

**Prequalification Team Inspection services
WHO PUBLIC INSPECTION REPORT
Vaccine manufacturer**

Part 1	General information
Manufacturers Details	
<i>Company information</i>	
Name of manufacturer	Bharat Biotech International Limited (BBIL)
Contact person	Mr Sai D. Prasad prasadsd@bharatbiotech.com
Inspected site	
Address of inspected manufacturing site	Genome Valley, Shameerpet Mandal, Ranga Reddy - 500078, Telangana, India. Bharat biotech DUNS: 8622 3673 4 Bharat Biotech : GPS coordinates: Latitude: 17.665269 Longitude : 78.605554
Manufacturing license number	The manufacturing license number 03/HD/AP/98/V/R for manufacturing of vaccines granted by the Drugs Controller General of India (DCGI), New Delhi and the Drugs Control Administration (DCA), State Government of Telangana.
Inspection details	
Dates of inspection	4 to 8 September 2017
Type of inspection	Initial inspection for Typbar-TCV [®] (Typhoid Vi Conjugate) 2.5 mL (5doses)
Representative from the National Regulatory Authority	The national regulatory authority (NRA) of the country where the inspection took place was informed and took part in the inspection:
Brief report of inspection activities undertaken	
Scope and limitations	
Areas inspected	<ul style="list-style-type: none"> • • PB2 facility is dedicated for Typhoid Vi Capsular Polysaccharide and Typhoid Vi Capsular Polysaccharide TT Conjugate Bulks and PO1 facility is dedicated for the formulation and filling of Typhoid Vi Conjugate Vaccine (2.5mL vial having five doses • PB2 dedicated for the manufacturing of purified and conjugated ViPS. • Building D for warehouse and quality control for chemical. • Building O for quality control for microbiology. • Building C for the storage of master and working seed banks.

	<ul style="list-style-type: none"> • Building F and B for water systems.
Restrictions	Not Applicable
Out of scope	Other than PB2, PO1, Building D, Building F & Building O
WHO product numbers covered by the inspection	Typbar-TCV [®] (Typhoid Vi Conjugate Vaccine) 2.5mL Vial (5 doses).
Introduction	
Brief summary of the manufacturing activities	<p>Bharat Biotech International Limited (BBIL) is a multidimensional biotechnology company specializing in the manufacture of Vaccines (Oral and Injectables), Bio therapeutics, and product-oriented Research and Development (R&D). Bharat Biotech International Limited was established in the year 1996.</p> <p>Bharat Biotech International Limited is specialized in vaccines drug substances manufacturing, formulation, filling, visual inspection, labeling, packaging, Quality Control and distribution of vaccines with product-oriented research and development (R&D).</p> <p>Vaccines, biopharmaceuticals, probiotics, gels and cream for human use are manufactured in designated facilities with provision for campaign based manufacturing of some products. The area is designed for the aseptic processing of injectable. There are separate production facilities which are utilized category-wise for bioprocess, formulation and filling in production of recombinant, bacterial, viral vaccines, biopharmaceuticals and probiotics.</p> <p>The portfolio of the vaccines, biopharmaceuticals and anti-diarrhoeal probiotic includes Recombinant <i>Hepatitis B</i> Vaccine, Vi-Capsular Polysaccharide Typhoid Vaccine, DTwP vaccine, DTwP + Recombinant <i>Hepatitis B</i> Vaccine, DTwP + Recombinant <i>Hepatitis B</i> + Hib-TT Conjugate Vaccine, <i>Haemophilus influenzae type b</i>-TT Conjugate Vaccine, DTwP + Hib (Combopack), Typhoid (Vi-Capsular Polysaccharide-Tetanus Toxoid Conjugate Vaccine), Poliomyelitis Vaccine, Purified BPL Inactivated Rabies Vaccine (Vero-cell derived), Purified Inactivated <i>Japanese Encephalitis</i> Vaccine, Adjuvanted H1N1 Vaccine Pandemic 2009, Rotavirus Vaccine (Live attenuated Oral), Recombinant Human Epidermal Growth Factor gel (For External Use Only), Silver Sulfadiazine, Chlorhexidine Gluconate and Recombinant Human Epidermal Growth Factor Cream.</p>
General information about the company and site	<p>BBIL is located on a site 40 kilometers away from Hyderabad, Telangana, India. All manufacturing, testing and release activities are carried out at BBIL manufacturing site.</p> <p>The total area of the site is approximately 7 hectares with a total of 19 Buildings. The overall built up area is 17500m² and the clean room area is around 7000m². Manufacturing facilities are segregated based on the type and nature of products, and separate areas have been provided for QAO, QAS, SAS QCD, Control Sample Storage Rooms, Warehouse, Utilities, Waste Water Treatment Plant, Incinerator, Animal Facility, Environment-Health-Safety (EHS), Administration Block and other Utilities.</p>
History	The last WHO audit was performed in February 2017.

