



**Prequalification Team
WHO PUBLIC INSPECTION REPORT
Vaccine Manufacturer**

Part 1: General information

Name of Manufacturer	LG Life Sciences Ltd (Osong Plant)
Unit number	NA
Production Block	Building 2 (1 st floor): Vial Line 1 Production Area and Packaging for Injection; Building 1 (3 rd floor): Quality control laboratories Building 1 (1 st floor): Warehousing
Physical address	Osong Campus, LG Life Sciences, Revision No. 151, Osongsaengmyeong1-ro, Osong-eup, Heungdeok-gu Cheongju-si, Chungcheongbuk-do, South Korea 363-951
Contact person and email address	Ms. Hyung-Shin (Helen) Kim: kimhs@lgls.com
Date of inspection	07 – 11 September 2015
Type of inspection	Initial GMP Inspection
Dosage forms(s) included in the inspection	Eupenta (DTP-HepB-Hib) liquid form pentavalent Vaccine Euvax (HepB) Vaccine Euforvac vaccine with Hib lyophilized component
Summary of the activities performed by the manufacturer	Warehousing, formulation, aseptic filling, quality control activities and distribution



PART 2: SUMMARY

General information about the company and site

LG Life Sciences was founded as the name of Lak Hui Chemical in 1947. It became LG chemical afterwards, from which LG Life Sciences Limited spin-off.

LG Life Sciences headquartered in Seoul, South Korea, including Business, Product Sales and Marketing Department while Research and Development Centre is located in Daejeon. There are three manufacturing sites: Onsan Plant, Iksan Plant and Osong Campus. Onsan Plant is for manufacturing intermediate agrochemical while Iksan Plant and Osong Campus are for manufacturing pharmaceutical products such as drugs, vaccines and human growth hormone.

Osong Campus has been under construction since 2010, in the area approximately 165,272m². Plant building for Oral Solid Line was built in 2010 and finished transferring the technology from Iksan Plant. The construction of vial line, pre-filled syringe line and human growth hormone bulk line is finished. All the lines are approved by Ministry of Food and Drug Safety (MFDS).

Major Changes in the Near Future

The company is planning to expand their manufacturing site for the following:

- Tech-transfer of D, T and wP bulks from BB-NCIPD LTD
- Tech-transfer from Intravacc
- Formulation (incorporation of IPV to Eupenta)

History of WHO and/or regulatory agency inspections

This is the initial WHO GMP inspection to the Osong site.

The MFDS carried out the following regulatory inspections:

- 1st GMP Approval for Oral Solid Dosage in 2010.
- Global Supply Practice Approval in 2011
- GMP Post-Approval Inspection in 2012
- Inspection for Injectable in 2013
- Inspection for Injectable & hGH API in 2015
- Inspection for Injectable in 2015

Focus of the inspection

The inspection focused on the production and control of Eupenta (DTP-HepB-Hib) Liquid form pentavalent Vaccine and Euvax (HepB) Vaccine as well as Hib lyophilized component for Euforvac vaccine. The inspection covered all the sections of the WHO GMP text, including premises, equipment, documentation, materials, validation, sanitation and hygiene, production, quality control and utilities.

Inspected Areas

- Quality Assurance
- Sanitization and hygiene
- Qualification and validation
- Complaints

- Recalls
- Self-inspection
- Personnel
- Training
- Personal hygiene
- Premises
- Equipment
- Materials
- Documentation
- Production
- Quality control

PART 3: INSPECTION OUTCOME

2.1 PHARMACEUTICAL QUALITY SYSTEM

Quality Assurance is in charge of controlling the quality management system of Osong Campus including sampling and control of retained samples, process and records review, GMP documentation control and issuing certificate of analysis, test results review and approval, validation review and approval, suppliers audit, complaints and recall, failed product management, change control, self-audit and annual product review.

Quality Risk Management:

Provisions for QRM were in place according to the implemented procedure.

