World Health Organization

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Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
of the Vaccine manufacturer

Part 1	**General information**
Manufacturers details	
Company information	
Name of manufacturer	Sinovac Biotech Co., Ltd.
Address of manufacturer	• No. 39, Shangdi Xi Road, Haidian District, Beijing 100085, P.R.China (Vaccine Bulk Workshop) • No. 15, Zhitong Road, Zhongguancun, Changping, Beijing (Formulation, Filling & Packaging workshop)
Contact person	Dr Weining Meng mengwn@sinovac.com
Inspected site	
Address of inspected manufacturing site if different from that given above	Global positioning system (GPS) coordinates in World Geodetic System (WGS) 84: Northern latitude: 40°03'38", East longitude: 116°30'50"
Inspection details	
Dates of inspection	22-26 May 2017
Type of inspection	Initial inspection
Representative from the National Regulatory Authority	The national regulatory authority (NRA) of the country was informed and took part in the inspection.
Introduction	
Brief summary of the manufacturing activities	Sinovac was found in 2001, is specialized in the vaccine manufacturing. Currently, Sinovac has four commercial vaccines (Hepatitis A vaccine, Hepatitis A and Hepatitis B vaccine, Influenza vaccine and Enteroviral EV71 vaccine) launched into market and two pandemic flu vaccine stockpiled by China government. Hepatitis A vaccine, Healive was launched into the market in 2002. Sinovac has an additional site located in Dalian for live attenuated vaccine.
General information about the company and site	Sinovac Biotech Co., Ltd. has two manufacturing sites: Shangdi and Changping. The Shangdi site is located at No. 39, Shangdi West Road, Haidian, Beijing and covers an area of about 2.2 hectare, 15.9 km from downtown. The surroundings of the Shangdi site are Dongbeiwang Road, Shangdi Xi Road and Sinovac Research & Development Co., Ltd. The Changping site is located at No. 15, Zhitong Road, Zhongguancun, Changping, Beijing and covers an area of about 2.93 hectare, 34.7 km from downtown. The surroundings of Changping site are Elekta (Beijing) Medical Device Co., Ltd, Zhongxin Guoan Mengguli New energy Techonology Co., Ltd, Beijing Sanjiu

	Pharmaceutical Co., Ltd, Beijing Huijia Vocational College, Beijing Radio Factory, Sanhuan Wakehua (Beijing) Magnetic Device Co., Ltd.
History	This is the initial WHO inspection. The previous inspections are presented below:

Date	National Authority	Result
2016.05.27-2016.05.29	Center for Food and Drug Inspection of China Food and Drug Administration	GMP routine inspection for Hepatitis A and B combined vaccine and influenza vaccine (split virion) passed.
2015.3.17-2015.3.18	Ministry of Health of the Republic of Kazakhstan	Inspection for inactivated hepatitis A vaccine and influenza vaccine (split virion) passed.
2014.10.30-2014.10.31	Beijing Food and Drug Administration	GMP routine inspection for inactivated hepatitis A vaccine, Influenza vaccine (split virion) and Hepatitis A and B vaccine passed.
2014.9.3-2014.9.5	Beijing Food and Drug Administration	GMP routine inspection for vaccine storage and distribution passed.
2014.8.26-2014.8.29 2014.9.1-2014.9.4	Ministry of Health of Turkey	GMP routine inspection for inactivated hepatitis A vaccine passed.
2014.2.24-2014.2.27	China Food and Drug Administration	GMP routine inspection for Influenza vaccine (split virion) passed.
2013.8.12-2013.8.16	COFEPRIS, Mexico	GMP certificate of inactivated hepatitis A vaccine and influenza vaccine (split virion) was approved, certificate No.: 14300CT110172 and 14300CT110173.
2012.12.23-2012.12.27	China Food and Drug Administration	Site inspection of 2010 GMP for inactivated hepatitis A vaccine bulk passed, certificate No.: CN20130107.
2011.3.16-2011.3.18	China Food and Drug Administration	GMP routine inspection for inactivated hepatitis A vaccine passed.

The major Changes in last 2 years regarding the Hepatitis A bulk product workshop comprises:

- Segregation and separation of inactivation area from virus area;
- Change of the gowning room of virus area to be unidirectional;
- Ensure segregation and passage through pass-box between cell area and virus area.

