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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHOPIR)
Quality Control Laboratory

Part 1	**General information**		
Inspected laboratory details			
Name of Laboratory	**Prime Health (Pvt) Ltd (PHPL)**		
Address of inspected laboratory site	Royal Plaza, Mezzanine Floor, 30 East, Fazal-e-Haq Road, Blue Area, Islamabad, Pakistan.		
Inspection details			
Dates of inspection	22-24 January 2020		
Type of inspection	Initial inspection		
Introduction			
Brief description of testing activities	**Type of Analysis**	**Finished Products**	**Active pharmaceutical ingredients**
	Physical/Chemical analysis	pH, Water content(Karl-fisher), Loss on drying, dissolution, uniformity of dosage units, Titration, polarimetry,	pH, Water content(Karl-fisher), Loss on drying, dissolution, uniformity of dosage units, Titration, polarimetry,
	Identification tests	HPLC, UV-VIS Spectrophotometer, FTIR	HPLC, UV-VIS Spectrophotometer, FTIR
	Assay, impurities and related substances Residual Solvent	HPLC (UV—VIS, DAD, RI detection), UV-VIS Spectrophotometer, Determination of related substances and impurities by comparison with reference standards, Residual Solvent GC, Atomic Absorption Spectroscopy, polarimetry	HPLC (UV—VIS, DAD, RI detection), UV-VIS Spectrophotometer, Determination of related substances and impurities by comparison with reference standards, Residual Solvent GC, Atomic Absorption Spectroscopy, polarimetry
	Stability studies	ICH conditions	ICH conditions
	Microbiological analysis	Not applicable	Not applicable

General information about the laboratory	Prime Health (Pvt) Ltd (in short PHPL) located at Royal Plaza, Mezzanine Floor, 30 East, Fazal-e-Haq Road, Blue Area, Islamabad-Pakistan. It is Pakistan's first laboratory to offer customer specific contract Pharmaceutical analytical services (Drug Substances and Drug Products). The goal of the laboratory is to be the premier provider of laboratory services worldwide while delivering an outstanding service experience. The PHPL covers the testing of Pharmaceutical dosage forms including Oral Tablets, Capsules, Suspensions, Ointments & Creams and Injectables, as well as active and inactive pharmaceutical ingredients. The PHPL was also engaged in stability testing.
History	This was the first WHO PQ inspection of the Prime Health (Pvt) Ltd. The PHPL has been awarded a Provisional Certificate for Contract Test and Analysis of Pharmaceuticals (API, Non-API and Finished Products), by the Drug Regulatory Authority of Pakistan (DRAP), Document # F.6-17/2018-QA & LT-574. The laboratory was: o accredited by the Pakistan National Accreditation Board for ISO/IEC 17025:2017 in October 2019; o certified to ISO 9001:2015 (certificate number 17760-QMS-001 dated 16 July 2019, expiry date 16 July 2022; o accredited to ISO 14001:2015 for Environmental Management System; and o certified to 45001:2018 for Health and Safety Management System.
Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	The scope of the inspection was limited to the activities of the drug physico-chemical laboratory with the inspection covering the following sections of the WHO Good Practices for Pharmaceutical Quality Control Laboratories (GPPQCL) text: o Organization and management o Quality management system o Control of documentation o Records o Data-processing equipment o Personnel o Premises o Equipment, instruments and other devices o Contract o Reagents o Reference substances and reference materials o Calibration, verification of performance and qualification of equipment, instruments and other devices o Traceability o Incoming samples o Analytical worksheet o Validation of analytical procedures

	○ Testing ○ Evaluation of test results ○ Certificate of analysis ○ Retained samples ○ Safety
Restrictions	None
Out of scope	The microbiology laboratory was outside the scope of this inspection
Abbreviations	**Meaning**
ALCOA	Attributable, legible, contemporaneous, original and accurate
API	Active pharmaceutical ingredient
CoA	Certificate of analysis
FPP	Finished pharmaceutical product
FTIR	Fourier transform infrared spectrophotometry or spectrophotometer
GMP	Good manufacturing practices
HPLC	High performance liquid chromatography (or high-performance liquid chromatography equipment)
KF	Karl Fisher titration
LIMS	Laboratory information management system
MB	Microbiology
MR	Management review
NC	Non-conformity
NCA	National control authority
NCL	National control laboratory
NRA	National regulatory agency
OOS	Out-of-specifications test result
PM	Preventive maintenance
PQ	Performance qualification
PQR	Product quality review
PQS	Pharmaceutical quality system
PW	Purified water
QA	Quality assurance
QC	Quality control
QCL	Quality control laboratory
QMS	Quality management system
QRM	Quality risk management
RA	Risk assessment
RCA	Root cause analysis
SOP	Standard operating procedure
URS	User requirements specifications
UV	Ultraviolet-visible spectrophotometry or spectrophotometer

