World Health Organization

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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
(WHO PIR)
of the Quality Control laboratory

Part 1	**General information**
Laboratory Details	
Name of the laboratory	SGS Lab Simon
Address of inspected laboratory	Vieux Chemin du Poète 10 B-1301 Wavre Belgium
GPS Coordinates	Latitude: 50.7070 Longitude: 4.5898
Address of corporate office, telephone number and fax number	Same as above
Dates of inspection	17-20 September 2019
Type of inspection	Routine
Introduction	
Brief description of testing activities	

Type of analysis	*Finished products*	*Active pharmaceutical ingredients*
Physico – Chemical analysis	pH, density, refractive index, optical rotation, viscosity, water content, conductivity, residual solvents, limit tests, tablet hardness, friability, disintegration, dissolution, uniformity of dosage units (mass, content), particular contamination (visible and sub-visible particles)	pH, refractometry, refractive index, optical rotation, viscosity, melting point, distilling range, loss on drying, water content, osmolarity, conductivity, heavy metals, residual solvents, limit tests, acid value, iodine value, peroxide value, ester value,

			hydroxyl value, saponification value
	Identification	HPLC (UV-Vis, PDA, RI, conductivity detection), GC-FID, TLC, UV-VIS spectrophotometry, IR, basic tests	HPLC (UV-Vis, PDA, RI, conductivity, fluorescence detection), GC-FID, MS), TLC, UV-VIS spectrophotometry, IR, basic tests
	Assay, impurities and related substances	HPLC (UV-Vis, PDA, RI, conductivity detection), GC-FID, UV-Vis spectrophotometry, AAS, FTIR, volumetric titrations	HPLC (UV-Vis, PDA, RI, conductivity detection), GC-FID, UV-Vis spectrophotometry, AAS, FTIR, volumetric titrations
	Biological tests	Sterility test, microbial limit tests, bacterial endotoxins test (LAL), microbial assay of antibiotics	Sterility test, microbial limit tests, bacterial endotoxins test (LAL), microbial assay of antibiotics
	Storage of Samples for Stability Studies	ICH conditions (long term and accelerated conditions) Ongoing Stability Studies)	Not applicable
General information	SGS Lab Simon is a QC-testing laboratory. This lab is not involved in activities of production, importation or distribution of medicinal products. The laboratory performs physical, chemical and microbiological testing of pharmaceutical products (raw materials and finished products) and medical devices according to the applicable pharmacopoeial monographs, or according to specific client test methods. The laboratory also carries out bacteriological monitoring for the pharmaceutical industry, such as microbial enumeration tests and identification of germs on settle plates and contact plates, microbial enumeration and identification of germs in water, growth promotion tests, sterility testing of culture media and testing of biological indicators.		
History	The laboratory was inspected by the Belgian Authorities for GMP: FAGG/AFMPS during Sep 2016, by Belac for ISO17025 during Feb 2019, by FDA during Sep 2017 and by Thailand GPO during Apr 2016. The site was previously inspected by WHO on 13-15 Oct 2010.		

Brief report of inspection activities undertaken – Scope and limitations	
Areas inspected	– Organization and management – Quality Management System – Data processing – Premises – Physico-Chemical and Microbiological laboratories – Evaluation of test results, including investigation of OOS – Personnel, including training and safety – Documentation and Records – Equipment – Calibration / Qualification – Performance check – Validation and verification of the methods – Traceability and records – Sample and material management, including water qualification – Suppliers and contractors
Restrictions	N/A
Out of Scope	N/A
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
GC	Gas chromatography or Gas chromatography equipment
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
QSHE	Quality, Security, Hygiene and Environment
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 findings and recommendations**

1. Organization and management

SGS is a Global company with over 95000 employees and about 2000 offices worldwide. A detailed presentation was provided; explaining the activities of the organization.

The laboratory was operating as SGS LAB SIMON. The organization and the management structure of the laboratory; responsibility, authority and interrelationship of the personnel were defined in the organizational chart. The organizational chart, dated Sep 2019 was associated with the respective SOP. The total number of staff was 139 at the time of inspection.