One recall has been recorded in the last five year regarding hepatitis A vaccine in syringe due to wrong printed information on the package box.

Brief report of inspection activities undertaken	
Scope and limitations	
Areas inspected	The Shangdi site: Buildings A1 and A2. The Changping site: Buildings B1 and B2.
Restrictions	NA
Out of scope	The inspection was limited to Hepatitis A manufacturing in the above mentioned Buildings.
WHO vaccine covered by the inspection	HEALIVE (hepatitis A Vaccine)

Abbreviations

AHU	air handling unit
ALCOA	attributable, legible, contemporaneous, original and accurate
ADS	active drug substance
APQR	annual product quality review
BMR	batch manufacturing record
BPR	batch packaging record
CAPA	corrective actions and preventive actions
CC	change control
CFU	colony-forming unit
CoA	certificate of analysis
DQ	design qualification
EM	environmental monitoring
FAT	factory acceptance test
FMEA	failure modes and effects analysis
FTA	fault tree analysis
FTIR	Fourier transform infrared spectrometer
GMP	good manufacturing practice
HACCP	hazard analysis and critical control points
HPLC	high-performance liquid chromatograph
HVAC	heating, ventilation and air conditioning
IR	infrared spectrophotometer
IQ	installation qualification
KF	Karl Fisher
LAF	laminar air flow
LIMS	laboratory information management system
LoD	limit of detection
LOD	loss on drying
MB	Microbiology
MBL	microbiology laboratory
MF	master formulae
MR	management review
NMR	nuclear magnetic resonance spectroscopy
NRA	national regulatory agency
OQ	operational qualification
PHA	*process hazard analysis*
PM	preventive maintenance
PpK	process performance index
PQ	performance qualification
PQR	product quality review
PQS	pharmaceutical quality system
QA	quality assurance
QC	quality control
QCL	quality control laboratory
QMS	quality management system

QRM	quality risk management
RA	risk assessment
RCA	root cause analysis
SOP	standard operating procedure
TAMC	total aerobic microbial count
TFC	total fungi count
TLC	thin layer chromatography
URS	user requirements specifications
UV	ultraviolet-visible spectrophotometer

Part 2: Brief summary of the findings and comments

1. Pharmaceutical quality system (PQS)

There generally appeared to be adequate resources available for the management of the PQS. Senior management demonstrated support to the system. Quality assurance and quality control activities were functioning with appropriate independence from the production unit.

Product quality review (PQR)

Provisions for PQR were in place. The period review is determined on the basis of production campaign. Annual PQR report of the bulk of inactivated Hepatitis A vaccine (Human diploid cell), 2015 QA0716019 that was approved in January 2017 after the change of adding dynamic environmental monitoring results and stability data was spot checked. The PQR for finished product made in 2016 (January to September) was also spot checked.

Quality risk management

Provisions for QRM were in place. QRM methods and tools in Sinovac consist of brainstorming method, FMEA and HACCP, etc…Quality Risk Management covers the lifecycle including organization, personnel, premises, facilities, equipment, materials, products, qualification & validation, documentation management, production management, quality control, quality assurance, product distribution, recall and self-inspection. An example reviewed for risk management related to the preparation of solutions for formulation. It covered a range of items of potential risk using FMEA tool.

Deviation management

Provision for deviations management was in place. The procedure "Deviation management" and its flow chart were discussed. The procedure was applicable to unplanned and planned deviations. Deviations were classified based on the impact to the quality of the product:

- Minor – no impact on product quality
- Major – potential impact on product quality
- Critical – may have severe impact on product quality safety and efficacy.

Deviations were classified by QA manager. According to the procedure unplanned deviations should be closed in 28 calendar days.

Deviation register for 2017 (all departments) was presented to the inspector. Deviations register for Hepatitis A vaccine for both bulk and formulation and filling manufacturing sites (2015 – 2017) was presented to the inspector.

Change control (CC) management

The change controls were managed as per the implemented procedures. The procedure "Change control management" and its flow chart were discussed. The procedure was applicable for GMP related changes. All changes should be approved by the qualified person. CC registers were maintained by QA.

