

Prequalification of Medicines Programme

WHO PUBLIC INSPECTION REPORT

(WHOPIR)

Quality Control Laboratory

The report is the property of the organization responsible for performing the inspection.

Part 1: General information about the inspection

Name of laboratory	TÜV SÜD PSB Singapore (Food and Pharmaceutical Testing Section)
Physical address	1 Science Park Drive, Singapore 118221
Postal address	As above
Telephone number	+6568851303
Fax number	+6567784301
Summary of all the activities performed by the manufacturer	The company was involved in: <ul style="list-style-type: none"> • Conventional chemical analysis • Instrumental analysis • Microbiological analysis • Biological testing • Stability testing • Pre-clinical trials
Scope of inspection	Prequalification inspection of QC laboratory.
Focus of inspection	<ul style="list-style-type: none"> • Quality system of the Quality Control Laboratory • Conventional chemical analysis • Spectrophotometric analysis (IR, UV) • Chromatographic methods (HPLC, GC) • Dissolution and Disintegration testing
Date of inspection	21 - 22 October, 2008 and 13 March, 2009
Programme	Prequalification Programme: Priority Essential Medicines.

Part 2: Summary

The TÜV SÜD PSB Singapore (Food and Pharmaceutical Testing Section)" at 1 Science Park Drive was inspected on 21st - 22nd October 2008 and 13 March 2009.

General information about the company and the site

TÜV SÜD PSB, headquartered in Singapore, provides services in product testing, certification, inspection and auditing. The company was previously known as the Singapore Productivity and Standard Board (PSB) and in April 2006, it was acquired by TÜV SÜD PSB Corporation Pte Ltd and further changed to its current name since April 2007.

The number of staff employed by TÜV SÜD PSB Singapore was more than 300 and total of more than 500 employees in the whole of ASEAN region. These ASEAN countries include Singapore, Indonesia, Malaysia, Philippines, Thailand and Vietnam.

TÜV SÜD PSB had more than 30 years experience in testing and certification. The company offers testing services in 3 major fields, these include chemicals and materials, electrical and electronics, and mechanical tests. The following listed the summary of the laboratory activities:

- 1) Chemical & Materials:
 - Food and pharmaceutical testing
 - Microbiological and DNA based testing
 - In vivo and in vitro testing
 - Micro-contamination analysis and surface analysis
 - Coatings evaluation and construction materials testing
 - Environmental monitoring and analysis
- 2) Electrical & Electronics:
 - Environmental and reliability tests
 - Electrical safety tests
 - Electromagnetic compatibility tests
- 3) Mechanical tests:
 - Building and industrial materials tests
 - Consumer product mechanical safety tests
 - Fire safety and security tests

The scope of these inspections covered the laboratory activities relating to the pharmaceutical product testing i.e. the pharmaceutical testing activities performed by the Food, Pharmaceutical & Biological Testing Section. The capabilities of TÜV SÜD PSB Singapore in pharmaceutical testing included chemical, microbiological and biological testing. Typically the type of Pharmaceutical products tested were Finished Pharmaceutical Products and APIs (Active Pharmaceutical Ingredients).



Table 1: The analysis performed by TÜV SÜD PSB Singapore on pharmaceutical products.

Type of Analysis	Finished products	Active pharmaceutical Ingredients
Physical / Chemical analysis	pH	pH
		Acid value
	Disintegration time	Iodine value
		Limit Tests
	Density	Apparent Volume
	Dissolution	Clarity & Colour of solutions
	Dimensions	Solubility
	Limit Tests	Acid neutralizing capacity
	Apparent Volume	Residue on Evaporation
	Color of solutions	Insoluble matter
	Uniformity of content	Heavy metals
	Uniformity of weight	Acidity/Alkalinity
	Minimum fill	Non volatile matter
Identification	FTIR	FTIR
	TLC	TLC
	HPLC	HPLC
	Spectrophotometry	Spectrophotometry
	Basic tests	Basic tests
Assay, impurities and related substances	HPLC(UV-VIS, PDA)	HPLC(UV-VIS, PDA)
	UV Spectrophotometry	UV Spectrophotometry
	FTIR	FTIR
	Volumetric Titrations	Volumetric Titrations
Type of Analysis	Finished products	Active Pharmaceutical Ingredients
Microbiological analysis	Microbial limit tests	Microbial limit tests
	Bacterial Endotoxins	Bacterial Endotoxins
	Sterility tests	Sterility tests
Method Validation	ICH Guidelines	ICH Guidelines



History of WHO or regulatory agencies inspections

The TÜV SÜD PSB Singapore was not previously inspected by the WHO.