Risk Management Quality System at Osong Campus in 2014 was presented. A risk review is in place, and unacceptable risk were reviewed for mitigation and further measures to consider mainly for SIP, CIP, mix up in packaging areas and EM for surface contact of operators.

Deviations and CAPA management:

Deviations were handled according to the implemented procedure. Deviations are categorized as major if considered as having an impact on the product quality directly/indirectly or a GMP system violation. Minor deviations have an indirect impact on the product or general violations such as simple errors that are easily correctable. The list of deviation since 2013 has been reviewed.

CAPA are handled according to Corrective and Preventive Action procedure.

Change control handling:

Change Controls (CC) were handled according to the implemented procedure. Changes are categorized as major, moderate and minor according to the impact to the product and need of approval from the authorities. The assessment of the change impact including the evaluation of the effectiveness of implemented changes is taken into account since the procedure revision effective 01/10/2014.

The list of change control initiated as from January 2014 was presented. Change controls were spot checked. Although provisions were implemented for change control management, the change control for the project Building 3 was not initiated. The change control regarding the scale up of Eupenta formulated bulk was not

initiated. The evaluation of the effectiveness of implemented changes was in place since 01/10/2014. However, for change control initiated according to the previous version of the change control procedures, ongoing activities related to change control process were not considered for effectiveness check of the implemented changes. The company has provided the remedial corrective and preventive actions adequately addressing the raised issues regarding the change control management.

Annual Product Quality Review:

The Procedures for the Annual Product Review was in place. The annual product review procedures for all products produced in Osong site have identified and the review of existing products reviewed annually from January to December of each year. The QA responsible for each product initiates the annual review. The approval for the review is happening before the mid of the following year. The QA manager is responsible for the approval.

Product Quality review of Eupenta injection vaccine has been provided as an example. The review was conducted for Eupenta for the year 2013 to 2014 to confirm the consistency of process and the compatibility of product control. The review includes the regulatory changes, change control during manufacturing process, specifications and deviations, validation and matters related to the utilities and facility.

2.2 GOOD MANUFACTURING PRACTICES FOR PHARMACEUTICAL PRODUCTS

Good manufacturing practices generally were implemented. Necessary resources were generally provided, including qualified and trained personnel, premises, equipment and services, appropriate materials, containers and labels, approved procedures and instructions, laboratories and equipment for in-process and other controls. Manufacturing steps were recorded in batch manufacturing and packaging records. Manufacturing processes were generally defined and reviewed. Qualification and validation were performed. Operators were trained to carry out procedures, and records were made during manufacture.

2.3 SANITATION AND HYGIENE

Manufacturing areas are provided with airlocks for personnel and materials entries and exits. Gowning procedures for access to the classified and self-contained manufacturing areas were in place. Programs for cleaning of manufacturing areas and equipment are in place.

Waste disposal procedures have been provided as per procedure. The procedure applies to the expired reagents and vaccine samples.

Cleaning and sanitisation procedures of incubators and biological cabinets have been provided.

The waste management procedures of solid and liquid materials have been issued on 02/09/2015 and 04/09/2015. These new established SOPs have not been circulated among the Osong site personnel of the Environment and Safety Department, QA and production plant personnel. Before establishing the above mentioned waste management procedures, the Manufacturer was following procedures issued by the Ministry of Korean Environment (Version I Environment, II Waste water, III waste

material). Additionally, the site follows the international standardisation ISO14001. Nevertheless, no internal SOPs were available. The company has provided the remedial corrective and preventive actions adequately addressing this issue.

2.4 QUALIFICATION AND VALIDATION

Osong Plant Validation Master Plan based on V-model including URS, Functional specification, DQ, Build, FAT, IQ, SAT, OQ and PQ. Required document for validation and qualification are defined. Policies for revalidation are in place in case of changes and for routine revalidation.