Changes were classified according to assessed risk as:

- Minor (type I)
- Major (type II) –authorities should be informed
- Critical (type III) - approval from authorities before implementation should be received

Closing time was specified for individual CC. In case timing was not followed CC procedure was initiated to postpone closing.

CC register for 2017 was presented to the inspector. CCs register for Hepatitis A vaccine for both bulk and formulation and filling manufacturing sites (2015 – 2017) was presented to the inspector.

Management review

The procedure "Production and quality meetings" was discussed. According to the procedure, production and quality meetings should be held monthly and quarterly. The following, but not limited, items were covered:

- Follow-up action's from previous reviews
- Changes to the production planning
- Change controls
- Deviations
- Corrective actions and preventive actions (CAPAs)
- Out of specifications (OOS)
- Utilities
- Materials
- Validation/qualification
- Documentation
- Training
- Complaints/recall
- Self-inspection/external audits

Last quarterly meeting was held on 19 April 2017. Meeting minutes were briefly discussed and found to be comprehensive.

Corrective actions and preventive action / root cause analysis (RCA)

The procedure "CAPA management" and its flow chart were discussed. According to the procedure, CAPAs were applicable to the:

- Complaints
- Product defects
- Recall
- Deviations
- OOS
- Self-inspections/ external audits
- Process performance
- PQ
- CC

The tools used for RCA were not specified in writing. It was said that mainly Ishikawa diagram was used. Written procedure on how to use Ishikawa diagram was not available, however when RCA was discussed it was noted that tool was used appropriately.

Batch release process

Qualified person is responsible for the issue of batch release taking into consideration the official Batch Release Certificate by CFDA.

2. Good manufacturing practices for pharmaceutical products

Resources were available, including qualified and trained personnel, premises, equipment and services, materials, containers and labels, procedures and instructions, laboratories and equipment for in-process and other controls. Qualification and validation of equipment, manufacturing processes and quality control testing methods were in place. Manufacturing processes were defined and reviewed. Qualifications and validations were performed. Deviations were recorded and investigated, root causes were determined and CAPAs were implemented. Systems were in place for handling complaints and recalling any batch of product from sale or supply.

3. Sanitation and hygiene

The premises were generally maintained at an acceptable level of cleanliness. The company had provisions for personal hygiene and sanitation in its production facility. Manufacturing areas are provided with airlocks for personnel and materials entries and exits. Gowning procedures for access to the classified manufacturing areas were in place. Cleaning, disinfecting and decontaminating procedures along with the environmental monitoring program were in place to control the non-viable and viable contamination levels in the production areas. During the inspection the gowning procedures appeared to be complied with no dress code violations noted. The level of sanitation and hygiene for premises and manufacturing equipment are considered acceptable.

4. Qualification and validation

Provisions for qualification and validation were in place and covers premises, equipment, utilities and systems, processes and procedures at periodic intervals and when changes have been made. VMP were established annually and the report on the completion was reviewed on monthly basis. Validation and qualification protocols and reports were spot checked as presented below.

The following validation and qualification reports were spot checked:

- Inactivation,
- Validation report of the sterile filtration,
- Extractibles, leachables and integrity of disposable bags used for the storage of Hepatitis A inactivated bulk, Hepatitis A formulated bulk and PBS,
- Media simulation test,
- Cleaning validation,
- Qualification of the filling volume of the vials (0.5 mL and 1 mL in 2 mL vials),
- Clean room qualification,
- Depyrogenation tunnel qualification,
- Autoclave qualification.

5. Complaints

The procedure “Complaints management” and its flow chart were discussed. Complaints were classified regarding product quality:

- Critical
- Major
- Minor

Complaints trends presented and organized by products and complaints categories, for example: packaging, production … etc.

Hepatitis A related complaints from 2015 – 2017 were spot checked. All complaints were classified as minor.

AEFIs:

To date, with only limited supply to external countries, the company experience with AEFI reporting and review has been with Chinese supply. Under the Chinese system, reports of AEFIs, to a large extent, are through CDC, which has already conducted some analysis of whether they consider an AEFI to be vaccine related. If so, this is indicated in the notification to the company but details of their investigation are not included in the notification. For grade 1 and 2 AEFIs feedback from government agencies ADR (national), CDC (provincial) will occur in real time. For grade 3 AEFIs, CDC provides yearly feedback to manufacturer.