Focus of the inspection

The inspection focused on the quality management system of the QC laboratory, and analytical activities. The areas of the Good Practices for National Control Laboratory guidelines covered in the inspection were as follow:

- Organization and personnel
- Quality management
- Premises and Equipment
- Documentation
- Sample flow and sample storage
- Reagents and reference substances
- Traceability
- Safety

Detailed summary of the inspection 21st - 22nd October 2008

Day 1 - AM	
OPENING MEETING – 8.30 AM	Introductions
	Objectives and scope of the inspection
	Confirmation of the proposed programme
	Recent changes
	Brief presentation of the laboratory
MANAGEMENT AND INFRASTRUCTURE	Quality system
	QM and quality policy
	Organization and management of the labs
	Documentation system
	Standard operating procedures
	Records including electronic
	Change control
	Customer contracts/agreements
	Complaints
	Out-sourcing of testing
<ul style="list-style-type: none"> • Supplier assessment • Contracts 	
Day 1 - PM	
MANAGEMENT AND INFRASTRUCTURE CONTINUED	Personnel <ul style="list-style-type: none"> • Organization chart • Job descriptions for key personnel • Training • Work allocation

	Self inspections
QC TESTING – GENERAL	Validation Master Plan
	Method validation
	Electronic systems
	Water system(s) <ul style="list-style-type: none"> • Validation • Operation • Specs and testing
DAY 2	
INSPECTION OF THE LAB	General working procedures
	Sample receipt
	Test methods and specifications
	Analytical records - raw data, workbooks
	Retained samples
	OOS result handling
	Preparation and control of reagents
	Control of reference materials/standards
	Handling of hazardous material
	Equipment <ul style="list-style-type: none"> • Environment • Operating procedures • Qualification • Calibration • Maintenance • Log books
	Glassware management
	Evaluation of test results
	Preparation and authorization of C of As
CLOSING MEETING	

Follow up inspection on 13 March, 2009 was focused on implementation on corrective actions.

2.1. ORGANIZATION AND MANAGEMENT

The organization of the TÜV SÜD PSB Singapore was defined in an organization chart. The laboratory had appropriate technical personnel with authorities to carry out their duties. The brief responsibilities of the personnel were defined in the Document Control Procedure.

The company had a central registry for incoming samples, reagents, chemicals etc, and the corresponding records were found to be in order.



The incoming samples were allocated to the designated technicians. The laboratory technicians filled in the necessary sample description in their laboratory samples log and form, and then assigned them with a unique In-house Identification Number (In-house ID) for the purpose of traceability.

The sample details that came together with the sample and form filled in by the laboratory staff formed a part of sample records. These sample records were passed to the company Sale staff and the Sale staff then checked various communication made with the customer i.e. customer requests by means of email, and created a Formal Quotation (FQ) in a database known as the End to End Test System (EETS). The print out of the FQ detailed the tests requirements and this printout also formed part of the sample records. This sample record was then passed back to the laboratory technicians for the necessary analysis.

Upon receiving the FQ together with other sample records, the laboratory technician generated the Job Number (JN) using the EETS. The generation of the JN number was either linked to the FQ number or In-house ID number (if the FQ number was not available).

The Job Number (JN) was the number found on the test reports and analytical raw data. There was no direct link between the JN to the In-house ID. The link between the JN to the In-house ID was made via the Formal Quotation Number (FQN) and the link between the FQN to the In-house ID was available via the EETS.

Test analysis carried out by the laboratory corresponded to the USP, BP and EP monographs and tests methods, as well as the customer in-house methods.

2.2 QUALITY SYSTEM

The quality management system of TÜV SÜD PSB Singapore was based on ISO 9001:2000 and ISO 17025 standard.

The quality manual and Quality assurance procedures were available during the time of inspection were available on the company intranet system. Work instructions were available on intranet as well as hard copies. The company's quality system was systematically reviewed by both internal and external audits

The change control system applied to equipment, methods, specifications, validations and calibration were available upon request. Any changes with respect to equipment, methods, specifications, validations and calibration were approved by the Technical Manager. The changes with respect to methods and specifications were implemented after customers' approval.