The site comprised of the following departments:

- Analytical Chemistry
- Microbiology
- R&D / Stability Studies
- Biopharmaceutical Testing

The laboratory had arrangements to ensure that its management and personnel were not subjected to commercial, political, financial and other pressures or conflicts of interest that may adversely affect the quality of their work. The laboratory had a policy in place to ensure the confidentiality of information contained in marketing authorizations and test reports. Confidentiality agreements, i.e. “Convention de secret” were randomly selected to be reviewed. They were found acceptable.

The Certification of accreditation from BELAC and issued on 7 Jun 2019 was available and valid until 21 May 2024.

2. Quality management system

Quality manuals defining the quality management system was available.

Two different Quality Manuals were available:

- A Global Quality Manual which defined the global policy of the company worldwide. The document was approved on 29 Mar 2019. This quality manual contained:
    - Annual management review
    - Performance evaluation of customers' perception of the company and the degree to which their needs and expectations were met
    - Survey to customers
    - Key performances indicators (KPI)
- Quality Manual "Benelux" (Belgium, Netherlands, Norway) was approved on 02 Jan 2017. The document contained:
    - Issuance statement
    - Policy statement
    - Organization of SGS
    - Description of the quality assurance system
    - Description of the document management
    - Internal review of the QHSE assurance system
    - Complaints management
    - Improvements
    - Safety, working conditions and environment
    - Global description of the processes
    - Personnel affairs
    - Security
    - SGS and its environment

The site's SOPs were electronically managed and monitored in accordance with SOP for Document control through a software system called "Master Control". SOPs were revised every 3 years and if a revision was not necessary, a new date for next revision would be assigned to the document. The SOPs were electronically organized and approved as described in the applicable procedure.

SOPs were available to the entire staff through the Master Control system. Hard copies of SOPs related to maintenance and technical equipment were provided, when applicable. Distribution and withdrawal of hard copies were managed by Master Control system.

The laboratory participated in proficiency testing schemes. The policy for participation in proficiency testing was described in the respective documents. The testing was organized in three control lines:
- First line control: Implementation of testing methods and verification of reference standards by analyst
- Second line control: Test was carried out under supervision of the QSHE coordinator and the Quality Manager.
- Third line control: Comparative study between laboratories

The results were recorded in an Excel spreadsheet and an Improvement Form would be issued in case of non-compliance. Randomly selected Improvement Forms were selected and reviewed.

Internal audits:
The activities of the laboratory were systematically and periodically audited internally in accordance with SOP for Audits.

The scope of the audit was determined by specific requirements, such as contracts, procedures or methods. Internal audits were carried out by the QA auditors in accordance with the established schedule or according to the arrangements agreed with the Manager or the concerned project leader.

There were three types of internal audits:
- System Audits
- Study audits
- Technical audits

Supplier -selection and evaluation:
The service providers were selected from an internal database of qualified suppliers.

The qualification of suppliers was assessed based on:
- the existence of a quality assurance system recognized by a certification body
- answers to an evaluation questionnaire
- where applicable, the result of a supplier quality audit

Management reviews (MR):
MRs were arranged in accordance with SOP for Management review.

The MR report, performed on 4 Apr 2019 and the respective records were available. The topics were properly predefined, and the statistics were provided, generally followed by a conclusion and actions proposed to be taken.

Change control:
Change Control requests were managed in accordance with the respective SOP. A change control Responsible Person was assigned by the Management, who proposed an action plan and obtained the approval of the change control committee before implementation of the respective proposal. The customer might be involved depending on the nature of the change. The recent change control SOP was effective since 12 Mar 2019.

Change control log was displayed as an Excel sheet which could not be considered as a validated e-system. However, a new software system, i.e. Track Wise system was designed to be implemented by the end of October through which the change control requests were also managed.

Handling of deviations and CAPA
CAPAs were raised through different processes, i.e. internal and external audits, deviations, OOS, complaints etc. They were recorded in an electronic system and assigned to the appropriate person to be handled.

Complaints:

Complaints were handled in accordance with SOP for Traitement des plaintes (complaints handling).

The Excel register of complaints was reviewed, as well as the documentation of the randomly selected examples.

The deficiencies identified on the Quality Management System were adequately addressed in the provided CAPA.

