World Health Organization

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Prequalification Team
WHO PUBLIC INSPECTION REPORT
Quality Control Laboratory

Part 1: General information

Name of the QC Laboratory	Testing Centre for Evaluation of Medicinal Products Quality of the Federal State Budgetary Institution "Scientific Centre for Expert Evaluation of Medicinal Products" of The Ministry of Health of The Russian Federation (FSBI "SCEEMP")
Physical address	Schukinskaya street 6, Moscow 123182, Russia
Date of inspection	23, 24, 25 September 2015
Type of inspection	Routine re-inspection
Type(s) of testing included in the inspection	Chemical, physical, microbiological
Summary of the testing activities performed by the QC Laboratory	

Type of analysis	*Finished products*	*Active pharmaceutical ingredients*
Physico – Chemical analysis	pH, density, refractive index, optical rotation, water content, loss on drying, residual solvents, limit tests, disintegration, dissolution, uniformity of dosage units (mass, content)	pH, density, refractive index, optical rotation, water content, loss on drying, residual solvents, limit tests, disintegration, dissolution, uniformity of dosage units (mass, content)
Identification	HPLC (UV-VIS, RI, DAD detection), GC , TLC, UV-VIS spectrophotometry, IR, basic tests	HPLC (UV-VIS, RI, DAD detection), GC , TLC, UV-VIS spectrophotometry, IR, basic tests
Assay, impurities and related substances	HPLC (UV-VIS, RI, DAD detection), GC (FID, TCD), UV-	HPLC (UV-VIS, RI, DAD detection), GC (FID, TCD), UV-

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		VIS spectrophotometry, volumetric titrations	VIS spectrophotometry, volumetric titrations
	Microbiological tests	Sterility test, microbial limit tests, microbial assay of antibiotics	Sterility test, microbial limit tests

Part 2: Summary

General information about the laboratory and site

The FSBI "SCEEMP" is formed of 4 expert divisions: the centre for finished pharmaceutical products evaluation, the centre for evaluation and control of medicinal immunobiological products, the testing centre for quality evaluation of medicinal immunobiological products, and the testing centre for medicinal products quality evaluation.

The Testing Centre for Medicines Quality Evaluation was formed of the following 11 laboratories:

- Control and coordination laboratory
- Laboratory of antibiotics (European directorate for the quality of medicines (EDQM), WHO)
- Laboratory of chemico-pharmaceutical preparations № 1
- Laboratory of chemico-pharmaceutical preparations № 2 (EDQM, WHO)
- Laboratory of nanomedicines, cell-therapy and genetic therapy products
- Laboratory of biotechnological products
- Laboratory of herbal medicinal products and homeopathic medicines
- Laboratory of vitamins, hormones and synthetic analogues
- Pharmacology laboratory and vivarium
- Microbiology laboratory
- Laboratory for control of radiopharmaceuticals and radiopharmaceutical reagent kits

The inspection's focus was on the Laboratory of chemico-pharmaceutical preparations № 2 and on the Laboratory of antibiotics, which was used to test anti-HIV, anti-TB products and antimicrobials.

Similarly to the last WHO inspection, the main function of the two laboratories was to test products, API and excipients as part of product registration using test procedures submitted by either applicants or directly by manufacturers. Reference materials with certificates of analysis were also supplied by applicants/manufacturers alongside with drug samples.

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History of WHO and/or regulatory agency inspections
This was the second WHO inspection of this site. The laboratory was also inspected by the EDQM and accredited to ISO 17025 standard. The accreditation certificate is valid until January 2018.

Focus of the inspection
The inspection focused on the quality management system and physical/chemical tests, identification, assay, impurities, related substances, and microbiological tests as the areas of quality control testing prequalified by the WHO.