The SOP for AEFI management includes provisions for reporting to government authorities ADR (national), CDC (provincial) any AEFIs directly reported to the company. The vigilance group (for all company products) is two pharmaceutical scientists. There is a company committee on safety of medicines which reviews grade 1 and 2 AEFIs. The SOP describes both regular and emergency meeting procedure. The committee includes expertise from: non-clinical, epidemiology, process research and statistics. In the event of a reported grade 1 or 2 AEFI, the procedure describes the associated quality investigation procedure. To date, it was indicated that there had been no serious AEFI that had been associated with a quality defect in the vaccine.

Under Chinese law, after a product have been registered for 5 years, the interval for preparation and submission of Periodic Safety Update Reports (PSURs) changes to five yearly.

There is limited international supply of Healive. The procedure in place describes management of AEFI reports from these countries. The quality agreements since 2015 with the distributor in recipient country have included a clause for AEFI reporting. However, to date, only letters indicating that there have been no adverse events have been received. The SOP describes reporting (with timeframes) on any such received notifications to relevant Chinese authorities.

6. Product recalls

The procedure "Product recall" was discussed. Recalls were classified as per CFDA guidelines:

- Class I - recall should be initiated within 24 hours
- Class II – recall should be initiated within 48 hours
- Class III – recall should be initiated within 72 hours

SOP stated that if there was no real recall, mock recall should be performed every year.
There was only one Class III recall recorded. This recall was initiated on February 11, 2014 for Hepatitis A vaccine, filled in syringes. Reason for the recall was wrong marketing authorization number printed on package.

7. Contract production, analysis and other activities

No contract manufacturing activities are reported by Sinovac Biotech Co., Ltd.

The contract analysis activities are limited to the testing of MSB (Identity and Virus Titre) and WSB (Identity, Virus Titre, exogenous factor (animal test), Bacteria and Fungus test, Mycoplasma test, mycobacteria, other exogenous factor with cell cultivation method.) of Hepatitis A virus by the national institute for food and drug control (NIFDC).

8. Self-inspection, quality audits and suppliers' audits and approval

The procedure "Audit" and its flow chart were discussed. Inspection was carried out by a nominated self-inspection team, conflict of interest was avoided. Self-Inspection was performed once per year. Self-inspection schedule for 2017 was presented to the inspector. Inspection was carried out using check lists. Inspection report was written by the Self-inspection administrator in QA department. CAPAs were addressed by the inspected department and implementation checked by department QA specialist.

The procedure "Materials suppliers selection and qualification" was discussed with regards to primary packaging materials manufacturers. According to the procedure, manufacturers of primary packaging materials on-site audits should be carried out at least every three years. Currently there was only one approved manufacturer of vials and rubber stoppers. It was noted that CC procedure to add another supplier of vials and stoppers was initiated. The last audit of the manufacturer of the vials was carried out in September 2016 by audit team consisting of 5 auditors during two days. The last audit of the manufacturer of rubber stoppers was carried out in May 2015 by audit team consisting of 3 auditors during two days.

The list of manufacturers supplying biological raw materials and adjuvants was spot checked.
The onsite audit of the supplier of the material was considered only in the case if the supplier is the manufacture and the distributor.
On site audit for new-born calf serum an onsite audit is scheduled every three years.
There were no on-site audits for the suppliers of the critical material including trypsin, lactalbumin hydrolase, sodium deoxycholate suppliers.

The supplier of the plastic bags used in the formulation was audited on 19 March 2014 by representatives from the production and QA from the company. No representatives from the quality control were involved in this audit. The audit was not addressing the details regarding the critical aspects of the plastic bags including the different involved parties in the manufacturing of the bags, the tubing, the connectors, the assemblies, the sterilisation, the quality control test methods and results.

The suppliers of the plastic bags used for the storage of the formulated bulks were not audited.

At the reception of the plastic bags used in critical processes of the manufacturing of Hepatitis A vaccines, the company relies only on a certificate of quality provided from the suppliers. There was no data or certificate of analysis provided for received plastic bags. In addition, at reception the control is limited to visual check of the external cartons/wrapping of the plastic bags. The control of the disposable bags was not considered acceptable.