3. Control of documentation

The laboratory had established and maintained an electronic system, i.e. Master Control software system to control all documents (preparation, revision, distribution, return, archiving); Refer to section 2 of this report for more details. Each controlled document had a unique identifier, version number, date of implementation and reference to the previous version. The master list of SOPs was arranged by the Master Control software system.

The access rights to the Master Control software system was defined as:
- Administrator
- Analyst
- Data reviewer
- Laboratory supervisor
- Supplier

At the time of inspection, the access rights were granted to 75 authorized members of staff.

The deficiency identified on the Controlled documentation was adequately addressed.

4. Records

Record were made of analytical tests, including calculation and derived data, method validations/ verifications, instrument use, calibrations and maintenance and sample receipt in log books containing consecutively numbered pages.

Besides the electronic data generated by the analytical instruments; the laboratory work was recorded by the technicians through paper supports, i.e. laboratory notebooks, annexes of procedures and laboratory templates. Customer instructions for testing were implemented into the LIMS system with the method specification as described in the respective SOP.

The records were complete and signed, alterations were commented, and references were made to appendices containing the relevant recordings, e.g. chromatograms and spectra. The specifications used were consistent with the information currently held in the dossier.

Records were archived in the archive facility for a period of 10 years. The retention samples were kept for a period of shelf-life plus one year. Access to the archive was restricted to authorized personnel.

The archiving procedure was explained in accordance with the applicable written procedure. The retrieval of documentation was recorded and supervised in an electronic system; i.e. Doc Tracy, operating through a barcode. A reminder was generated to control the return of the documentation in a timely manner.

Pest control was also performed throughout the whole laboratory. A pest control-visit was carried out every two months, and if any pests were found, another additional inspection would be requested. The contract with the company for pest control was reviewed. The last visit was performed on 3 Sep 2019.

5. Data processing equipment

An inventory of all computerized systems, as a validation master plan, with all required information was available.

Records on hardware configuration, installation and changes (incl. software updates) were kept for computerized systems which were components of test equipment. Electronic data was protected from unauthorized access and cyber-attack by installing the appropriate program.

Physical access to servers, system documentation, wiring closets and back-up media were controlled and access to the electronic data was restricted through individual passwords.

Backups were performed on each working day, alternately on two different archiving servers. These were located on 2 different sites. The restoration of data was properly performed based on a request form. The last evidence of annual restoration of data was reviewed.

Computer systems were validated in accordance with GAMP5, 21 CFR part 11, GLP monograph 116, EU-GMP annex 11.

Qualification tests, including IQ, OQ and PQ tests were performed according to the corresponding protocols, based on the provided URS and the results were described in the respective reports. A final summary report was written. Based on this report, the computerized system was released by the Quality Assurance Department. During validation of computerized systems, the frequency, roles and responsibilities were established based on a documented and justified risk assessment.

Validation documentation of Empower chromatographic software system for chromatography, including the access rights, privileges granted to each category and the respective SOP was thoroughly presented. The URS was authorized by the QA on 12 Jul 2013. The chromatographic software systems were connected to the acquisition station which was under supervision of IT-personnel, only.

Spreadsheets (e.g. Excel®) were created based on requests with all required information and managed through the change control system. The request was considered as URS which should be authorized by QA. All cells including calculations were locked so that formulas could not be accidentally overwritten. Free access was only given to cells to be filled in with data. Calculation algorithms were tested with another validated software or by a pocket calculator. A known dataset was used for the verification of the software. The sheets were stored in a folder which was sealed by a pass-name. The pass-name was created as a formula which would be changed as soon as the spread sheet was removed and replace by a revised version. The creation of the Excel spreadsheets was managed in accordance with SOP for Spreadsheet validation work instruction, and the respective annex A01 for Excel sheet validation request.

The deficiency identified on the Computerized systems was adequately addressed.

6. Personnel

The laboratory had sufficient personnel with the necessary education, training, technical knowledge and experiences for their assigned functions. CV and Job Descriptions of randomly selected staff was reviewed and commented. CVs needed to be regularly updated to record all the training areas that employees received in the workplace.