The procedure validation and control applies when there is introduction or change of manufacturing procedure, analytical method, facility or equipment. Water systems validations are performed considering DQ, IQ, OQ and PQ. PQ is performed in 3 phases I, II and III.

HVAC systems:

HVAC system validation was DQ, IQ, OQ and PQ. PQ was performed in phase I, II and III. Phase I conducted 3 times for all classified areas considering non-viable and viable particles at rest conditions. Phase II conducted 2 to 4 times considering viable and non-viable particles at rest conditions. After phase II, alert and action limits are established. Phase III was based on the monitoring. The qualification at “in operation” conditions of classified areas was not considered. Requalification and reclassification policies and frequency for HVAC and classified areas was implemented according to HVAC system control.

Cleaning validations:

Vial Line equipment system validation status was presented. CIP was performed for equipment in a loop and samples are taken from each tank individually. SIP was performed for equipment connected.

CIP qualification process for tanks and hard pipes in the preparation, formulation and filling rooms are qualified once a year as per SOP/policy. Qualification tests include conductivity, endotoxin, pH and bioburden tests.

Cleaning in place was performed before the production steps of a bulk while rinsing was performed immediately after production. Conductivity test was performed after each CIP and rinse. Purified water is used to flash pipes and tanks which it follows flashing with NaOH solution. Final rinsing is with PW and WFI as described in the procedures OP-IN-006. Samples collected from the final rinse with WFI are tested for conductivity, endotoxin, TOC and bioburden.

Incubation room:

Qualification of the incubation room for Media Fill was performed.

Lyophilizer:

Lyophilizer was undergoing CIP/SIP before each run. Nitrogen gas filter was tested after each lyophilizer run via WIT test with WFI as wetting agent. Lyophilizer was yearly qualified for CIP/SIP. The temperature mapping was initially performed in February 2013. The lyophilizer was equipped with around 62 probes. The cooling chemical agent in the ducts of the lyophilizer is polydimethylsiloxane.



Depyrogenation:

Depyrogenation tunnel was qualified every year. Integrity test and particles counting are performed every 6 months. The Depyrogenation tunnel was equipped for aerosol injection. 3ml, 5ml, 20ml - PQ report of Tunnel sterilizer was spot checked. 3 runs were performed for each vial size using 20000 vials for each. 8 thermocouples and 8 endotoxin spiking were considered for distribution of heat. The results were considered conform according to the established specifications by the company.

Sterile Filtration:

The sterile filtration validation was reviewed. Additional data were provided by the company after the inspection. The company has adequately addressed the raised issues regarding the sterile filtration validation.

Process validation:

Process validations include mixing and homogenisation of formulation for filling steps, integrity tests for liquid. Process validations for single dose vial and 10 doses vial have been reviewed. The equipment and process involved in the validation studies were the mixing, filtration, pressure and transfers. The studies involve the steps of preparations and filtration, final bulks and filling. Integrity tests of filters (bubble point) on the preparation solution were also performed on all bulks. All results during validations studies including QC tests are within the acceptance criteria.

Media simulation:

Media Fill Test (MFT) was performed with TSB 3% filtered in house. All aseptic processes are simulated including the presence of maximum number of operators. Media Fill test of Injection 1 Line (Aseptic processing validation) was reviewed. In routine 3mL, 5mL and 10mL vials used for MFT. Initially 3 runs were performed with 5mL.

A summary of the results of the MFT performed since 12 January 2012 to 29 June 2015 was presented by the company. All are claimed as pass.

Worst case scenario such as the maximum number of the aseptic operations during the MFT was not considered. In routine process, during aseptic formulation, up to 8 containers of WcP and Aluminium gel are transferred to the container in the formulation Box. The mixed solution was transferred afterward to the formulation tank. During the MFT only the transfer of 2 containers instead of 8 containers were considered. It has been highlighted that the environmental monitoring within the formulation box during aseptic processes was not considered by the company.