Part 2	Summary of the findings and comments (where applicable)

1. Organization and Management

Prime Health (Pvt) Ltd is a contract pharmaceutical quality control testing facility. It is a sub-group of the SPARS Group of companies in Pakistani. It holds a Certificate of Incorporation B002196, incorporation number 0096983 dated 25 January 2017; Membership Certificate of Trading from the Islamabad Chamber of Commerce and Industry, dated 22 March 2019 and renewal on 31 March 2020; and was registered by the Pakistani Drug Regulatory Authority (DRAP) on registration number F03-77/2018-QC(266-CLB), dated 07/01/2019.

The DRAP had inspected the Laboratory according to the local regulations which made reference to WHO guidelines and issued a provisional certificate dated 27th Sep 2018 as a contract test and analysis laboratory for pharmaceutical products, valid for one year up to 27th September 2019. There were no formal rules regarding such laboratories in Pakistan.

The Laboratory had two separate sections one for chemistry and the other for microbiology.

The Laboratory Manual "Manual of the Laboratory Management system", was based on the ISO/IEC 17025:2017 and WHO GPPQCL guidelines (*TRS No. 957, Annex 1).*

Internal audits
The SOP described the procedure for carrying out internal audits. It was noted that internal audits are conducted biannually. The schedule for 2020 was available.

Change controls management
Change control procedure covered changes related to documents, test methods, equipment etc. The changes were categorised as critical, major and other/minor.

Deviation management
Deviation procedure was in place. The objective was to provide procedure to raise, investigate and approve or reject any deviations. Deviations were classified as planned and unplanned; however, definition was found to be ambiguous. Planned deviation was defined as "when a decision to carry out a process or procedure in a different way exactly as written from its established procedure". The procedure also described tools to be used for performing investigation of deviation. Based on the risk assessment, deviations were divided into Level 1 (critical), Level II (major) and Level III (minor).

Quality risk management (QRM)
QRM procedure was in place. The scope of the SOP included quality and safety risks, review of process and continual improvement. The FMEA method was used for risk assessment (severity 1-10, probability 1-8 and detectability 1-4) and RPN was assigned (critical: 201-320, major: 101-200 and minor:1-100). The forms included risk identification form, risk logbook, risk analysis before mitigation and risk analysis after mitigation.

Proficiency testing / inter-laboratory comparison program
The PTS procedure was in place. The general policy stated that participation is on an annual basis, with minimum one activity for each sub discipline within the laboratory's scope. The LGC was used for PT scheme.

Management Review
Management review (MR) was held twice a year.

2. Quality management system

Quality Management System of Prime Health, comprised of different levels of documentation, such as Level I, Level II and Level III documents, which includes, but not limited to following procedures:

a) Document Management
b) Training Procedure
c) Selection and Qualification of Contractors
d) Quality Risk Management
e) Corrective action and preventive action (CAPA) system
f) Change Control Management
g) Deviation Management
h) Master Validation Plan
i) Laboratory Instruments Qualification
j) Calibration and Maintenance of Laboratory Instruments
k) Internal Audit
l) Investigation Procedure
m) OOS Test Results
n) Customer Complaints
o) Annual Test Review
p) Waste Disposal
q) Data Integrity
r) Management of Review Meeting

3. Control of documentation

Management of document control was in place. The objective of the procedure covered handling of internal and external documents. Document distribution record for the Quality Manual was available. The obsolete date was correctly indicated on the list of obsolete documents. The obsolete SOP was also properly stamped "Obsolete".

4. Records

Control of records procedure was in place. The records were basically paper based. The test data generated electronically (e.g. by the chromatography software, Excel worksheet, etc.) were printed out.

5. Data processing equipment

Major testing equipment like HPLCs, were designed to comply with 21 CFR 11.

6. Personnel

The following laboratory personnel were engaged:

Activity	Number
Chief Executive Officer	01
Chief Operating Officer	01
Business development	01
Human Resource/ Admin	01
Finance	02
Procurement	01
Information Technology	01
Chief Quality Operations	01
Analysts	02
Microbiologist	01
Quality assurance	01
Laboratory Assistant	01
Cleaner	01

7. Premises

The Laboratory was situated on mezzanine floor and comprised of the Chemistry Laboratory on West side and Management Offices/ Microbiology Laboratory on East side. The Laboratory was well designed, had modern construction, and was tidy. There was orderly placement of laboratory equipment, fixtures and fittings. It had adequate safety equipment.

