

**Prequalification Team Inspection services  
WHO PUBLIC INSPECTION REPORT  
of the FPP manufacturer**

<b>Part 1</b>	<b>General information</b>
<b>Manufacturers details</b>	
Company information	
Name of manufacturer	<b>Anhui Biochem Bio-pharmaceutical Co., Ltd</b>
<b>Inspected site</b>	
Address of inspected manufacturing site if different from that given above	No. 30 Hongfeng Road, Hi-Tech Development Zone, Hefei, Anhui, People's Republic of China
Unit / block / workshop number	Oral Solid Dosage (OSD) workshop, building 2
<b>Inspection details</b>	
Dates of inspection	15 – 18 August 2016
Type of inspection	Follow-up inspection
<b>Introduction</b>	
Brief summary of the manufacturing activities	Manufacture including production, quality control and release of: <ul style="list-style-type: none"> <li>• Tablets</li> <li>• Hard capsule</li> <li>• Soft capsule</li> <li>• Therapeutic biological products</li> <li>• Granules</li> </ul>
General information about the company and site	<p>Anhui Biochem Bio-pharmaceutical Co., Ltd is pharmaceutical entity established in 2003, focused on the production of anti-HIV and anti-hepatitis B products.</p> <p>The company is subsidiary of Anhui Biochem United Pharmaceutical Co. Ltd and located at Hi-Tech development zone of Hefei city.</p> <p>The authorized activities were following: manufacturing, packaging, labeling, testing, storage, and distribution for FPP.</p>
History	
Brief report of	

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inspection activities undertaken	
Scope and limitations	
Areas inspected	See Part e below
Restrictions	N/A
Out of scope	N/A
WHO product numbers covered by the inspection	HA656 Lamivudine/Zidovudine Tablet, Film-coated 150mg/300mg

Abbreviations		
	AHU	air handling unit
	ALCOA	attributable, legible, contemporaneous, original and accurate
	API	active pharmaceutical ingredient
	APQR	annual product quality review
	BDL	below detection limit
	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
	CpK	process capability index
	DQ	design qualification
	EM	environmental monitoring
	FAT	factory acceptance test
	FBD	fluid bed dryer
	FG	finished goods
	FMEA	failure modes and effects analysis
	FPP	finished pharmaceutical product
	FTA	fault tree analysis
	FTIR	Fourier transform infrared spectrometer
	GC	gas chromatograph
	GMP	good manufacturing practice
	HACCP	hazard analysis and critical control points
	HPLC	high-performance liquid chromatograph
	HVAC	heating, ventilation and air conditioning
	ID	identity
	IR	infrared spectrophotometer
	IPC	In process control
	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
NIR	near-infrared spectroscopy
NMR	nuclear magnetic resonance spectroscopy
NRA	national regulatory agency
OQ	operational qualification
PHA	preliminary 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
RH	relative humidity
RM	raw materials
RS	reference standard
SAP	system applications products for data processing
SFG	semi-finished goods
SOP	standard operating procedure
STP	standard test procedure
T	temperature
TAMC	total aerobic microbial count
TFC	total fungal count
TLC	thin layer chromatography
TMC	total microbial count
URS	user requirements specifications
UV	ultraviolet-visible spectrophotometer
VMP	Validation Master Plan
WS	working standard

**Part 2**
**Brief summary of the findings and comments (where applicable)**
*Brief summary of the findings and comments*
**1. PHARMACEUTICAL QUALITY SYSTEM (PQS)**
Principle

In general PQS was implemented. Production and control operations were specified in written form and GMP requirements were generally followed. Managerial responsibilities were specified in job-descriptions. Product and processes were monitored and the results taken into account in batch release; regular reviews of the quality of pharmaceutical products were conducted. There was a QA department responsible for the quality assurance system headed by the QA Manager/QP (one person holding two positions) and the deputy QA manager.