	<p>The last joint inspection was carried out from 28th June 2017 to 29th June 2017 by the team of officers from CDSCO (HQ), New Delhi, Technical expert, CDL Kasauli, CDSCO Zonal Office, Hyderabad and DCA, Telangana for assessing the GMP compliance as per Schedule M, WHO guideline requirement and adequacy of data for post approval change in accordance with the requirements of CDSCO guidance for industry.</p>
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Abbreviations	AHU	Air Handling Unit
	ALCOA	Attributable, Legible, Contemporaneous, Original and Accurate
	APQR	Annual Product Quality Review
	APS	Aseptic Process Simulation
	bOPV	Bivalent Oral Poliomyelitis Vaccine
	BMR	Batch Manufacturing Record
	BPR	Batch Production Record
	CA	Compressed Air
	CAPA	Corrective Actions and Preventive Actions
	CC	Change Control
	CFU	Colony-Forming Unit
	CIP	Cleaning In Place
	CoA	Certificate of Analysis
	CPE	CytoPathic Effect
	CpK	Process capability
	DQ	Design Qualification
	DoM	Date of manufacturing
	DoE	Date of Expiry
	EDI	Electronic DeIonization
	EM	Environmental Monitoring
	FMEA	Failure Modes and Effects Analysis
	FTA	Fault Tree Analysis
	GMP	Good Manufacturing Practices
	GPT	Growth Promotion Test
	HEPA	High Efficiency Particulate Air
	HVAC	Heating, Ventilation and Air Conditioning
	IPQC	In Process Quality Control
	IQ	Installation Qualification
	LAF	Laminar Air Flow
	LIMS	Laboratory Information Management System
	MB	Microbiology
	MBL	Microbiology Laboratory
	MF	Master Formulae
	MFT	Media Fill Test
	MR	Management Review
	NCA	National Control Authority
	NCL	National Control Laboratory
	NRA	National Regulatory Agency
	OMCL	Official Medicines Control Laboratory
	OQ	Operational Qualification
	PHA	Process Hazard Analysis
	pH	(-ve) logarithm of H ⁺ concentration
	PLC	Programmable Logic Controller
	PM	Preventive Maintenance

	PQ	Performance Qualification
	PQR	Product Quality Review
	PQS	Pharmaceutical Quality System
	PS	Polysaccharide
	PS-TT	Polysaccharide-Tetanus Toxoid
	PSF	Product Summary File
	PW	Purified Water
	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
	RO	Reverse Osmosis
	SIP	Sterilization In Place
	SMF	Site Master File
	SOP	Standard Operating Procedure
	SAS	Sterility Assurance Services
	STP	Standard Testing Procedures
	TOR	Time Out of Refrigerator
	TT	Tetanus toxoid
	UN	United Nations
	UNICEF	United Nations Children's Fund
	URS	User Requirements Specifications
	UV	Ultraviolet-Visible Spectrophotometer
	VVM	Vaccine Vial Monitor
	WFI	Water for Injection
	WHO	World Health Organization

Brief summary of the findings and comments**1. Pharmaceutical quality system**

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

The Manufacturing operations are supported by Quality Operations (QO) consisting of Quality Assurance Systems (QAS), Quality Assurance Operations (QAO) Sterility Assurance Service (SAS) and Quality Control Departments (QCD).