The maximum batch size of 200L which normally used in routine process for 10 doses of Eupenta vaccine was not considered during Media Fill Test in order to make sure that the whole contact surface of equipment was covered.

The company has provided adequate corrective and preventive action plan addressing these issues.



2.5 COMPLAINTS

Complaints are handled according to the implemented procedure applied to all drug substances and pharmaceutical products in LG Life Sciences Osong Campus. A designated person from QA is appointed for complaint handling. *Timeline for dealing with complaints was not considered adequate.* The company has adequately addressed this issue.

No vaccines complaints were recorded as there were no Eupenta and Euvax B vaccines supplied for UNICEF Agencies or PAHO.

2.6 PRODUCT RECALLS

Provisions for recall were in place as per the implemented procedure. The responsible for recall was corporate quality assurance (CQA). Designated responsible for product recall as well as complaint was available. The purpose of the SOP was to explain the steps required to follow in case of any complaints or detection of deviation in safety of products post marketing (locally and internationally). The road map of recall procedures was available for easy reference.

No recall incident for any vaccine produced by Osong site was recorded. However, one recall case on 2014 for oral solid tablet was reported. Customers complaint were received, investigation and recall of the product was initiated. The cause root of the deviation was identified and a CAPA was initiated. The LG responded within 1 day post complaint/report. The investigation revealed that there was an operator error due to not following the standard procedures. Appropriate CAPAs were applied.

The management of adverse event following immunisation AEFI (Pharmacovigilance plan) for domestic marketing has been developed for local registered vaccines. The telephone number of the Company was added in the carton label for any possible reporting of adverse event. A designated person to deal with any domestic adverse event has been identified to be within 24/7.

For international marketing of Eupenta another contract to deal with pharmacovigilance cases has been established as per LG life Sciences Pharmacovigilance Plan. The pharmacovigilance contract includes the contact details of LG officer and the response should be available within 3 days.

2.7 SELF INSPECTION AND QUALITY AUDIT

The internal audit was performed as outlined in Annual Audit Master Plan at least once a year for every department. Raised observations in audit are communicated to the responsible department for implementation and CAPA (Corrective Actions and Preventive Actions) are documented.

QA manager is responsible for establishing an annual self-inspection plan. The procedure has been established, internal audit check list provided and found to be satisfactory.

Supplier qualification:

Suppliers of raw materials, intermediates and finished product used in LG Life Sciences Osong Plant are qualified according to the implemented procedure: Evaluation and approval for manufacturers and suppliers. The supplier evaluation was

carried out by documentation review, sample test, supplier audit and quality evaluation of the supplier. Approved companies are registered in ERP system so that purchase order for material could be only from qualified/Certified suppliers.

Aluminium gel labels suppliers were added to ERP in the qualified list of suppliers *however, these were not qualified as per the qualification procedures of supplier*. Rubber stoppers material was not in the list of material from qualified supplier. Appropriate CAPAs adequately addressing the raised issues were provided.

The audit of supplier was performed as per the implemented procedure. Annual audit plan was in place. According to the criticality of the material and the history of the suppliers a plan for next audit is prepared. Supplier of level A are audited every 5 years, supplier of level B every 3 years, supplier of level C audited the following year and supplier of level D are disqualified. The audit vendor plan for most of the material was every 5 years based mainly on the history records of suppliers *but not taken into account the criticality of the material to the process*. Thiomerosal, Sodium Phosphate, 13 mm (white) aluminium caps and sterile filters were not included in the audit of vendor Plan. Appropriate CAPAs adequately addressing the raised issues were provided.

2.8 PERSONNEL

LG Life Sciences at Osong Campus was staffed by around 113. Quality Assurance (15), Quality Control (28), Production (35), Warehouse & Planning (6), Production & Development (22), Utility (3) and Safety & Environment (3).

Organizational chart showing the relationships between different areas including quality assurance, production and quality control, with identification by name and title of key personnel (Heads of Production, QA, QC, Warehousing, Engineering) was provided in the SMF and the presentation during the opening meeting.

