

## WHO PUBLIC INSPECTION REPORT (WHOPIR)

### Quality Control Laboratory

#### Part 1: General information about the inspection

Name of laboratory	The Laboratory of Pharmaceutical Analysis of PE “State Pharmacological Center” Ministry of Health, Ukraine
Physical address	14, Ezhena Pottier St., Kyiv, Ukraine
Postal address	As above
Telephone number	+38445361338
Summary of all the activities performed by the laboratory	The laboratory was involved in: <ul style="list-style-type: none"> <li>• Conventional chemical analysis</li> <li>• Instrumental analysis</li> <li>• Microbiological analysis</li> <li>• Biological testing (contracted out)</li> </ul>
Scope of inspection	Prequalification inspection of QC laboratory
Focus of inspection	<ul style="list-style-type: none"> <li>• Quality system of the Quality Control Laboratory</li> <li>• Conventional chemical analysis</li> <li>• Spectrophotometric analysis (IR, UV)</li> <li>• Chromatographic methods (HPLC, GC, and TLC)</li> <li>• Dissolution, disintegration and friability testing</li> <li>• Microbiological analysis</li> </ul>
Date of inspection	17 and 18 December, 2009
Programme	Prequalification of Medicines Programme

#### Part 2: Summary

The Laboratory of Pharmaceutical Analysis of PE “State Pharmacological Center” Ministry of Health, Ukraine on 17 and 18 December, 2009.

#### *General information about the laboratory*

The Laboratory of Pharmaceutical Analysis of PE “State Pharmacological Center” Ministry of Health, Ukraine was established in 1994.

The laboratory was involved in pre-registration control of substances and of finished medicinal products; quality control of finished products designed for clinical trials; conduct-

---

 WHOPIR:

The Laboratory of Pharmaceutical Analysis of PE “State Pharmacological Center”  
 Ministry of Health, Ukraine  
 December, 2009

ing trials to confirm compliance of quality of samples of medicinal products submitted for pre-registration control or designed for clinical trials with their specifications, and reproducibility of analytical methods indicated in registration materials; *in vitro* comparative studies to justify equivalence of medicinal products in oral solid dosage forms for systemic use; run-time arbitration quality analysis of medicinal products; counseling and methodic assistance to institutions and organizations concerning quality analysis of medicinal products.

The laboratory quality policy was based on “General requirements for competence of testing and calibration laboratories” and ДСТУ/DSTU ISO/IEC 17025-2006.

**The Laboratory of Pharmaceutical Analysis of PE “State Pharmacological Center” was performing the following analysis:**

Type of Analysis	Finished products	Active pharmaceutical Ingredients
Physical / Chemical analysis	pH	pH
	Friability	Acid value
	Disintegration time	Iodine value
	Tablet hardness	Peroxide value
	Density	Ester value
	Dissolution	Hydroxyl value
	Dimensions	Saponification value
	Limit Tests	Unsaponifiable matter
	Delivered Volume	Nitrogen by sulphuric acid digestion
	Clarity & Colour of solutions	Water semi-micro determination
	Uniformity of content	Clarity & Colour of solutions
	Uniformity of weight	Limit Tests
	Minimum fill	Solubility
	Acid value	Density
	Iodine value	Acid neutralizing capacity
	Peroxide value	Residue on Evaporation
	Ester value	Heavy metals
	Hydroxyl value	Acidity/Alkalinity
	Saponification value	Refractive index
	Unsaponifiable matter	Optical rotation
Nitrogen by sulphuric acid digestion	Viscosity (capillary & rotating)	
Water semi-micro determination	Melting point	
Residue on Evaporation	Loss on drying	
Heavy metals	Conductivity	
Acidity/Alkalinity		

WHOPIR:

The Laboratory of Pharmaceutical Analysis of PE “State Pharmacological Center”  
 Ministry of Health, Ukraine  
 December, 2009

	Refractive index	
	Optical rotation	
	Viscosity (capillary & rotating)	
	Loss on drying	
	Conductivity	
<b>Identification</b>	NIR-spectrophotometry	NIR-spectrophotometry
	TLC	TLC
	HPLC	HPLC
	GC	GC
	UV-VIS Spectrophotometry	UV-VIS Spectrophotometry
	Atomic absorption spectrometry	Atomic absorption spectrometry
	Basic tests	Basic tests
<b>Assay, impurities and related substances</b>	HPLC (UV-VIS, DAD, Fluorescence, Refraction)	HPLC (UV-VIS, DAD, Fluorescence, Refraction)
	GC (incl. Head-space)	GC (incl. Head-space)
	UV-VIS Spectrophotometry	UV-VIS Spectrophotometry
	Atomic absorption spectrometry	Atomic absorption spectrometry
	Volumetric Titrations	Volumetric Titrations
<b>Biological (Microbiological) analysis</b>	Microbial limit tests	Microbial limit tests
	Bacterial Endotoxins	Bacterial Endotoxins
	Sterility tests	Sterility tests
	Microbiological assay of antibiotics	Microbiological assay of antibiotics
	Pyrogens (contracted out)	Pyrogens (contracted out)
	Abnormal toxicity (contracted out)	Abnormal toxicity (contracted out)

### *History of WHO or regulatory agencies inspections*

The laboratory was previously inspected by the WHO on the 9<sup>th</sup> and 10<sup>th</sup> of December 2008.