Each new employee was informed of his tasks and responsibilities in a job description to be signed by the holder. The new employee received an introduction training concerning the organization of the company and its main procedures. The basic technical training of the new employee was defined and assigned by the concerned manager. An ability test was performed by the analyst and the obtained results were evaluated based on pre-established acceptance criteria. The laboratory also maintained the records of all technical personnel, describing their qualifications, training and experience. Laboratory tests were performed only by trained personnel who had performed the ability tests successfully. An annual GMP-training was delivered to all people involved with GMP.

Staff were trained on new and revised SOPs. Personnel were trained in accordance with the respective SOPs. Monthly meetings were also arranged to discuss the technical issues, SOP updates, CAPAs etc.

The deficiency identified on the Personnel was adequately addressed.

7. Premises

The activities of SGS Lab Simon S.A. were distributed in buildings A, B, C and D. Detailed lay-out of the premises were given in the Appendix 02 in LIF. Access to the laboratory facilities was restricted to designated personnel. The laboratory facilities were generally of suitable size and design to suit the functions and to perform the operations to be conducted in them. Separate storage facilities were maintained for the secure storage of samples, retained samples, reagents, laboratory accessories and reference substances, if necessary under refrigeration (2-8°C) and frozen (-20°C). The temperature of these rooms was monitored and controlled. Inflammable Reagents were kept in A345-Flammable storage cabinets, designed in accordance with specifications set for the Fire Protection Association.

The facility for sterility testing purposes was managed in accordance with SOP for Qualification of the sterile laboratory. The intermediate report of maintenance and qualification of the Microbiological facility by service provider CMI – Cleanroom Management International was reviewed. The qualification was performed twice a year, recently in June 2019. All the requirements and acceptable range were defined in the respective SOP. The location of the air-sampling and plates for viable particles was determined based on a risk assessment.

A weekly monitoring of viable particles in areas classified as A, B and C was performed for viable particles according to the applicable requirements. The environmental monitoring plan was defined in the respective SOP.

SOP for cleaning of sterility room and the respective logbooks, together with SOP for Monitoring of the microbio-contamination of air, surfaces and working stations in the incubation room of the sterility suite were reviewed.

The qualification report of the pass-box located between the grade B and C was available.

The deficiency identified on the Premises was adequately addressed.

8. Equipment, instrument and other devices

A list of equipment was provided. Equipment, instruments and other devices used for the performance of tests, calibrations, validations and verifications were randomly selected and inspected to verify whether they met the applicable requirements. The required test equipment and instruments for the performance of laboratory activities, including preparation of samples and the processing of and analysis of test and/or calibration of data were available. Calibration certificates provided by external providers were properly reviewed and certified.

The usage of the equipment was not recorded in a bound and paginated logbook, but only documented in the analytical worksheets. After the completion of the test, the worksheets were paginated, signed, stamped and scanned in the LIMS system. The equipment was traceable through their ID numbers.

Volumetric glassware was provided only as Class A. Glassware was calibrated every three years based on a 11-years risk assessment study in accordance with the respective SOP.

The following equipment and/or related qualification documentation were reviewed to verify the adequacy of their calibration/validation certificates:

- Temperature mapping of the refrigerator. The mapping was done in accordance with the applicable SOP.
- Incubator. The SOP for Qualification of incubators was revised to be in accordance with the applicable requirements. In the new version, the incubator should also be qualified when the equipment was fully loaded. The stability of temperature, uniformity of temperature distribution and time required to achieve equilibrium conditions were properly tested and recorded in the respective certification issued by the service provider. The uncertainty of measurement was calculated.
- Evisense digital thermometer for continuous monitoring of the temperature in all required storage facilities.