Access to some parts of the laboratory e.g. Sample Retention Room, and the main laboratory was through biometric access control system. CCTV cameras were also installed in critical laboratory areas like the entrance to sample retention room, and several rooms in the laboratory.

The Chemistry Lab, covered an area of 2288 sq. ft., with the following sections:

- Change Room
- Sample Retention Room with compact mobile racks
- QA Office
- Stability section
- Wet Chemical laboratory
- Balance Room
- GC & AA Lab
- Instrument lab
- Washing/ Glassware storage area
- Chemical Storage area
- Janitorial Cabinet

The Microbiology Lab, covered an area of 668 sq. ft., and comprised of the following sections:

- Main Microbiology laboratory
- Washing Area/ Water purification System
- Media preparation section
- Air Lock1 & 2
- Gowning/ De-gowning
- Sterile section

The Administration – covered an area of 1592 sq. ft. with the following offices:

- Reception/ Admin
- COO Office
- IT Office
- CQO Office
- Record Room
- Rest Rooms

The Chemical laboratory was supplied with fresh air handing unit with exhaust system as well as air-conditioning that provided a temperature-controlled environment between 22 to 30ºC. An Uninterruptable Power Supply (UPS) system rated at 20kVA supported critical equipment like the stability chambers.

8. Equipment, instruments and other devices

The required test equipment and instruments were available and well designed.

The laboratory had two stability chambers (40ºC/75%RH and 30ºC/65%RH). Annual calibration was performed by the external service provider.

9. Contracts

No testing activity was outsourced by the PHPL; with only calibration, qualification and preventive maintenance activities outsourced.

10. Reagents

The laboratory confirmed that reagents were freshly prepared. The laboratory used water that was purified through reverse osmosis unit and distillation. The purified water was required to comply to USP specifications.

11. Reference substances and reference materials

The Laboratory mainly used chemical reference substances supplied by clients.

12. Calibration, verification of performance and qualification of equipment, instruments and other devices

Calibration of the major laboratory equipment was outsourced. The calibration of the dissolution apparatus and HPLCs were performed by external service provider. Calibration certificates and stickers placed on equipment were verified during the inspection.

13. Traceability

Laboratory results were generally traceable to the equipment and reference standard used.

14. Incoming samples

Request for analysis from the customer was in place. Samples were received to perform tests for assay, identification, impurity and dissolution as per pharmacopoeial requirements. Upon receipt of the samples a Checklist was used with the Logbook indicating the sample.

15. Analytical worksheet

The Laboratory used both Analytical Note books and Analytical worksheets. The Analytical worksheet for the testing of a product in place. Each page of the worksheet was serially numbered.

16. Validation of analytical procedures

Analytical method verification protocol and report was in place.

17. Testing

The laboratory receives samples from different clients which were requested to be tested as per the pharmacopoeia. The working standard was provided by the client along with the certificate of analysis.

18. Evaluation of test results

Out of specification (OOS) was in place.

19. Certificate of analysis

Certificates of analysis (CoA) were issued to clients. It provided for all the required information.

20. Retained samples

Retained samples were kept in the sample store.

21. Safety

During the inspection of the wet chemistry and instrumentation laboratories, it was noted that adequate safety equipment (overhead shower and eye-shower stations) were located in strategic positions. The laboratory was equipped with modern work benches and fume hoods. Fire extinguishers were also strategically located in the building.

Part 3	Conclusion – Inspection outcome

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, ***Prime Health (Pvt) Ltd,*** located at ***Royal Plaza, Mezzanine Floor, 30 East, Fazal-e-Haq Road, Blue Area, Islamabad, Pakistan***was considered to be operating at an acceptable level of compliance with WHO GPPQCL Guidelines.

All the non-compliances observed during the inspection that were listed in the full report were addressed by the manufacturer, to a satisfactory level, prior to the publication of the WHOPIR.

This WHOPIR will remain valid for 3 years, provided that the outcome of any inspection conducted during this period is positive.