9. Personnel

Organizational charts showing the relationships between different departments, including QA, Production, QC, Warehouse and Engineering with identification of the key personnel are provided. Curricula vitae and the job responsibilities for key personnel, with qualification, experience and responsibility are provided. Measures were in place to prevent unauthorized people from entering production, storage and QC areas.

10. Training

Provisions for personnel training and evaluation of its effectiveness were in place.

The procedure "Visual inspector's qualification procedure" was discussed. Newly recruited visual inspectors had to pass written theoretical exam and practical exam. Visual inspector's re-qualification by written exam (open questions and questions with pre-given answers) was carried out twice per year and practical exam once per year. According to the procedure, inspectors were given 1000 vials/syringes, with acceptance

criteria NMT 0.4% fail. It was allowed to repeat test 3 times on different days. Visual inspectors eye sight checks were performed every 6 month by ophthalmologist.

Training/qualification records of experienced visual inspector and newly recruited were discussed.

The procedures "Qualification of QC analysts" and "Training and qualification template" were discussed. To be qualified for GC tests, analyst had to perform three analysis of the same sample, acceptance criteria were STP requirements.

12. Premises and equipment

Overall, exposed surfaces were smooth, impervious and unbroken. Changing rooms were designed as airlocks and used to provide physical separation of the different stages of changing. Premises were cleaned and disinfected according to written procedures. The layouts and drawings of the manufacturing areas including the classification, differential pressure, flows of personnel, materials, products and waste, air handling units and water systems were provided in the site master file and presented during the briefing meeting. Rest and refreshment rooms were separate from manufacturing and control areas. The warehouse has two independent areas for storage of starting materials, consumables and hazardous chemicals. The warehouse has storage areas for refrigerated products. The principle FEFO (First expires first out) are taken into consideration to deliver material to production. Storage areas were of sufficient capacity. Sufficient space was given to avoid mix ups and cross-contamination. Storage space was provided for samples, reference standards, reagents and records.

The production of Hepatitis A Vaccine (Human Diploid Cell) inactivated is divided into dedicated manufacturing facility and utilities of bulk in the "production workshop of Bulk of HAV" in the Shangdi site, and production area of final bulks and finished products in the "formulation workshop" and "packaging workshop" in the Changping plant. The Bulk of HAV is transported from the Bulk of HAV workshop at Shangdi site to the packaging workshop at Changping plant.

- **Shangdi site for Hepatitis A inactivated bulk:**

Bulk production areas are divided into four functional units including cell cultivation area, virus production area, virus inactivation area and preparation area.

Cell culture area is of grade C equipped with local laminar air flow hoods.

Virus production area of grade C is used for inoculation, harvest, purification and inactivation of hepatitis A virus.

- **Changping site for Hepatitis A formulation and finished products:**

The Formulation, Filling and Packaging Workshop is divided into formulation area, solution preparation area, syringe filling area and vial filling area, clean clothes washing area and packaging area.

The production process and manufacturing site layouts were discussed and visited.

- **Water system**

The procedure "PW and WFI system No I sampling" was discussed. WFI endotoxins and bioburden tests were performed daily. PW and WFI systems No I and II were discussed. PW and WFI action and alert limits of the test results were based on historical data.

13. Materials

Overall, the reception, sampling, testing, storage and releasing or rejecting of starting materials, packaging materials, bulk and finished products is performed according to implemented specifications and SOPs.

Controls are in place at receipt, checking, sampling, storage, release, storage of approved materials in segregated areas (quarantine, approved and rejected) with adequate labeling.

The procedures "Materials sampling" and "Packaging materials sampling" were discussed. The procedures were applicable for raw materials and excipients sampling and for primary packaging materials, VVMs and printed packaging sampling.

According to the SMP BJ-SOP-SA-063/01 "Packaging materials sampling"
$N \leq 3$ samples taken from all boxes
$3 < n \leq 300$ samples taken according to the formula $n\sqrt{} + 1$
$N > 300$ samples taken according to the formula $n\sqrt{}/2 + 1$

Raw materials and excipients were received and sampled at Shangdi site. Physical-chemical tests, including identity tests were also performed at Shangdi site.