- Autoclave. The qualification was performed in accordance with SOP for Utilisation, maintenance and qualification of autoclaves for decontamination. The thermal indicators; EZtest Vapeur from MesaLabs were also used and documented on the respective template. The indicators were properly attached to the template. The thermal indicators' CoA was available, with proper expiry date.
- HPLC instrument.
- Weight 20g, certified on 2 Mar 2017 by Economie service provider, including the uncertainty of measurement.
- Weight, used for calibration of the selected Balance.
- Dissolution apparatus
- Disintegration apparatus, including the thermometer used for measuring of the temperature of the water bath. The periodic performance qualification was carried out in accordance with the applicable SOP.
- UV-vis, including the incorporated software system. The calibration was performed in accordance with the manufacturer's specifications.
- UV lamp
- Analyseur d'air M Air T
- GC
- TLC (Thin Layer Chromatography) equipment
- Friability tester
- pH-meter, with magnetic agitator
- AAS (Atomic Absorption Spectrophotometer)
- IR system Spectrum 100 FT-IR. It was verified that the associated audit trail was permanently activated.
- Randomly selected stability chambers
- Water purification ELIX system from MILLIPORE and the respective SOP for production of purified water and SOP for maintenance of the equipment.

The deficiencies identified on the equipment, instruments and devices were adequately addressed.

9. Contracts

The selection and purchasing of services and supplies was centrally managed by Benelux in accordance with SOP for Purchasing; effective 7 Jul 2019. Nevertheless, the subcontractors were managed locally by the laboratory management.

The laboratory had subcontracted number of testing to companies/organizations listed in Annex 4 of LIF which was updated on 21 Jun 2019.

Randomly selected agreements/certification of system management were reviewed.

10. Reagents

The reagents used were of appropriate quality and correctly labelled. Labels of reagent contained: content, manufacturer, date received and date of opening of the container, concentration, if applicable, storage conditions, expiry date and retest date, as justified. The writing and approval of purchase orders were made via the applicable software system, available on the computer network.

Reagents, solvents and reference substances were ordered by the Supply Management team. Supply Management used a computer system designed to manage and trace the standards-reagents in the warehouse. This system was also used to select and segregate the products that would expire during the next following month and to order products that were below the minimum stock. The Material Safety Data Sheets were entered in the system and printed out when the analysts came to collect the necessary products for the analyses that had been assigned to them.

The expiry date was assigned to each container after it was opened based on a risk assessment performed in 2013, including stability study.

Media were purchased as "Ready to use". Growth promotion and sterility of the media were tested at each arrival.

Reagent solutions prepared in the laboratory were labelled by name of the reagent, date of preparations and initials of technician or analyst, expiry date or retest date, as justified, concentration, if applicable.

Volumetric solutions prepared in the laboratory were also properly labelled.

The quality of water was regularly verified to ensure that the various grades of water met the appropriate specifications as per the European Pharmacopoeia monographs and the respective SOPs.

Columns were labelled with a unique ID number. They were handled and used in accordance with SOP for utilization of column. The columns were not verified upon their receipt. However, they should meet the method requirements during the system suitability verification. The SOP was reviewed and confirmed. The number of theoretical plate were recorded until 30 % of the column capacity before it was discarded.

The detergent used for dishwasher for glassware was specified in SOP for utilization, maintenance of the dishwasher for glassware.

The deficiencies identified on the equipment, instruments and devices were adequately addressed.

11. Reference substances and reference materials

a. Reference substances and reference materials

Reference substances were initially tested, released, stored and periodically monitored according to the required provisions in the respective SOP. They were stored and used in a manner that did not adversely affect their quality. All information about the reference standards was available in the corresponding analytical worksheets. A register of all reference substances was available through the same database which was also used for the reagents. In case the results of the retesting were non-compliant, a retrospective check of tests performed using the reference substance since its previous examination was carried out.

b. Reference cultures

Reference cultures were used for establishing the acceptable performance of media, for validating methods, for verifying the suitability of test methods and for assessing and/or evaluation of ongoing performance. The biological reference materials were commercially sourced, clearly labelled and stored appropriately.

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

Each instrument was uniquely identified. Labels indicated the status of the calibration and the date when recalibration was due. Generally, the equipment underwent IQ, OQ and PQ, following a plan established by the laboratory, when applicable.

Balances were checked daily using internal calibration and regularly using suitable test weights. Requalification was regularly performed using certified reference weights.

Records were kept for items of equipment with information to identify the device, current location, maintenance carried out, history of damage, malfunction, modification or repair.

13. Traceability

Test results were traceable, and where appropriate, references to the primary substances was available. All calibrations or qualification of instruments were traceable to certified reference materials.

The deficiency identified on the traceability was adequately addressed.