Annual Product Review (APR):

Provisions for the APR were in place according to the implemented procedure. The APR shall be prepared within 120 working days after the receipt of last available data from analysis for the respective drug product.

The APR of Typbar TCV[®] covering the manufacturing period from January to December 2016 was spot checked.

- APR for Typbar-TCV[®] (Typhoid Vi Conjugate Vaccine) 2.5 mL for 5 doses manufactured in 2016 were spot checked.
- No batch failed to meet the established specification/s for Typbar-TCV[®] (Typhoid Vi Conjugate Vaccine) 2.5 mL for 5 doses during 2016.
- Review of critical in-process controls and finished product results.

There was no change to the critical in-process controls in Typbar-TCV[®].

No out of specification were observed. There was no fail. All the test results of Typbar-TCV[®] filled in 2016 met the pre-determined specification limits.

Quality Risk Management (QRM):

Provisions for the QRM were in place according to the procedure in place. A formal risk assessment programme was in place and this programme was found to be active. The risk assessment (RA) procedure provided guidance on a number of quality risk management tools which could be used, including Ishikawa (fish bone) analysis and FMEAs.

The following RAs were spot checked:

- Example RA concerning operations in the building bulk production (the manufacturing facility for typhoid and typhoid-TT drug substances) were reviewed.
- Retrospective risk assessment is placed. The spillages are dealt with according to the implemented procedures.
- Production activity for Purified bulk of typhoid Vi capsular polysaccharide in respective facility.

• Change Control (CC) Management:

Provisions for CC management were in place as per the procedure in place. CCs were categorized as critical, major and minor according to the impact to the quality, safety and/or the efficacy of the product. Timelines for the closure of the CCs were implemented. All critical, major and minor changes shall be closed as per the action plan provided by the initiating department therefore; no time frame for the closure of CC has been specified the list of change control initiated in 2015 to 2017 for manufacturing of Typhoid Bioprocess and final product (PO1) was spot checked.

Deviation Management:

Provision for the deviation management was in place as per incident and deviation management procedure. The deviations management procedure included the incident, unplanned and planned deviations. Critical, major and minor categorizations were assigned for unplanned deviations. For planned deviations, a RA is performed and accordingly, the planned deviations with high risk are rejected, with moderate risk shall be approved conditionally and with low risk shall be approved by QAS. Timelines and periodic review of incidents and deviations was in place.

The incidents classified as minor are closed within 30 days and critical and major deviations are to be closed as proposed by the initiating department head and agreed by the QAS

Corrective and preventive actions (CAPA) management:

Provisions for the CAPA plan were in place.

Management review:

Provision for the management review was in place. Quality Management meetings were held monthly with the participation of QA Director, QA heads, QC Managers, Production Director, Workshop Director, Engineering and representatives from other department. Monthly reports of the management review meetings were recorded.

Batch release procedure for vaccines:

Random samples of a vaccine lot are collected by relevant department personnel for QC analysis. These samples are tested against approved specifications in the QC. Accordingly, the CoA is issued. The BPR is reviewed for compliance with GMP. The vaccine lot is sampled by relevant department and QA send these samples to CDL, Kasauli, India. Once approved by CDL, the QAO will release the batch to dispatch and subsequent distribution for sale. Furthermore, relevant department personnel collect the samples to be retained for all the batches manufactured and these samples are given to QC for storage. These samples are stored until one year after the expiry of the batch.

However, it is the current practices of the company to send sample from batches with GMP violation and batches not intended for commercial supply for the official batch release by CDL. In addition, the data package submitted to CDL for official batch release was silent with regard to these GMP violations.

