculation of sensitivity and specificity yields the following:

- Sensitivity= 47.2% (95% CI: 30.4, 64.5)
- Specificity= 93.2% (95% CI: 87.1, 97.0)

Sensitivity was particularly impaired as a result of two EMs:

- Although the failure rate for Minilab quality tests of Aspirin 500mg tablets was already relatively high, a reasonably high proportion of "passed" Aspirin tests also failed when tested using the Gold Standard (8/12 or 75%).
- Although none of the samples of Aminophylline 100mg tablets failed the Minilab quality tests, 6/6 samples sent to India failed when tested using the gold standard

Specificity was particularly impaired as a result of one EM:

- All 8 samples of Salbutamol 4 mg tablets which "failed" when tested by the Minilab, tested "passed" upon examination by the lab in India.

This indicates that there are three specific EMs that need to be more carefully reviewed in close collaboration with the manufacturers of the Minilab in order to ensure that errors of these types are avoided during the subsequent round. Other medications were not of immediate concern.

Dropping aspirin, aminophylline and salbutamol from the calculations for sensitivity and specificity based on the assumption that the testing of these three medications were due to either human or methodological errors that can both be corrected when identified, yields a sensitivity of 77.8% and a specificity of 100%, suggesting that overall, the performance of MiniLabs as a tool to identify substandard drugs does yield relatively robust results.

DISCUSSION

Drug quality

Although the pharmaceutical products failing the Stabicon and GPHF-Minilab® tests cannot be considered representative of all the pharmaceutical products in Afghanistan for reasons mentioned earlier, it seems that those failing the tests are, more often than not, common molecules that are dispensed in large volume to the population. Although the larger-scale substandard EMs identified (aspirin, paracetamol and chloramphenicol) are not considered immediately life-saving (except chloramphenicol), we must add the high potential impact of untoward events if the substandard products supplied also contain toxic impurities, in addition to the risk of therapeutic failure.

The results are most certainly not representative of the overall quality of drugs for either BPHS or EPHS facilities. The 15% failure rate as measured by the Stabicon testing is indicative at national level only, given that the total sample size of collected medications was smaller than intended due to delays in getting permissions to collect drug samples from health facilities. This will be corrected during the following round of DQA.

As evidenced by the list of manufacturers/suppliers provided, the origins of the substandard pharmaceutical products found in this analysis correspond mainly to Afghanistan's neighbouring countries. This is in line with the limited available literature, explaining that countries suffering from conflict have very permeable borders; their regulatory authorities are thus unable to control the quality of medicines entering their pharmaceutical market. Further readjustment of data collection tools is necessary, however, in order to more clearly discern the manufacturing origin of all samples collected as well as manufacturing and expiry dates.

Pharmaceutical export companies may not be subject to the same regulatory requirements as those that operate (and are enforced) in their countries of origin. As such, unscrupulous drug manufacturers may adapt the quality of their products to the requirements (or lack thereof) of the 'client country', in order to maximize their profit. This pinpoints the need for cross-border initiatives that tackle the problem of substandard medicines in the region.

The use of the GPHF-Minilab® and tablet based data entry

The use of tablets for data entry of Minilab results was piloted during the current survey. The perception of the data management staff has not been encouraging. The tablet database program was not perceived to be convenient, since it contained insufficient internal consistency checks. As a result, data entry was not always correct, and it took considerable time for the data management staff to ensure the data quality. The data manager frequently had to resort to the paper based forms in order to correct the data transferred by the tablets. For the next DQA round the database entry consistency checks need to be further improved. The intention is to perfect the data entry process using tablets because of the inherent positive elements in their use in this assessment as well as others.

The Minilab failed to test certain samples (2 out of 25 drug formulations), which was unanticipated. The standards and methodology for fixed combination anti-TB drugs were also not available at the times of assessment. Further review will take place with the Minilab manufacturers before a new selection of 30 EMs is made for the subsequent round.

The sensitivity of the Minilab as was used currently is low at 47.2%. The specificity is acceptably high at 93.2%. Three EMs are of concern in relation to the validity of the Minilab results: Aspirin 500mg tablets (for which not all "failed" samples were identified by the Minilab), Aminophylline 100mg tablets (which "passed" the Minilab tests but failed the Stabicon quality checks) and Salbutamol 4mg tablets (which all "failed" Minilab quality tests yet they passed the Stabicon tests). The potential sources of these errors will be investigated. If these are corrected, current data (measured by dropping the three EMs of concern from the analysis) suggests that overall sensitivity and specificity of the Minilab can be as high as 78% and 100%, respectively.

Dataset and further analysis

The analysis contained in the present report should be considered exploratory and descriptive. The data were demonstrated to be internally consistent yet further work on the dataset could prove useful, for example by comparing data with those of the BSC to check consistency on the stock outs which are possibly on the high side, or to explore relationships between the variables in the datasets. In order to facilitate this type of analysis the possibility should be explored to include the same drugs in the BSC questionnaires that are shown in the DQA.