14. Incoming samples

SGS Lab Simon was not involved in collection of sampling. This task was the customer's responsibility.

As soon as the samples arrived at the laboratory, the "Sample Management" department proceeded to check the samples for integrity, packaging, labelling, conformity between the sample and the analysis request and then stored them according to the procedures.

If a problem was observed with a sample (broken container, leaking, illegible label information) or with the accompanying documents or the sample submission form, the "Sample Management" department would contact the customer immediately so that the latter sent new samples or completed/corrected the request.

The samples were registered in the LIMS (Laboratory Information Management System) by the Administration group. The Sample Management Officer entered the sample identification data and, based on the analysis request, encoded the tests to be performed. The LIMS assigned a unique identification code of the sample type with limited number of labels.

The "Sample Management" department identified the samples by a self-adhesive label issued in limited numbers by the LIMS and containing the SGS code of the sample ("SampleID"), the laboratory concerned, the name of the product, the batch number and the storage conditions of the sample. After the completion of the tests, the usage of sample identification labels was not reconciled.

The "Sample Management" department removed the number of units needed for retention samples to be kept in the sample library.

A test request, together with a copy of analytical method accompanied each sample submitted to the laboratory and contained the following information:
- description of the sample
- specification to be used for testing
- required storage conditions

The test requests were reviewed by the laboratory to ensure that the laboratory had the resources to meet them and that the selected tests/methods were capable to meet the customers' requirements. Once approved, the test appeared on the "Planification" list in the system.

Prior to testing, the samples were stored safely in a dedicated room, taking into account the storage conditions for the sample. The samples were sent for testing to the specific unit together with the test request by the responsible person.

The samples remaining after the completion of testing, were stored under the appropriate conditions for a period of one month after issue of the CoA (or 3 months in case of OOS). After this period, the samples were disposed as described in the respective SOP, unless otherwise instructed by the customer.

The deficiencies identified on the incoming samples were adequately addressed.

15. Analytical worksheet

A roadmap (called "Lab Sheet") was issued through LIMS, containing the order number (sequential number, also called "assignment ID"), the SGS identification code of the sample ("sample ID"), the name and customer reference, turn-around time, date of registration, name of the product to be tested and lot number, list of tests to be performed, reference of the test methods, specification limits for each test , the price of the test and information relating to the sending of the certificate of analysis / test report and / or raw data to the customer.

The analysts recorded information about samples, test procedures, calculations and results in analytical worksheets, which were completed by raw data. Analytical worksheets from different units related to the same sample were assembled together.

The worksheets contained the following information:

- the date on which the analysis was started and completed;
- reference to specifications and full description of the test methods, by which the sample were tested, including the limits; identification of test equipment used; reference substances, reagents and solvents employed;
- interpretation of the results and
- the conclusion whether the sample was found to comply with the specifications;
- any deviation from the prescribed procedures (which were approved and reported).

All values obtained from each test, including blank results, were immediately entered in the analytical worksheet and all graphical data, whether obtained from recording instruments or plotted by hand, were attached or were traceable to the electronic record file or document where the data was available.

The completed analytical worksheets were signed by the responsible analyst, quality controlled by data reviewer and verified, approved and signed by the supervisor.

For corrections the old information was deleted by putting a single line through it. Alterations were signed by the person making the corrections and the date for the changes was inserted.

The deficiency identified on the analytical worksheet was adequately addressed.

16. Validation of analytical procedures

The procedures employed for testing were suitable for the intended use, successfully demonstrated by either full validation, partial validation or transfer of method. Validation of analytical methods were managed by respective SOPs.

Method verification was required if an official analysis method (standard, compendium) was used exactly as described for the first time. Guidelines on the characteristics to be validated, depending on the type of test, were included in the applicable SOP. Method verification (except for microbiological methods) was handled in accordance with written procedure.

All verification, validations and transfer of methods performed by the laboratory were recorded in a list to be traceable for future use.

Appropriate system suitability tests were employed prior to the analytical tests for verification of pharamcopoeial methods and/or validated analytical procedures.

17. Testing

Test procedures were described in detail and allowed analysts to perform the analysis in a reliable manner. Deviations from the test procedures were approved and documented.