Computerized systems:

Policy on computer systems validation was in place.

2. Good manufacturing practices for pharmaceutical products

Resources were available, including qualified and trained personnel. Premises, equipment, laboratories, materials, containers and labels, procedures and instructions were in place. Qualification and validation of equipment, manufacturing processes and quality control testing methods were in place. Manufacturing processes were defined and reviewed. Records were made for the production operations. Deviations were recorded and investigated, root causes were determined and corrective and preventive action were implemented. Systems were in place for handling complaints and recalling any batch of product from sale or supply.

3. Sanitation and hygiene

Most of 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.

4. Qualification and validation

Overall, 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. Validation master plan (VMP), validation and qualification protocols and reports were spot checked as presented below.

- Media Fill for Typbar-TCV[®]
- Aseptic process simulation for Typbar-TCV[®]
- Process validation for Typbar-TCV[®]
- Validation/Revalidation of PB2 & PO1 autoclaves.
- Cleaning validation for Typbar-TCV[®]
- Qualification /Requalification of PO1 for Typbar-TCV[®]
- Incubators
- Smoke studies
- Hold time studies
- Filing and sealing machines
- HVAC
- Market complaints and AEFI's for Typbar-TCV[®]

5. Complaints and Adverse Event Following Immunization

At the time of the inspection, there was no commercial batch available regarding Typhoid conjugate 2.5 ml in vial.

6. Product recalls

Product Recall procedures were spot checked. The purpose was to describe the procedure for conducting the product recall for the statutory recalls, voluntary recalls and recall originate from market/customer complaints. Terminologies were defined for clarification. The procedure has further defined types of classification of recall with the timelines which include Class I; Class II Class III. The procedure also provided for types of product recalls. Recall Product Log book was reviewed and there was no complaint related to the product or similar products under consideration in the year 2017.

Procedure for mock up recall was in place. The purpose of the procedure was to evaluate effectiveness of any product recall from depot and distribution.

7. Contract production, analysis and other activities

No manufacturing process used in the production of Typbar-TCV[®] Vaccine is contracted to outside companies or premises. The external laboratories used for testing processes are approved as per the instructions and information given in the procedure "Approval of Contract Testing Laboratories".

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

Self-inspection:

The company conducted self-inspection as per approved procedure. A self-inspection program for each manufacturing line and supporting department was in place. After completion of self-inspection, report was generated, main deficiencies were identified and drawn as critical, major and others. Accordingly, the CAPAs were initiated. Inspection report clearly summarized closed, open and total findings in table.

Schedule for 2016 and 2017 prepared as per procedure were reviewed and a self-inspection summary report, for the self-inspection were in line with the schedule and clauses of the procedure. There were no data integrity issues according to the report.

Vendor approval:

Vendor qualification was done as per implemented procedures “vendor qualification for material” and “vendor control for service provider”. Vendor qualification procedure classified raw material suppliers into four categories according to the criticality to the product. The qualification process includes questionnaires, onsite and sample testing. The suppliers which scored high would be subject to onsite audit.

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.

10. Training

Procedure for training was spot checked. The procedure covers different types of training and the schedules for training the new and currently employed personnel including on the job training. The schedule for new training is identified by different departments (i.e. QA and HR) and prepared in December for the coming year. The evaluation report of training was also included in the procedure.

Employees training record was provided for January 2017. Training questionnaire and evaluation report for individuals was presented for review.

In addition in this new version, individual training is introduced. The new system is implemented for bio process, formulation and filling. The evaluation report of training was also included in the procedure.

Employees training record was provided for 2017. Training questionnaire and evaluation report for individuals was presented for review. Training records for three production staff were spot checked.

Vaccination and hygiene

SOP for vaccination and personal hygiene is placed

Personal hygiene

Formal procedures were in place governing personal hygiene aspects for staff and visitors entering into the production premises.

12. Premises and Equipment**Production areas:**

The 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. Changing rooms were flushed with filtered air. Premises were cleaned and disinfected according to written procedures.