Building local capacity in cost-effective and sustainable drug quality testing

The second objective of the drug quality assessment was to build local capacity in cost-effective and sustainable drug quality testing. This was achieved through the use of the Minilabs as the initial screening tool for drug quality assessment. Minilabs are cost-effective and have already been adopted by the Ministry of Public Health as a tool for drug quality screening to be rolled out throughout the country.

We have used 5 Minilabs for this round of the DQA, each of which was manned by a laboratory technician. These technicians have had the opportunity to use the labs intensively, and gain considerable experience in testing the drugs selected for inclusion in this round of DQA.

Additionally, by including the quality checks by a WHO reference laboratory as part of the DQA, we have been able to validate what works and what does not work in drug quality testing in the Afghan context. We will be working closely with the Minilab developers to ensure that the tests for Aspirin, Aminophylline, and Salbutamol will be improved. This will further improve the quality of drug testing in Afghanistan in the future, which is especially important if the use of Minilabs will be considerably scaled up in Afghanistan.

SUMMARY OF KEY FINDINGS

Indications of stock-outs and the presence of counterfeit or substandard EMs

- The proportions of sampled EMs which are out of stock are unacceptably high at 46%, even though the figures may be biased upwards due to refusal to cooperate by some health facilities.
- From the samples tested with Minilab and Stabicon, it is estimated that up to 15.1% of EMs collected could be sub-standard; notwithstanding the difference between Minilab and Stabicon results, this is a strong evidence suggesting the presence of substandard essential medicines in the public pharmaceutical sector in Afghanistan. Although the percentage of samples failing these tests is relatively low when compared to the limited literature available, which cites rates up to 30%, the extent of the problem cannot be fully ascertained yet. The sampling procedure will be reviewed in light of these results as many items were out of stock at the time of sampling and not all medicines are equally prone to be counterfeit or falsified. Furthermore, specific families, such as anti-TB drugs, must be sampled in future quality assessments.
- High fail rates were found for Aspirin and Paracetamol 500mg tablets using Minilab tests, results which were confirmed by the WHO reference laboratory. These are not immediately life-saving drugs, but could result in a lack of trust by the population in the quality of health services if they are not perceived to 'work'.
- Of concern is the relatively high fail rate for the life-saving drugs Chloramphenicol 1g powder for injection (9%) and the Aminophylline 100mg tablets, as measured by the WHO certified laboratory.

Performance assessment on Storage

- The average score on the checks on storage is 7.5 out of 10. Compared to the results of pharmaceutical market assessments carried out in other developing countries (which include assessment of compliance to internationally recognized standards (WHO) of Good Storage and Distribution Practices), the overall score for this indicator is high, suggesting that degradation may have a limited effect on the quality of EMs. The following DQA rounds will be used for validating these findings.
- The distribution of positive checks by implementers show that some implementing partners have received very high scores, at the level of 9 or 10 points out of 10, while there are also lows of 1-5. The latter implementers should be the focus of attention.

RECOMMENDATIONS

Substandard drugs in Afghanistan

DQA is a useful tool in identifying and addressing the issue of substandard EMs in Afghanistan. For future rounds of DQA, the sample size must be increased and more detailed data must be collected on manufacturers/distributors in order to attain more robust results.

The results outlined in Table 18 should be used in identifying the suppliers of these EMs. Given that most of the implementing agencies were found to have substandard drugs in their facilities, all implementing agencies and MoPH should take note of the problem suppliers and problem EMs and take this information into consideration when ordering and receiving supplies of EMs.

Use of Minilabs

Minilab testing was able to identify problems with two types of drugs in Afghanistan, results that were verified by the reference laboratory:

- Aspirin
- Paracetamol

Nevertheless, there is room for improvement in the testing methodology. Three EMs are highlighted that need follow-up for both internal and external quality assurance in order to identify the source of error.

- Aspirin
- Aminophylline
- Salbutamol

Overall, results of the Minilab tests were robust enough to validate its wider use as a screening tool for drug quality in Afghanistan. Cautions should nevertheless be used in the interpretation of results for the three EMs outlined above.

The continued verification of Minilab results is essential to ensure the quality of results.

Drug stock-out

Efforts must be made to reduce drug stock-outs at health facilties, with particular attention to BPHS facilities.

Drug storage conditions

Although the results of the WHO checklist indicate that storage conditions for EMs in Afghanistan are overall better than in other developing economies, there is still room for improvement, particularly in the field of temperature control:

- availability of cold storage and temperature monitoring as part of storage facilities
- greater attention to ventilation and the avoidance of direct sunlight.

Those implementing agencies receiving a lower score (below 5) on the drug storage assessment are advised to review storage conditions in their health facilities according to the checklist provided.