The endotoxin testing (BET) was performed in the Microbiology laboratory according to the SOP for Endotoxin testing by kinetic turbidimetry. The described method corresponded to the method C of the EP monograph (2.6.14) current edition. Practical examples of analytical records for endotoxin testing were reviewed.

Specific tests were carried out by another unit or by specialized external laboratory.

For More details, refer to section 18 of this report.

18. Evaluation of test results and OOS investigation

SOP for Handling procedure of OOS, OOE and OOT results, effective 30 Oct 2017 was in place describing the investigation of test results. When a doubtful result (suspected OOS result) was identified, a review of the procedures applied during the testing process was undertaken by the supervisor and the analyst.

Doubtful results were rejected only if an error could clearly be identified.

If the investigation was inconclusive, the SOP gave clear guidance on the number of retests allowed.

Once an error was identified, corrective and preventive measures were recorded and implemented. All individual results (all test data) with acceptance criterial was reported.

Analytical test reports were issued by the laboratory based on information recorded in analytical worksheets.

The test reports further included the following information:
- the background and the purpose of the testing;
- reference to the specifications and methods used;
- the results of all tests performed (or numerical result with the SD of all tests performed);
- the statement whether the sample complies with the requirements.

For the day to day management, there was an Excel sheet with the list of OOS results. Nevertheless, the OOS ID number was generated through the LIMS software system.

Randomly selected analytical reports, including chemist notebook, method validation / transfer of method OOS investigation, all related raw data and traceability of devices were reviewed and verified.

The deficiencies identified on the Evaluation of test results were adequately addressed.

19. Certificate of analysis

When reviewing the test files, the QP ensured that the work was carried out in accordance with the analysis request and the respective procedures.

The impact of deviations on the validity of test results was assessed by the QP who decided whether deviations needed to be considered in the interpretation of the reported results. Deviations were described in the « Evaluation/Comment » section of the certificate of analysis.

Certificates of analysis were released after being electronically signed by the QP in the LIMS.

A certificate of analysis was prepared for each sample/batch of a substance or product and contained series of information, among others:
- the results of the tests performed with the prescribed limits and
- a conclusion as to whether the sample was found to be within the limits of the specification.
- The date on which the tests were completed.

20. Retained samples

Samples were divided in three portions at the time of receipt of the samples. Retained samples were kept in boxes sealed and identified by unique identification number, managed by Sample Management team and stored immediately in the sample library of the company in their final pack, as required by the legislation. The boxes were stored in the archive facility segregated from paper documentation.

21. Safety

At the time of inspection, staff were observed wearing laboratory coats, appropriate footwear and, suitable eye protection. Special care was taken in handling highly potent, infectious or volatile substances. Highly toxic and/or genotoxic samples were handled in safety cabinets. Safety showers including eye wash statins were installed. Rubber suction bulbs were used on manual pipettes. Safety data sheets were available for all stored chemicals.

The deficiency identified on the Safety was adequately addressed.

Miscellaneous	
Assessment of the Laboratory Information File	The Laboratory Information File (LIF) provided introductory information of the organization. However, the LIF didn't cover all information required by the guidelines for Preparing a laboratory information file (WHO Technical Report Series, No. 961, 2011, Annex 13). According to this guideline, a LIF is a document prepared by the laboratory. It contains specific and factual information about the operations carried out at the named site and any closely integrated operations of the laboratory. If only some of the operations are carried out on the site, the LIF needs to describe only those operations, e.g. sampling, chemical analysis or stability testing. It is expected that the laboratory gives a short description of its activities under each of the identified headings. Policy or essential steps for each activity should be described and reference to a standard operating procedure (SOP) or other supporting documents should be given, where applicable. Where appropriate, supportive documentation should be appended. Nevertheless, all activities pertaining to physico-chemical and microbiological laboratories were described in the laboratory's Quality Management System.
Annexes attached	N/A

Part 3 – Conclusion – Outcome of inspection

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, ***SGS Lab Simon*** located at ***Vieux Chemin du Poete 10, B-1301 Wavre; Belgium*** 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 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.

Part 4	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/
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Short name: WHO GDRMP guidance or ***WHO TRS No. 996, Annex 5***
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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.
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