Inspected Areas
The following areas of the WHO good practices for quality control laboratories were covered in this inspection:

- 2.1 Quality system
- 2.2 Control of documents
- 2.3 Records
- 2.4 Data-processing equipment
- 2.5 Personnel
- 2.6 Premises
- 2.7 Equipment, instruments and other devices
- 2.8 Reagents
- 2.9 Reference substances and reference materials
- 2.10 Calibration, verification of performance and qualification of equipment, instruments and other devices
- 2.11 Traceability
- 2.12 Incoming samples
- 2.13 Analytical sheet
- 2.14 Validation of analytical procedures
- 2.15 Testing
- 2.16 Evaluation of results
- 2.17 Certificate of analysis
- 2.18 Retained samples
- 2.19 Safety

(please note that the sections below have a different numbering than those of the WHO good practices for quality control laboratories.)

2.1. Organization and management

As noted during the last WHO inspection, 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 their job descriptions.

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2.2. Quality management system

Management Review

It was performed once per year. The last management review was done in May 2015. The last 2 management review reports were requested. The review of 2013 (review performed in 2014), was reviewed. According to the management review standard operating procedure in Russian (SOP) No. EIC-OA-017, version 6, valid until 01/06/2018, management reviews covered:

- Analytical results and results of internal audits
- Proficiency testing, non-conformances
- Management of quality system records
- Corrective and preventive actions
- Complaints
- Customer responses
- Changes in the work plan
- Staff training
- Resource planning
- Results of the previous management review
- Recommendations to improve the quality system.

Salient points of the 2013 review included a description of the non-conformities obtained for the different laboratories. Out of specification test results and corrective and preventive actions were reviewed, as well as complaints. Internal and external training was described to have been performed according to the program for 2013. Newly recruited staff passed the introductory training according to the plan. There were 16 new hires in 2013. Conclusions drawn at the end of the management review report including a series of corrective measures to be taken, such as the usage of standardized templates for analytical results and to improve the quality of documentation in the analytical reports.

Out of specification (OOS) test results and non-conformities

In 2014, there were 11 OOS in the antibiotics laboratory and 17 in the Laboratory of chemico-pharmaceutical preparations № 2. See section 16 of this report for further details.

Corrective actions

The Russian procedure entitled “Corrective actions” valid until 19.10.2015, was reviewed. It described two types of corrective actions. Immediate corrective actions and long-term corrective actions were defined along with the responsible persons. The corrective actions had to be approved by the head of the centers.

There was a description of how the corrective actions were performed, starting with the registration of the non-conformity, a registration of the corrective action, drafting and approval of a plan, followed by implementation and evaluation. Effective ness of the corrective action is reviewed, and adjustments are made if necessary. All corrective actions were reviewed during management review but were raised during OOS investigations and internal audits. There was a register available.

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Preventive actions
The Russian procedure entitled "Preventive actions" SOP valid until 02.06.2017, was reviewed. There was no register for preventive actions but a plan for the year was drafted further to internal audits and out of specifications, and was reviewed during management review.

Internal audits
An internal audit report from 2 April 2014 was reviewed. It was performed in accordance with ISO 17025 and WHO guidelines. Observations and corrective actions, responsible person, timeline and date of completion were documented in a table drafted for each audit report.

The Russian SOP entitled "Organization and performance of internal audits", valid until 16.10.2017, was reviewed. The plans were drafted ahead of time and the audits were required to be performed at least once a year. The plan for 2015 was reviewed.

2.3. Control of documentation
The Russian language procedure SOP entitled "Management of standard operating procedures and working instructions", was reviewed. It stated that by November 30, a work plan was established listing all of the SOPs, working instructions to be developed and reviewed for the next year.

Hard copies are distributed to responsible persons and a register is kept for each document of distribution. Each document has a validity of 3 years, after which it is reviewed. If there are no changes, validity is extended for another 3 years but version number remains the same. Documents can be reviewed prior to 3 years if required. Before implementation of a new SOP, when a document is approved by the deputy general director, after its signature, the old version of the SOP is withdrawn and the new version is distributed and training with implementation should be done within 15 days of sign-off.