Primary packaging materials vials and stoppers were received and stored at Changping site. Sampling of primary packaging materials was carried out in QC laboratory under LAF.

Temperature mapping re-qualification for finished products storage cold room was discussed. Study was carried out from 1 January 2017 till 4 January 2017. 152 T sensors were used and located at three levels. Temperature was recorded every 2 minutes. T mapping was performed twice per year – winter and summer. Temperature sensors calibration certificates were presented to the inspector.

14. Documentation

Documents were available and included SMPs, SOPs, protocols and records. Documents discussed were generally being followed and staff appeared appropriately knowledgeable as to their content. Documents were approved, signed and dated. Documents were regularly reviewed and kept up to date.

The procedure "GMP documentation management" was discussed. If no changes, documents were valid for 5 years. Before July 2016 documents validity was specified 2 years. Reason to change from 2 years to 5 years was explained that Chinese Pharmacopoeia is changed every 5 years and products marketing authorization also should be renewed every 5 years. According to the SMP all documents, including BMRs, BPRs and analytical raw date were retained permanently in documentation archive room.

15. Good practices in production

Access to production premises was restricted to authorized personnel. Seed and cell lots are stored in qualified equipment with adequate temperature monitoring and inventory system. In general production operations followed defined procedures and master formulas. Deviations from procedures were recorded and investigated. Dedicated facilities were in place for manufacturing Hepatitis A bulks.
Manufacturing of Hepatitis A vaccine was discussed.
The intermediate products and the finished product are stored according to Chinese Pharmacopoeia, Registration Specification of Hepatitis A Vaccine, inactivated. The storage time and temperature of the intermediate products and finished products were discussed.

16. Good practices in quality control

The QC function was independent of other departments. Adequate resources were available to ensure that all the QC arrangements were carried out. QC personnel had access to production areas for sampling and investigations as appropriate.

Quality control laboratories include:

- Chemical & Physical Laboratories,
- Cell/microbiology Laboratory,
- Biological Laboratory,
- Sampling Weighing Room,
- Sampling Warehouse,
- Animal House.

The performance of the in-vitro relative potency assay was observed. This assay uses kits prepared by the manufacturer. In house reference IgG is calibrated against the international reference Antibody from NIBSC. Reading of the assay is performed on a reader connected to a standalone PC. The reader is externally calibrated once per year by an external company using a standard absorbance material. The raw data is transferred to Excel for analysis.

Retention samples were stored in cold room at 2 – 8 ºC. Storage period for finished product was expiry date + 1 year and for APIs was 2 years after finished product release.

17. Distribution Shipping

For local supply, Hepatitis A vaccine is distributed in active refrigeration. However, the company has performed a validation of packaging for international shipment, using passive insulation system, according to the WHO guideline. The data-loggers used were Log-tag Trix-8 and the certificate of analysis from the manufacturer indicated an accuracy of ±0.5°C. These were distributed as required in that guideline. The methodology indicates that samples, boxes and cooler bricks were conditioned to 2-8°C before packing an activation of the recorders. However it was noted that for test at high ambient temperature the initial temperature of the loggers was 6.7-8.4°C while in the low ambient temperature test they were 11.00-17.5°C. The explanation given for this is that the company uses different packaging configurations for delivery to hot or cold destinations and cooler bricks may be of different temperature. However no such description is made in the document which indicates only one configuration of cooler bricks and that all are at 2-8°C before use. In response to the question about routine procedure SOP, it was stated that the SOP did not contain instructions on pack configuration for different conditions.

Study also reviewed (2014) of transportation of bulk between sites. Routine transportation uses active refrigeration. Study was performed both in summer and winter conditions using two potential transport routes. Data logger distribution was based on prior temperature study of van.

QC samples requiring refrigeration taken at Shangdi site are transported to Champing site using passive cooling system. Box is conditioned at 2-8°C for 30 minutes before sample loading with 3 cooler bricks. (routine process). For the study simulation fully loaded samples in box. Incubation was at 37°C for 3 hours. Data loggers showed maintenance of appropriate internal temperatures.

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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 deficiencies listed in the Inspection Report, as well as the Corrective Actions taken and planned, Sinovac Biotech Co., Ltd 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 inspection report as well as those reflected in the WHO Public Inspection Report (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.