Part 5	List of WHO Guidelines referenced in the inspection report

1. WHO Good Practices for Pharmaceutical Quality Control Laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 1.
   Short name: WHO GPPQCL Guidelines or ***TRS No. 957, Annex 1***
   http://www.who.int/medicines/publications/44threport/en/

2. WHO good practices for pharmaceutical microbiology laboratories. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 2.
   Short name: WHO TRS No. 961, Annex 2
   http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

3. WHO good manufacturing practices: water for pharmaceutical use. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fourth-sixth Report. Geneva, World Health Organization, 2012 (WHO Technical Report Series, No. 970), Annex 2.
Short name: WHO TRS No. 970, Annex 2
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_970/en/

4. WHO guidelines for sampling of pharmaceutical products and related materials. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Thirty-ninth Report. Geneva, World Health Organization, 2005 (WHO Technical Report Series, No. 929), Annex 4.
Short name: WHO TRS No. 929, Annex 4
http://whqlibdoc.who.int/trs/WHO_TRS_929_eng.pdf?ua=1

5. Guidance on good data and record management practices. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fiftieth Report Geneva, World Health Organization, 2016 (WHO Technical Report Series, No. 996), Annex 5.
Short name: WHO GDRMP guidance or ***WHO TRS No. 996, Annex 5***
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex05.pdf

6. WHO good manufacturing practices for pharmaceutical products: main principles. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-eighth Report Geneva, World Health Organization, 2014 (WHO Technical Report Series, No. 986), Annex 2. ***Short name: WHO GMP guidelines*** or ***TRS No. 986, Annex 2***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_986/en/

7. WHO good manufacturing practices for active pharmaceutical ingredients. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 2. ***Short name: WHO TRS No. 957, Annex 2***
http://www.who.int/medicines/publications/44threport/en/

8. WHO Good Practices for Pharmaceutical Products Containing Hazardous Substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fourth Report. Geneva, World Health Organization, 2010 (WHO Technical Report Series, No. 957), Annex 3.
Short name: WHO TRS No. 957, Annex 3
http://www.who.int/medicines/publications/44threport/en/

9. WHO good manufacturing practices for sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 6.
Short name: WHO TRS No. 961, Annex 6
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

10. WHO guidelines on transfer of technology in pharmaceutical manufacturing WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 7.
Short name: WHO TRS No. 961, Annex 7
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

11. Model guidance for the storage and transport of time-and temperature-sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 9. ***Short name: WHO TRS No. 961, Annex 9***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

12. General guidelines for the establishment maintenance and distribution of chemical reference substances. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-first Report Geneva, World Health Organization 2007 (WHO Technical Report Series, No.943) Annex 3. ***Short name: WHO TRS No. 943, Annex 3***
http://whqlibdoc.who.int/trs/WHO_TRS_943_eng.pdf?ua=1

13. Guidelines on heating, ventilation and air-conditioning systems for non-sterile pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 8. **Short name: WHO TRS No. 1010, Annex 8**
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_1010/en/

14. WHO guidelines on quality risk management. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 2. ***Short name: WHO TRS No. 981, Annex 2***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

15. WHO guidelines on variation to a prequalified product. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-seventh Report Geneva, World Health Organization, 2013 (WHO Technical Report Series, No. 981), Annex 3. ***Short name: WHO TRS No. 981, Annex 3***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/trs_981/en/

16. WHO guidelines for drafting a site master file. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-fifth Report Geneva, World Health Organization, 2011 (WHO Technical Report Series, No. 961), Annex 14. ***Short name: WHO TRS No. 961, Annex 14***
http://whqlibdoc.who.int/trs/WHO_TRS_961_eng.pdf?ua=1

17. WHO Guidelines on good manufacturing practices: validation, Appendix 7: non-sterile process validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 3. ***Short name: WHO TRS No. 992, Annex 3***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

18. WHO General guidance on hold-time studies WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 4. ***Short name: WHO TRS No. 992, Annex 4***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

19. WHO Technical supplements to Model Guidance for storage and transport of time – and temperature – sensitive pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Forty-ninth Report Geneva, World Health Organization, 2015 (WHO Technical Report Series, No. 992), Annex 5. ***Short name: WHO TRS No. 992, Annex 5***
http://www.who.int/medicines/areas/quality_safety/quality_assurance/expert_committee/WHO_TRS_992_web.pdf

21. Supplementary guidelines on good manufacturing practices: validation. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fortieth Report. Geneva, World Health Organization, 2006 (WHO Technical Report Series, No. 937), Annex 4.
Short name: WHO TRS No. 937, Annex 4
http://whqlibdoc.who.int/trs/WHO_TRS_937_eng.pdf?ua=1

22. Stability testing of active pharmaceutical ingredients and finished pharmaceutical products. WHO Expert Committee on Specifications for Pharmaceutical Preparations. Fifty-second Report Geneva, World Health Organization, 2018 (WHO Technical Report Series, No. 1010), Annex 10.
Short name: WHO TRS No. 1010, Annex 10
http://www.who.int/medicines/publications/pharmprep/WHO_TRS_996_annex10.pdf