The same procedures were applicable to both the antibiotics laboratory and the Laboratory of chemico-pharmaceutical preparations № 2.

2.4. Records
Electronic records of HPLC analyses were saved on the c:/ drive of each instrument. Back-ups were performed once per month on a portable 1 TB hard-disk. It was performed by selecting the main folder were all analyses were stored, which is acceptable. The Russian language SOP entitled "Archivation of primary data obtained in drugs testing" was reviewed. It applied to all equipment capable of recording electronic data. Back up frequency was specified as not less than once in two weeks in the SOP if connected to the network, but once a month if standalone.

The data was stored on a cluster of servers that are located as clouds in different areas.

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HPLC data was not named in a systematic manner and took time to be retrieved. There should be more systematic means of naming data to ensure full traceability.

The system for registration of archivation processes did not contain information about when data backups were performed.

2.5. Data-processing equipment

HPLCs, GC, dissolution (UV), UV and IR instruments were linked to computers operated by their respective software. See section 2.3 above for details.

All excel calculation spreadsheets were revalidated once per year by entering the same values (initial data) as before and reentering it. If they get the same results as initially, it confirms that the formulas were still the same. All cells were protected. All cells that contain formulas were password protected. They were located on a specific section of the central server.

2.6. Personnel

The Russian language SOP entitled “Organization of training for employees of the testing centers”, valid until 28.08.2016, was reviewed. Initial training, periodic and unplanned training were described.

After practical training via mentoring by an experienced staff member, the analysis of a known sample was done. An example was reviewed for Karl Fisher qualification of a new analyst that had joined the laboratory in 2014. The percentage of RSD was compared by the laboratory for 3 replicate tests by the new analyst vs. the experienced analyst. A theoretical exam was also taken in accordance with the requirements of the Ministry of Health.

The example of a chart listing the induction training that was given on SOPs to an employee in 2014 was reviewed.

2.7. Premises

As seen during the initial inspection, the laboratory premises were spacious, well maintained, clean, and tidy and provided adequate room for laboratory activities. The laboratory environment was appropriate for performing different tests. Separate small laboratories were dedicated to different analyses such as high performance liquid chromatography (HPLC), gas chromatography (GC) and physical tests (dissolution and disintegration).

2.8. Equipment, instruments and other devices

The equipment in the Laboratory of chemico-pharmaceutical preparations № 2 was inspected in detail. There were 18 HPLCs and 1 GC. There were 2 functional dissolution testing apparatus. Similar equipment was found in the Antibiotics Laboratory. Corrective actions and preventive actions (CAPAs) made further to the last inspection were acceptable. As stated further to the initial WHO inspection, the laboratory was well equipped to perform almost all pharmacopoeial tests for finished dosage forms.

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2.9. Contracts

This area was not reviewed in detail due to time constraints.

2.10. Reagents

The Russian language SOP entitled "Planning and organization of purchasing of laboratory equipment and material supplies for the testing centres", SOP EIC-OA-024, version 3, expiring on 15.04.2017, was reviewed. Each laboratory had a responsible person to check the inventory. The reagents were usually ordered from Merck and Sigma, or according to the catalogue numbers which are indicated in the dossier by the companies.