The Drug Substances of Typhoid Vi Capsular Polysaccharide Bulk, Typhoid Vi Capsular Polysaccharide Bulk Tetanus Toxoid Conjugate Bulk are manufactured in PB2 Facility. The PB2 Facility is dedicated for the Bio-process of Vi Capsular Polysaccharide Typhoid and Typhoid Vi Conjugate Bulk.

PO1 facility located in the ground floor of Building ‘O’ is used for formulation and filling of Vi Capsular Polysaccharide Typhoid Vaccine (0.5 mL, 2.5 mL and 5.0 mL Vial presentation) and Typhoid Vi Conjugate Vaccine (0.5 mL and 2.5 mL Vial presentation).

Both Quality Assurance and Cell and Virus Bank Storage Area are located in 1st floor of Building C. The Cell Banks are stored in liquid nitrogen and the Virus Banks are stored at -70°C in a secure location, and are under the control of QAO. Additionally the company also stores Cell and Virus Bank materials at an alternate site located on the 1st floor of Building A.

Warehouse:

The warehouse is located on the ground floor of building D. It is used for storage and dispensing of raw and packing materials used in the manufacture of different drug substances and drug products. The intermediates such as the bulk antigens used in formulation and filling of finished products are stored at recommended storage conditions and issued as per requirement upon requisition. The finished products are packed and transferred to the dispatch area after clearance from QCD and QAO Departments.

Storage and distribution areas of finished products:

The finished products are stored in a cold rooms located in Building D. Due to the scarce capacity of this warehouse (max 19 lots), storage is outsourced to a third party located 15 km away from BBIL and where one cold room at 2-8°C and one room at minus 20°C are dedicated to BBIL products.

Other key areas include Pure Water (PW) storage tank located on Top of Building F from which Water for Injection (WFI) and Pure Steam (PS) are produced and distributed to other buildings.

Quality Control Department (QCD)

QCD has 5 divisions:

(a) Chemical Laboratory, (b) Microbiology Laboratory, (c) Virology Laboratory, (d) Animal Facility and (e) EHS.

14. Materials

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.

Vaccine vials were sterilized prior to filling by passing through the PO1 depyrogenation tunnel. The vials were stoppered using stoppers sourced ready packed for sterilization and then autoclaved in house.

15. Documentation

The batch manufacturing records (BMR) for finished product of typhoid lot (2.5mL/5dose), manufactured in 2016 were spot checked. The final product was formulated from respective Typhoid –TT conjugated bulk. Relevant seed lot number was used in the production of respective Typhoid-ViP batch. The seed lot system is well described including the in-house QC test performed. The BMR documents were in details, clear and of a good standard.

The quantities in each manufacturing step have been reviewed for Typhoid Vi Capsular Polysaccharide and Typhoid Vi Capsular Polysaccharide Conjugation with TT Bulk and finished product starting from steps namely; Culture medium and inoculum preparation, Fermentation, Upstream process (precipitation and concentration and

diafiltration), Conjugation with TT bulk formulation and filling into 2.5mL/vial. Routine and In-process tests and specifications for intermediates and final product were reviewed.

16. Good practices in production

The 2.5mL 5 dose is containing the following:

SN	Ingredient	Quantity dose	per Function
1	Purified Vi-Capsular Polysaccharide of <i>S. typhi</i> Ty2 conjugated to Tetanus Toxoid	25µg	Active Immunizing Ingredient
2	Sodium chloride	4.5mg	Buffer
3	2-Phenoxyethanol	5mg	Preservative
4	Water for Injections	q.s to 0.5mL	Diluent

Typbar-TCV™ vaccine, is filled in vials of USP Type 1 clear tubular (3mL for Multi dose), stoppered with 13mm grey bromobutyl siliconised rubber stoppers and sealed with 13mm aluminum flip off seals.