Organisation management and job description procedure has been spot checked during the inspection.

2.9 TRAINING

Procedure for training program was in place. Schedule of training was based on the type of training program required for each area. List of training required for personnel by the department was provided in this procedure.

Proficiency certificate policy for operators was demonstrated as per procedure (Analyst training evaluation and qualification). The procedures include GMP training, QC training and on job training (OJT) program. The document was reviewed as satisfactory.

Training history of operators was spot checked and proficiency test for total polysaccharide assay used in the Eupenta vaccine accelerated test was reviewed. Certification for training on 6 times for this assay has been provided along with validation report of total polysaccharide tests that the operator performed.

Backup system for operators dealing directly with critical manufacturing process (formulation and filling) was in place. For QC tests at least 1 operator was trained and certified to perform assays.



2.10 PERSONAL HYGIENE

All employees are trained to practice good sanitation and health habits. Each of the production units was equipped with washing, changing and rest areas. Different working uniforms are provided to the employees depending on the classification of working areas. Smoking, eating, drinking and storage of food are prohibited and restricted to certain designated areas. According to the individual hygiene checklist, all personnel are monitored for clothing, health status and hygiene. The microbial contamination was checked regularly on the surface of clothes and hands of employees who work in critical area. The procedure regarding the control of Personal Hygiene document was spot checked.

2.11 PREMISES

The Manufacturing buildings involved in the production of Euvax B, Euforvac and Eupenta vaccines at Osong Plant are in general terms considered suitable to the operations to be carried out. The company has provided an acceptable Site Master File with relevant documentation regarding the manufacturing processes, buildings, utilities and maintenance plans.

Osong campus was built as two of three-story building:

- 1st floor of pharmaceutical plant is separated into the production office, oral solid line, vial line, pre-filled syringe line and warehouse. The storage for starting material and packaging material is located in the 1st floor.
- 2nd floor consists of human growth hormone bulk line, 100L antibody line and 2000L antibody line.
- 3rd floor for central office and the Quality Control laboratory.

The facility is provided with Purified Water, Water for Injection (WFI), Clean steam and HVAC systems for classified and unclassified environments. Utility building consists of purified water, compressed air, plant steam, chilled water, emergency power generation and waste water treatment system.

During the facility tour the following was observed:

Filling line is equipped with doors. Doors of filling line at the accumulation table of vials coming out from the depyrogenation tunnel and at the rubber stopper bowl side, open/swing into grade B areas.

Isokinetic probes for particles monitoring in the formulation room are long and having curves which could impact the particles counting.

Auto and Visual inspection

Rejected vaccine vials from auto inspection were collected in trays that were labelled with the same colour for pass vials. The available procedure identifies that “another colour” label should be used in the rejected trays. *The company has provided satisfactory corrective and preventive actions to eliminate the risk of mix ups.*

Storage room for finished product and raw material at 2 to 8 °C was routinely temperature monitored via 3 probes in 3 locations. The mapping has been performed as empty and at 70% pattern loads of the storage room.



2.12 EQUIPMENT

Product contact equipment (pipelines and tanks) are made of 316L stainless-steel. Silicone hoses are used for liquid transfer where transfer lines are not used.

Equipment and utensils employed in production of drug substance and drug products are subjected to applicable cleaning at regular intervals and, where appropriate, immediately before and/or after use according to implemented procedures.

Major production equipment includes filling machines, automatic washing and sterilization machine, autoclaves, hot air sterilizer, tanks, fermenters, and various chromatographic separation and purification columns. Equipment are periodically inspected in accordance with the maintenance master plan.

Preventive maintenance (PM) activities are performed and recorded, and corrective actions are taken as necessary according to the provisions in place.

2.13 MATERIALS

Provisions for incoming materials, intermediates and finished products are in place for reception, quarantine and release processes. Appropriate storage conditions are provided.