The Russian language SOP entitled "Receipt, inventory and storage of reagents and materials in the center", No. EIC-OA-026 was reviewed. It stated that upon receipt, the delivery documents and certificate of analysis or other certificates, were checked. A warning was given that if certificates of analysis were not available, the reagents could not be accepted. There were different rules regarding what have to be verified for local vs. international manufacturers. For locally sourced products, month and year of production, the shelf life and storage conditions were specified, if the shelf life was less than 6 months, the date, month and year of production were specified. For the reagents made outside of Russia, the reagents must have the name of the manufacturer, the name of the product, the expiry date or retest date, the quality of the reagent, like HPLC, GC quality or otherwise, when the analysis was done, number of the batch or lot number and the storage/transportation conditions. The expiry date should be verified (not more than 60% of the shelf-life should have been elapsed). If there was no expiry date, or range, it cannot be used in the laboratory. When the materials were stored in cupboards, they were registered/added to the inventory. When reagent bottles were opened, the nature of the reagent was taken into consideration and the expiry date was set to 3 years after opening the bottle for stable and dry reagents, but not more than half of the expiry date given by the manufacturer. For liquids and non-stable solids, a shelf life of 1 year or no more than half of the expiry date given by the manufacturer was set from date of opening. If there was no manufacturer information on the expiry date or shelf-life, the laboratory requests an expert to determine stability/shelf-life of the reagent. The inventory was maintained both electronically and in the laboratory.

The Russian language SOP entitled "Preparation of media" was reviewed. It stated that the pH meter had to be calibrated before starting the work, as well as the analytical balances. The media batch number had to be assigned. The Russian pharmacopoeia or manufacturer's instructions were followed. The pH was checked before and after. There was a separate SOP for media sterilization.

The Russian language SOP entitled "Sterilization of Media" was reviewed. There were 11 chemical indicators used for every run.

When a batch of media was received, the quality was verified by doing growth promotion test.

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2.11. Reference substances and reference materials

The Russian language SOP entitled "Handling of reference standards", valid until 27. 09. 2016 was reviewed. It stated that on receipt the integrity of packaging and expiry date were verified. There were 2 types of reference standards. For pharmacopoeial reference standards, validity was verified on the internet and manufacturer's working or reference standards, on the certificate of analysis. Mostly pharmacopoeial reference standards were used.

The Russian language procedure entitled "Procedure of drug sample acceptance for conduction of drug quality evaluation in pursuance of tasks set by the Ministry of Health of the Russian Federation", valid until 02.08. 2016, was reviewed. They get reference standard substances only with specific work orders. The amount of reference standards is usually only sufficient for the task performed. They do not use previously opened standard.

The reference standards, once opened, were stored in their own separate refrigerator for opened standards. As noted during the initial WHO inspection, all reference and impurity standards required for analysis were supplied by either applicants or manufacturers. Each reference material was supplied with its certificate of analysis. On receipt, reference materials were stored at appropriate storage conditions until required by analysts.

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

The calibration programme was the same as during the last WHO inspection.

The Russian language SOP entitled "Level III" qualification of liquid chromatographs, was reviewed.

A register of qualification and calibration was reviewed for 2014. It was provided in a tabular format and included all equipment at the laboratory. The example of Agilent 1100 VWD, RID, pump number DE43619243, equipment number X10/OA028, was reviewed. It was done using an inbuilt test with "pass" or "fail" for wavelength accuracy and for intensity of the detector light source that was done by in-house staff. Further testing was performed by a service engineer and by the state metrological center (annually). The state metrological center provided a certificate for the data. The certificates were kept in the dossiers of each piece of equipment and were supported by the detailed data with calculations.

The qualification documentation from Agilent for 1100 VWD RID was reviewed. It was also performed once a year. It did not contain any information about audit trails.

For gas chromatography, the Russian language SOP entitled "Qualification of gas chromatographs", was reviewed. It specified all of the necessary qualification requirements. This was done in house, but the state metrological testing still had to be done annually.

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Labels indicating equipment qualification and calibration status were affixed to all equipment and instruments.

For dissolution, the Russian language SOP entitled "Qualification of the instrument used for dissolution testing", valid until 08.04.2016 was reviewed. It specified shaft verticality tests, eccentricity, vessel verticality, basket positioning, and temperature testing was carried out twice per year. This was done by the laboratory metrology department. Chemical testing was done twice per year by laboratory employees using prednisolone testing. Degassing was now done using a Distek equipment or through heating and stirring, or filtration through a 0.45 micron filter. The prednisolone test results done on 27 August 2015, for the 30 minute time-point, were shown and were considered satisfactory and in line with USP requirements. Mechanical calibration records from 25.August 2015 were reviewed for the equipment located in the Laboratory of chemico-pharmaceutical preparations № 2 (OA code) and included all of the necessary records.