The manufacturing process involves five stages namely media preparation and inoculum preparation, fermentation, downstream process and conjugation with tetanus toxoid bulk. This is elaborated in a flow chart including the building where each stage is carried out and the in process controls applied along with applicable storage condition for each stage of manufacture.

The master and working cell banks MWCB of *S. typhi* Ty2 strain cells were adequately labeled, stored and inventoried. Each stage of seed preparation has been clearly described with indication of the processing conditions such as type of media, processing time, speed and temperature and the yields.

The downstream process includes four precipitation steps, concentration and diafiltration and sterile filtration conditions methods and storage of the product.

The conjugation with Tetanus Toxoid Bulk is comprehensively described.

Formulation and filling starts with the addition to the Vi Capsular Polysaccharide-TT Conjugate Bulk of saline solutions prepared in the stainless steel (SS) mixing vessel in the Excipient Solution Preparation (ESP) area. The pH is adjusted using NaOH solution. Final Bulk is stored in the mixing vessel that is maintained up to overnight. Final Bulk is transferred to the filling vessel in a closed SS loop.

Prior to the filling process the vials are washed sterilised and depyrogenated. After fill volume is adjusted, filling operation starts, followed by stoppering and sealing with flip-off aluminium seals. This is done in a grade A environment. The vials are packed as summarised in table below:

Presentation	Packing	Target fill Volume	No. of doses
2.5mL	USP Type 1 Glass Vial (3mL)	3.1mL	0.5mL x 5 doses

The filled vials are inspected before labeling. Vials with particulate matter and other defects like defective sealing and inadequate volume are rejected. The labelled vaccine vials with VVM30 are packed in mono-cartons that form a multi-carton and are transferred to Warehouse for cold storage at 2 to 8°C until dispatch.

The facility operates in three shifts.

A formal environmental monitoring programme was in place covering microbial and non-viable particulate monitoring. Settle plates for use in class C and D areas were made in house while those for use in class A and B areas were purchased. The company's water monitoring programme was also considered; EM and water sampling was performed by QC staff.

17. 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

Environmental monitoring:

Media for EM are containing tween and lecithin as stabilizers. Disinfectants used, didecydimethyl ammonium chloride, glutaraldehyde 1,6- dihydro 2,5 dioxahexane, benzalkonium chloride dodecylbispropylene triamine, 1,6 dihydroxy, 2-5 dioxahexane, glutaraldehyde, benzalkonium chloride, alkyl urea derivatives and 2-propanol, 1-propanol ethyl-hexadecyl-dimethyl ammonium-ethyl sulfate..

Water monitoring:

The site has one generation plant for PW located in building F with two PW generators, which feeds 2 independent water systems for PW and WFI: one is in building F and is dedicated to rotavirus manufacturing facility; the second is located in Building B and produces water for building B &C, Building C where polio vaccine is manufactured and Quality Control Building.

In building B, one mother tank of PW is present, from which pure steam and WFI are produced. The initial qualification of the old PW generator was conducted in B.

The utility in building F was visited and found clean and well maintained. Trends for all required test including regular controls of temperature, pH, conductivity, TOC and microbiological counts are performed according to an appropriate sampling plan. Trends related to Jan-Dec 2016 and Feb-July 2017 were reviewed and no observations were raised.

The Out of Specification (OOS), out of trend (OOT) and out of limit (OOL) handling:

Procedures handling OOS, OOT and OOL were in place. It describes the handling of OOS and OOT's and process for investigation, documentation, tracking and trending results and to take the corrective and preventative action in order to prevent the reoccurrence of the OOS and OOT. Procedures for management of sterility test failures were in place

18. Distribution and dispatching

Qualification and validation of international shipping:

The transportation of TT purified bulk from the manufacturing third party company to BBIL warehouse was reviewed. The bulk is transported in insulated box which contains 16 gel packs and an electronic temperature device to assure temperature at 2 to 8°C. The current transit time is estimated with 15 hours which temperature stability is assured.

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, BBIL 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.