Starting materials and packaging materials are purchased from approved suppliers. For each delivery, the containers are checked for integrity of the package and seal and for consistency between the delivery note and supplier's labels. Incoming starting materials are stored in quarantine area with quarantine labels until tests are completed. Procedures for sampling with adequate equipment in suitable sampling rooms are in place. After approval of sample testing, starting and packaging materials are properly labelled with released labels and moved to the storage area.

Starting materials are weighed by warehouse personnel and cross-checked in weighing room of warehouse before use in production. The first in/first out (FIFO) principle was adopted for starting materials dispensing.

Rejected material storage area with locking system was available.

Management procedures of residuals of any bulk materials used in the formulation step has been identified in the SOP for Management of Raw Materials.

Procedures for non-conformance occurrence based on human visual inspection and/or OOS procedures conformed by QA have been provided. These procedures cover the handling and reporting, labelling and segregations of items in non-conformance area (warehouse).

Labels Management:

Printed packaging material should be destroyed and its disposal recorded. In the storage room for labels, returned labels were found in the storage labels room. The company has provided adequate corrective action to make sure that *printed packaging material is destroyed and its disposal recorded*.



2.14 DOCUMENTATION

In general, documents were designed, prepared, reviewed and distributed with care. Documents were approved, signed and dated by the appropriate responsible persons. Documents were regularly reviewed and kept up to date. Records were made or completed when any action was taken.

A documentation system was in place to guide production and control of products. These included Validation Master Plans (VMP); standard operating procedures (SOPs); Batch Manufacturing and Packaging Instructions and records (MIs, BMRs, BPRs); specifications of starting materials, packaging materials, packaging components and finished products; standard testing procedures, analytical records and certificates of analysis; qualification and validation protocols, schedules and reports; training schedules and records. There were corresponding records in form of reports, forms, checklists, logbooks, registers maintained as evidence of compliance with the procedures and specifications.

Document control procedures were in place.

Batch record review:

The manufacturing date was the date of issuing manufacturing instruction and not from the date of filling and the expiry date of monovalent bulk of DS used in the formulation process was considered.

Batch record was reviewed.

Summary protocol documentation was provided along with the Batch Record. Purified diphtheria toxoid DS received from bulk supplier. Internal check list document was used to confirm that the product produced/imported from the bulk supplier complies with the specifications.

Batch release specifications were compared with the Summary protocol documentation. The company has adequately addressed the issues raised for the batch record review.

2.15 GOOD PRACTICES IN PRODUCTION

The Diphtheria, Tetanus, and whole cell Pertussis bulk concentrate are manufactured by the bulk supplier. The HBsAg and the *Haemophilus influenzae* type b - tetanus toxoid are manufactured by LG Life Sciences in Iksan site. Formulation, filling, testing, packaging, and release of the vaccine are performed by LG Life Sciences in Osong Campus.



The Process flow chart for Eupenta Inj was provided.

The approximate number of vials and doses for each fill size and presentation:

- 1 dose (0.5 mL) presentation: approximately 300,000 vials per batch
- 10 dose (5.0 mL) presentation: approximately 30,000 vials per batch

10 doses vial presentation

Component	Material	Reference
Vial, 10 mL	Colorless, Borosilicate Type I glass	USP
20 mm Rubber stopper	Grey, chlorobutyl	EP
Aluminum seal 20 mm with polypropylene flip-off cap	Aluminum seal, flip-off cap	Pharmaceutical quality

1 dose vial presentation

Component	Material	Reference
Vial, 3 mL	Colorless, Borosilicate Type I glass	USP
13 mm Rubber stopper	Grey, chlorobutyl	EP
Aluminum seal 13 mm with polypropylene flip-off cap	Aluminum seal, flip-off cap	Pharmaceutical quality

The Process flow chart for Euvax B was provided:

1 dose presentation is filled in 3 mL vials, 10 doses in 5 mL vials for paediatric and in 20mL vials for adult.