2.13. Traceability

Test results were traceable to analyst, analytical instruments, equipment, reagents, reference substances and test procedures. This was generally acceptable.

2.14. Incoming samples

As noted during the previous WHO inspection, records were kept for all incoming samples as per standard operating procedures of the laboratories. There was a central registry recording registration and distribution of the samples. Records of incoming samples were properly kept by logging them in a register. A sample laboratory sheet with tests to be performed and limits was generated for each sample at the time of logging. Samples were inspected on receipt and appropriately stored until testing started.

2.15. Analytical worksheet

As noted during the previous WHO inspection, analysts recorded tests performed, raw data, calculations and results in laboratory notebooks. Calculations were randomly checked by supervisors. Sufficient details were recorded in books to establish traceability.

2.16. Validation of analytical procedures

The Russian language SOP on method transfer entitled "Method translation", was reviewed. It specified that only system suitability testing was performed for pharmacopoeial methods for active pharmaceutical ingredients. For related substances tested in active pharmaceutical ingredients, if a method was used for related substances which were not listed in the monograph, then transfer was required. For finished products, system suitability, repeatability, precision and accuracy had to be done for assay. System suitability, repeatability and sensitivity had to be done for related substances tested in finished products. If a manufacturer's method was used, method transfer consisted of system suitability, repeatability and accuracy for assay. System suitability, repeatability and sensitivity was done for related substances. An example was reviewed and included verification of peak asymmetry, column effectiveness, peak area precision (% RSD for 6 injections – 10.0% limit for peak area in the example that was seen, with reference to the

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manufacturer limits), retention time, separation, accuracy of the preparation of the standard solutions using 2 standard preparations. The laboratory stated that they injected sample as part of method verification but that was not stated in any procedure.

Manufacturers usually submitted method validation along with the dossiers which was reviewed by the laboratory. When discrepancies were noted with the manufacturer's results, an investigation was done by the laboratory on the root cause. Sometimes, the method specified chromatographic conditions which were discrepant with those of validation. The manufacturer was usually informed of any discrepancy in test results and a decision was taken based on the response. In most of the cases, when a laboratory informs a manufacturer of difficulties in method transfer, the issue will be resolved through the provision of supplementary method transfer data.

2.17. Testing

Methods received with incoming dossiers from the Ministry of Health were scanned. When the task from the Ministry of Health arrives, an expert commission has access to the database. The testing center counts the number of samples necessary and transmits the information to the Applicant. The analyst got the full documents. The sample, the reference standard and the documents accompanying the sample and the reference standard come at the same time. Storage and transportation conditions from the manufacturer to the center were described in the documents accompanying the samples. The samples were then shifted to the laboratory. Any expert or analyst, who had access to the specific product samples and dossiers, got the scanned documents. The specification and test procedure were accessed electronically. In the archive room, only documents from 2015 were kept. Documents from 2014 were kept in another archive. Documents were kept for up to 2 years – after 2 years, they were kept by an external archiving company for an undetermined period (permanently kept).

Audit trails were checked in a HPLC system located in the Antibiotics Laboratory on the second day. It was equipped with Chemstation a, b and c versions. The c version was consulted and the audit trail function was unavailable (the laboratory could not enable it since it had not been activated by the supplier).

Azithromycin 500 mg film coated tablets batch number 131013-MC, sample identification number 0615/AH/15, was selected as an example from the sample receipt logbook of the Antibiotics Laboratory and the full analytical report and protocol (certificate of analysis) was reviewed by inspectors. The analyst logbooks were consulted. The balance logbooks were also shown (in the Antibiotics Laboratory, there was no balance print-out.) The balance logbooks included the weight, batch number, date, time, name, who did it. Traceability to all of the logbooks and to the raw data was very good.