### *Focus of the inspection*

This inspection focused on:

- implementation of corrective actions from previous inspection
- evaluation and investigation of out of specification (OOS) results
- dealing with reference materials
- specific equipment and tests such as:
  - HPLC
  - GC

---

 WHOPIR:

The Laboratory of Pharmaceutical Analysis of PE "State Pharmacological Center"  
 Ministry of Health, Ukraine  
 December, 2009

- UV
- IR
- AAS
- Dissolution
- Disintegration
- Analytical balances

## **2.1. ORGANIZATION AND MANAGEMENT**

The organization of the laboratory was defined in an organization chart. The laboratory had appropriate technical personnel with authorities to carry out their duties. The responsibilities of personnel were defined in job descriptions. The laboratory had a central registry. Records were kept for all incoming samples. The laboratory had an appropriate system for archiving the documents and handling the samples.

## **2.2 QUALITY SYSTEM**

The Quality system was implemented in 2007 and was based on CTY/DSTU ISO/IEC 17025-2006 standard. Quality assurance documents were approved and available for the laboratory employees.

The Quality Manager was appointed and had direct access to the head of the laboratory.

The quality system was systematically reviewed by internal audits.

A complaint SOP was available.

In general observations from last inspection were adequately addressed and corrective actions were implemented.

## **2.3 CONTROL OF DOCUMENTATION**

There were procedures in place to generate and approve documents including SOP' s, records and analytical work sheets as well as procedures for the issuance of certificates of analysis. Distribution of the documents was controlled.

## **2.4 RECORDS**

Training records, analytical work sheets and sample logs were available. The records included the identity of the personnel involved in the preparation and testing of the samples. Spot checks showed that written procedures were available for the performing of the work.

## **2.5 DATA PROCESSING EQUIPMENT**

---

WHOPIR:

The Laboratory of Pharmaceutical Analysis of PE "State Pharmacological Center"  
Ministry of Health, Ukraine  
December, 2009

The HPLC systems, GC, UV and IR equipment were linked to the computers operated by their respective software. All the related test reports such as chromatograms were stored electronically and as hard copies.

## **2.6 PERSONNEL**

An organization chart was showing the arrangements, responsibilities and reporting lines in the laboratory.

Current job descriptions were available; documents were signed and dated by the relevant employees.

The personnel met during the inspection were experienced, skilled and conscientious.

## **2.7 PREMISES**

The laboratory was located on the third floor of a larger building. The laboratory premises were well maintained and clean. The laboratory environment was appropriate for the tests to be carried out. In general there was sufficient space available to separate different types of analysis. It was noted in some rooms that more floor space would be beneficial for convenient activities.

The laboratory had suitable testing equipment.

In general storage conditions were acceptable. A separated room in the cellar was also used for storage.

## **2.8 EQUIPMENT, INSTRUMENTS AND OTHER DEVICES**

Operational and calibration SOPs were available for all equipment. A calibration schedule was available.

The list of laboratory equipment was available.

## **2.9 SPECIFICATION ARCHIVE**

The specifications were provided by the applicants for the Marketing Authorizations. Applicant's specifications were handled according to the confidentiality agreements signed by the laboratory employees.

## **2.10 REAGENTS**

The reagents were purchased from reputable manufacturers.

The preparation of reagents was performed according to Pharmacopoeia methods. Volumetric solutions were standardized according to the relevant Pharmacopoeia methods.

Upon receiving, reagents were inspected visually. Certificates of analysis were available. An approved vendors list was available. The inventory of the reagents was available and was up-dated.

In general the reagents were stored appropriately, special storage conditions were provided for certain chemicals.

## **2.11 REFERENCE MATERIALS**

In general official reference substances were used for the analysis. The reference substances were normally supplied by the applicants or if necessary ordered by the laboratory staff. The reference substances register was maintained. An identification number referring to the sample number was assigned to the reference substances.

## **2.12 CALIBRATION, VALIDATION AND VERIFICATION OF THE EQUIPMENT, INSTRUMENTS AND OTHER DEVICES**

Equipment items were uniquely identified.

Equipment was calibrated by the State metrological service according to the calibration schedule. Labels indicating equipment calibration status (of calibration and due day) were affixed to all equipment and instruments.

pH meters were verified with standard buffer solutions every day.

## **2.13 TRACEABILITY**

Traceability of results was assured by:

- Keeping appropriate records of observations
- Verifying observations, calculations and results
- Using primary reference standards
- Regularly calibrating instruments and equipment
- Performing system suitability tests as specified in relevant compendia monographs

## **2.14 INCOMING SAMPLES**

Incoming samples and corresponding documents which were submitted for analysis were registered in the samples registration book. Incoming samples were allocated to the des-

igned technicians. A unique registration number was allocated to the samples and was traceable through all the operations.

Upon receiving samples, these were visually checked. The amount of material / product for each sample was sufficient for analysis and for sample archiving purposes.

### **2.15 ANALYTICAL WORKSHEET**

The analytical work sheets were checked, signed and dated by the analysts, then checked and signed by the Quality Assurance manager. Worksheets contained required information. Changes were done in a correct manner.

### **2.16 TESTING**

Values obtained from the tests were entered on the analytical worksheets and graphical data were attached. System suitability criteria were fulfilled when defined in the method.

In the microbiological laboratory steam sterilization was used for sterilization purposes.

Pyrogen and toxicity tests were contracted out to the external laboratory. The contract laboratory was audited.

### **2.17 EVALUATION OF TEST RESULTS**

The test results were evaluated by the Quality Assurance manager. Test reports in general contained the required data. The SOP dealing with OOS was available for inspection.

### **2.18 RETAIN SAMPLES**

Retain samples were kept for a predefined duration - at least 6 months if testing results were within the specifications and at least 12 months if testing results were OOS.

### **2.19 SAFETY**

Personnel at the laboratory had to wear protective clothing. Safety instructions were followed.

## **Part 3: Conclusion**

The Laboratory of Pharmaceutical Analysis of PE “State Pharmacological Center” Ministry of Health, Ukraine was considered to be operating at an acceptable level of compliance with WHO Good practices for national pharmaceutical control laboratories.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the laboratory, 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.