The company Customer Complaints procedure classified complaints as high and low risk complaints. All complaints were reviewed and if the company deemed it necessary, the corrective and preventive actions would be carried out.

2.3 CONTROL OF DOCUMENTATION

There were 7 levels of documents. The Quality Manual, testing procedures and testing laboratory procedures were available only on the company's intranet and staff were able to print out hard copies if required. The company mode of communication of any up-version of documents or new documents released on the company intranet was by e mails.

Other documents such as test methods and work sheets were available in hard copies and these documents were kept in the laboratory.

Other procedures such as generation, review and approval records and analytical reports, as well as procedures for the Issuance of Certificates of Analysis were also found available.

2.4 RECORDS

Training records, analytical reports and sample logs were reviewed during the inspection.

Analytical raw data were available upon request and all raw data were attached together with other sample records. All analytical raw data were available as in accordance to the tests required by the customers i.e. on the Formal Quotation Report. The analytical raw data identification was either by the customer number or job number which ever was shorter and such numbering or identification was not procedural..

2.5 DATA PROCESSING EQUIPMENT

The HPLC systems, GC, UV and Infrared equipment were linked to the computers operated by their respective software. Computer software programs were validated by the equipment suppliers. The samples numbering system - EETS - was validated by simulation.

2.6 PERSONNEL

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

All employees received induction training. Training for new employees such as laboratory technicians) were carried out by experienced staff through a "buddy system" and these training was carried out in accordance with a check lists system. Training for laboratory chemists was based on their qualifications and work experiences.



Training on the quality system was carried out quarterly.

Training records and training evaluation records were documented in an individual training records file. Effectiveness of the training was evaluated. It was noted that there were several ways for the evaluation of on-job training.

Current job descriptions were available, but documents were not signed, dated and approved.

2.7 PREMISES

The TÜV SÜD PSB Singapore premises were well maintained and clean. The laboratory was of suitable size and design and provided for adequate separation of activities. The laboratory had suitable testing equipment.

Samples, retained samples and reagents were stored in the cupboards located in the laboratories.

2.8 EQUIPMENT, INSTRUMENTS AND OTHER DEVICES

SOPs for equipment and instrument calibration, operation and preventive maintenance were not available. Calibration, preventive maintenance schedules and their corresponding records were also not available at the time of inspection. These observations were corrected by appropriate corrective actions.

2.9 SPECIFICATION ARCHIVE

Document master copies as well as obsolete document copies were kept in a documents archive.

2.10 REAGENTS

The preparation of reagents was performed according to Pharmacopeia methods. Liquid volumetric solutions were properly labeled. Volumetric solutions were standardized according to Pharmacopeia methods.

Certificates of analysis (CoA) for reagents and approved suppliers list were available upon request.

Reagents were stored in the cupboards located in the laboratories.

There was a check in place in ensuring the reagent used for the analysis was within the expiry date.

2.11 REFERENCE MATERIALS

Only Compendia (official) reference standards were used.

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

pH meters were calibrated before use however, balances were verified every day.

2.13 TRACEABILITY

Traceability to international standards was assured.

2.14 INCOMING SAMPLES

Incoming samples to the laboratory were checked and registered in the log book. A unique registration number was allocated to the samples.

2.15 ANALYTICAL WORKSHEET

Data generated and results obtained were compiled into analytical reports. The analytical report was written up, checked, signed and dated by the analyst, then checked and signed by the technical manager. Certificates of analysis were drawn up according to the specifications once the results had been authorized. The certificate was written, checked, signed and dated. The final approval for release of a result was granted by the technical manager.

2.16 TESTING

Values obtained from the tests were entered on the analytical worksheets and graphical data were attached.

2.17 EVALUATION OF TEST RESULTS

All test results and raw data were evaluated by the supervisor or the head of section. Analytical test reports were issued based on the analytical work sheets.

Calculation was carried out by means of an Excel program and spreadsheet.

2.18 RETAIN SAMPLES

Retain samples were kept for a predefined duration (3 month) in the cupboards located in the chemical laboratory.

2.19 SAFETY

Personnel at the TÜV SÜD PSB Singapore had to wear protective clothing during analysis. Staff who did not conduct analysis were not required to wear protective clothing. Safety instructions were followed. A water shower was provided.

Part 3: Conclusion

The QC laboratory **TÜV SÜD PSB Singapore (Food and Pharmaceutical Testing Section)**, 1 Science Park Drive, Singapore 118221, 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.