Microbiology:
Special equipment was used for environmental monitoring and the media used was purchased already made.

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A sterility test report for rifampicin was reviewed as an example. Tests were done with media with and without product using bacillus subtilis, clostridium sporogenes, pseudomonas aeruginosa, staph aureus, candida albicans, aspergillus brasiliensis, and bacillus subtilis. The number of passages was documented. Results were recorded.

The Russian language SOP entitled "Environmental monitoring" was reviewed. It stated that an AirportMD8 was used. They also used 2 different types of BACTair^{TM} test kits containing Sabouraud Agar and TSA media. The sterility testing area was grade A and the surrounding area confirms to grade B. The number of sampling points depended on the room space - if it was less than 15 m^2, monitoring was done in only 1 spot; all rooms in the microbiology area of the Laboratory of antibiotics are less than 15 m^2. Monitoring was performed before and during the work. The operator's gloves were also sampled by swabbing or through the use of contact plates. Contact plates and swabs were used. They do swabbing for 24-30 cm^2. When growth was found, morphological identification was performed on site. Genetic identification, if needed, was done through another contract laboratory to which the samples got sent.

The Russian language SOP entitled "Procedure of performing sterility testing of antibiotics using membrane filtration and recording of results" was reviewed. The membrane had to be rinsed using isotonic 0.9 % sodium chloride. The incubation was 14 days (20-25)^{o}C or (30-35)^{o}C in accordance with USP pharmacopoeial requirements. If no growth was found, it was considered sterile. The test could only be repeated if in the negative control there was growth, if there was growth during environmental monitoring, and if they can prove that this is due to the mistake or fault of the operator, or closure of the system/test.

If the repeated test was acceptable, it was accepted, but if there was growth a second time, it was declared non sterile.

The Russian language SOP entitled "Growth promotion test of digest media", was reviewed. The SOP stated that the growth promotion test was performed for each batch of media.

Media storage period was following Russian pharmacopoeia requirements. If was usually used quickly, but always checked for sterility and growth promotion. The media preparation logbook was reviewed. Adequate detail was recorded.

Growth promotion records were reviewed as examples for the microbial enumeration and sterility test.

In the microbiology area of the antibiotics laboratory refrigerator at 2-8^{o}C, prepared media was seen to have shelf life of 3 months (media No. 1, 3, 8, 9 were seen to be labelled with a 3 month shelf-life). This was verified to be consistent with the Russian Pharmacopoeia and in any case, the growth promotion test was always performed in parallel. Also, one of the dry media bottles did not have a label which is inconsistent with the SOP instructions of labelling upon receipt. The number of test tubes was recorded

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when subdividing a sub-culture. Not more than 3 sub-cultures were performed. Disks were assumed to be at the 2nd passage level. They think that from the test strain, the lyophilization and it was put on the disk, counts for 2 passages. The maximum that they could use were 5 passages from the master strains.

Autoclaves were equipped with thermocouples. Temperature and pressure was printed out during sterilization cycles. First vacuum test for each media sterilization cycle was validated?. These were shown to inspectors along with the printouts. The sterilizer was tested once every 3 months using a Bowie Dick. The last sterilization of media was carried out on 16 September. The sterilization cycle was exactly 15 minutes. The number 00745 was linked to the media, which ensured data traceability. How many loads were validated was unclear. There was no validation to cover different potential load patterns. The biggest amount of media was sterilized in one load. The smallest volume was 300 mL. When performing validation, did you have thermocouples inside while verifying penetration and distribution. They put the probes inside the sample. This was stated to be in the Russian language SOP. Only a chemical color changing test was used inside the flasks. At least, for the validation, was not done, empty, minimum and maximum load. See observations under “Part 5”.