Critical aseptic operations for formulation (including weighing of wP and transfer of wP to a container as well as the transfer of Aluminium gel to the container covered with aluminium foil and then transfer via peristaltic pump to the formulation tank transfer) took place in a box supplied by HEPA filtered air of grade A from the ceiling of the formulation room. The company has adequately addressed the raised issues regarding the aseptic operations.

2.16 GOOD PRACTICES IN QUALITY CONTROL

Quality control department is in charge of Testing and reporting of test results on raw materials, intermediate product, final product, validation of test methods, establishment of specifications and test methods, environmental monitoring and water monitoring, stability test and the management of laboratory equipment and instruments and the management of standards and reagents.

Quality Control department consists of five working groups including Chemical, Instrumental, Biological, Microbiological analysis and Animal laboratory.

Procedures for controlling and managing of raw materials and procedures for test and management of samples were spot checked.

Provision for Out Of Specification:

OOS procedure was in place. The procedure identifies the steps for investigation on the event of OOS test results occurs in the Osong site. A follow up steps including CAPA if requested has been identified.

OOS report related to Eupenta accelerated stability samples was spot checked. The OOS of test result was about the lower level of total polysaccharide in Eupenta FC

vaccine for two batch numbers at 6 month time point at 25°C. The test was performed as part of stability study and maximum shelf life at 25°C has been concluded to be up to 3 month.

Method validations summary reports for identification tests of Hib antigen and quantitation method for total free PRP in Eupenta vaccine using Bio-LC was spot checked. Three lots of Eupenta finished product for validation were used also 3 analyst were participated and assay characteristic were performed as per ICHQ2.

Method validations summary report for Hep B antigen in vitro potency measurement by ELISA test and quantitation method for total PRP in Eupenta vaccine using Bio-LC was spot checked.

Stability of Eupenta vaccine development-1 lots of 1D and 10D. Stability data for up to 36 months have been provided for both presentations 1D and 10D.

Stability of Eupenta vaccine development-2 lots of 1D and 10D. Stability data for up to 12 months for 1D and 18 months for 10D have been provided.

Stability of Eupenta vaccine commercial lots of 1D and 10D. Stability data were presented for up to 6 months for 1D and 12 months for 10D.

Environmental Monitoring:

Trends for entire clean room area of final product manufacturing department in the second quarter 2015 has been claimed as acceptable by the company. However, the microbial specifications for grade B were not in line with the GMP specifications. The company has provided corrective and preventive action plan adequately addressing the raised issue.

The water monitoring test results has been reviewed and found within acceptable limits.

2.17 DISTRIBUTION AND SHIPMENT

Shipping validation of HepB bulk from Iksan to Osong has been reviewed. Three bulks were used for validation study. Eleven bottles of twenty litres were used on each study. Four TempTale data loggers were used in different positions inside the truck. The truck was already validated with 24 different positions of data loggers. QC tests were performed before and after transport. Results have been reviewed and deemed satisfactory.

Shipping validation report for Eupenta vaccine has been reviewed and found acceptable. The study indicates that 10 dose vials of 10 vials per box with a total of 140 boxes were packed within two Styrofoam boxes. Two sets of CPM and Ice packs were used to support the study. These ice packs are being stored in 2 to 8°C before packing. Two sets of temperatures were used in the study as per WHO recommendation, - 5°C and + 40°C. The validations study found to be satisfactory.

The validation process of the international shipment, packing and transportation have been reviewed and found satisfactory.

Domestic shipment has been reviewed and deemed to be acceptable.



PART 4: CONCLUSION

Based on the areas inspected, the personnel met and the documents reviewed, and considering the findings of the inspection, including the deficiencies listed in the Inspection Report, as well as the Corrective Actions taken and planned, LG Life Sciences Ltd (Osong Campus) was considered to be operating at an acceptable level for compliance with WHO GMP guidelines.

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

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