2.18. Evaluation of test results

The Russian language SOP was reviewed. It stated that evaluation of 3 replicates was performed using % RSD – with limits specified depending on the number of retests (maximum of 6 specified).

The register was maintained on Excel spreadsheets for 2013, 2014 and 2015. Examples of OOSs from 2015 were selected for review.

The Russian language SOP entitled “Control over the tests non-compliant with the established requirements”, was reviewed. It contained a flow chart describing the process to be followed. It stated that if no root-cause was found, the results were evaluated by another analyst, or by another laboratory. Reference was made to the Russian language SOP entitled “Test result evaluation” valid until 17.04.2017.

The example of an OOS dating from 18.02.2015, obtained by the Laboratory of chemico-pharmaceutical preparations № 2 was reviewed for dosage uniformity, related substances and assay being out of specification. After investigating the OOS and determining their possible root causes, the confirmation of OOS was performed by the Laboratory of antibiotics.

Another OOS was reviewed as an example. It was obtained on 20.02.2015. It was due to a mismatch of the retention time for the related substances, which were found to be the same as those of the placebo. The problem was with the standard test method which did not give good reproducibility. The tests were therefore not repeated and the quality assurance department noted that the analyst had not written down the number of the column that was used, but this was not considered to be related to the issues with the method.

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A third example was reviewed. Impurity E was higher than requirements for amlodipine and valsartan tablets. It was validated as being due to a product quality defect. The test was repeated by the same analyst and the result was confirmed. The test was also repeated further to this in another laboratory which also obtained an out of specification result.

If there was a discrepancy in test results obtained for the first retest (based on results of a single retest), but no root cause identified the sample was sent to another laboratory.

The Russian language SOP entitled "Test results evaluation", was reviewed. It stated that analytical results were first checked by the group lead, who checks the analytical worksheets, formulas and calculations, followed by the head of the laboratory, who only performs an overall check. There was a leading expert who will receive the sample and do the main tests and then there was a supporting expert who would do another test like Karl Fisher titration or other test. It was the expert's responsibility to transfer the data to the computer to print out the report (called protocol) of the analysis. The report (or protocol) was signed by the expert who was responsible for the analyses and by the head of the laboratory.

2.19. Certificate of analysis

This area was generally acceptable.

2.20. Retained samples

Retained samples were appropriately stored. The samples were kept until the end of their expiry date. Considering the purpose of testing, this was considered satisfactory.

2.21. Safety

Laboratory personnel wear appropriately attired with protective clothing while working in the laboratory and safety instructions were followed. However, no emergency water shower was available in the Chemical laboratory. The main stock of flammable liquids and organic solvents were kept outside of the laboratory in a separate building.

New chemicals, when received, were stored in the MSDS sheet registry.

Before analysts started their analyses, they were required to read the MSDS sheets associated to the reagents that they had to use. A general safety procedure had to be read and this fact documented by each analyst. The laboratory did not verify whether analysts actually read the MSDS sheets.

The Russian language SOP entitled "Management of the liquid chemical waste", was reviewed. The name of the waste and where it should be stored was included. For instance, acetonitrile and organic solvents had to be placed in polyethylene canisters of not more than 2.5 L. Hexane had to be placed in non-transparent glass bottles. Acetic acid had to be placed in glass bottles (used for Karl Fisher). There was a detailed list and table of chemical reagents with precautions to be taken.

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Part 3: Conclusion

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, as well as the corrective actions taken the Testing Centre for Evaluation of Medicinal Products Quality of the Federal State Budgetary Institution "Scientific Centre for Expert Evaluation of Medicinal Products" of The Ministry of Health of The Russian Federation, located at Schukinskaya street, 6, **was considered to be operating at an acceptable level of compliance** with WHO Good Practices for Pharmaceutical Quality Control Laboratories.

All the non-compliances observed during the inspection that were listed in the full report 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.