#### Management review

The SOP “Management review” was discussed. MR was carried out at least once in a year. The following topics were included, but not limited:

- Previous review
- Product status
- Retained samples
- Stability
- CC
- Deviations
- OOS/OOT
- CAPA
- Self-inspection
- External audits
- Complaints
- Recall
- Returns
- Supplier management
- PQR EM
- Water monitoring
- Regulatory and SOP status

Till the date of inspection one MR meeting was carried out. Quality System MR Minutes for 2016 was discussed.

#### Quality Risk Management (QRM)

The SOP “Quality risk assessment” was discussed. The quality risk management was initiated in case of:

- New/modified product, process, equipment, utilities, facility
- Change control
- Self-inspections, customer audits, complains, recalls, deviations, OOS, validation, PQR, MR
- And any other items as appropriate

According to the SOP the following tools could be used for the RA:

- FMEA
- FMCA
- FTA
- HACCP
- HAZOP
- PHA

- Risk classification

RA was carried out by RA team. As a tool FMEA was mainly used.

The SOP “SOP for failure mode effect analysis” was discussed. Scoring system to calculate RPN was: 2, 4, 6, 8 and 10.

RA No XXXX and YYYY were discussed.

Product Quality Review (PQR)

The SOP “Annual product review” was discussed. PQR report should be completed by the end of February next year. “TAI YOU” software was used to calculate Cpk. The Cpk results were reconfirmed by excel calculations.

According to the SOP the following shall be covered by the PQR:

- Raw materials
- Packaging materials
- Excipients
- IPC results
- Finish product results
- OOS
- OOT
- Deviations / CAPA
- CC
- Stability
- Retain samples
- Complaints
- ADR
- Returns
- Recall
- Equipment / facilities
- Regulatory affairs
- EM
- Water
- Contracts
- Quality incidents
- GMP status
- Validation, re-validation
- Conclusion

The PQR for 2015 Lamivudine/Zidovudine Tablet film coated 150mg/300mg was reviewed.

Deviations

The SOP, flow chart and log book were discussed. Deviations were classified as:

- Critical
- Non-critical

- Planned
- Unplanned

Deviation No XXXX was discussed.

#### Corrective actions and preventive actions (CAPA)

The SOP “Corrective and preventive actions” was discussed. The SOP was applicable to the:

- Deviations
- OOS/OOT
- Recall’s
- Complaints
- Rejection of materials
- Self-inspection
- External inspection
- PQR

Root cause determination was specified in the CAPA SOP, tool used was 5 Why’s.

According to the SOP CAPA should be approved by the quality manager and implementation monitored by the QA. QA should organize also evaluation of the effectiveness of CAPAs. CAPAs register for 2016 was presented to the inspectors.

#### Change control

The SOP “Change control” and flow chart were discussed. Change control investigation was initiated amongst the following cases, but not limited to: raw material, excipients, packaging materials, facility, equipment, test method, specification, and manufacturing/packaging process, computerized systems. The investigations were recorded and had unique identifications. The CCs were classified as:

- Major
- Minor

CC No XXXX was discussed.

## **2. GOOD MANUFACTURING PRACTICES (GMPs) FOR PHARMACEUTICAL PRODUCTS**

In general good manufacturing practices were implemented. The necessary resources were generally provided. Qualification and validation were performed. Significant deviations were recorded and investigated. Records covering manufacture and distribution, which enable the complete history of a batch to be traced, were retained.

## **3. SANITATION AND HYGIENE**

Premises and equipment were maintained at acceptable level of cleanliness. The scope of sanitation and hygiene covered personnel, premises, equipment and apparatus, production materials and containers, products for cleaning and disinfection.

#### Personnel hygiene

The SOP “Employee Hygiene Control” was discussed. Eating, drinking, smoking, jewelry, cosmetics and personal medicines were not allowed in production and QC areas. Persons having an apparent illness or open lesions were not allowed to handle starting materials, packaging materials, in-process materials.

#### **4. QUALIFICATION AND VALIDATION**

##### Validation Master Plan (VMP)

The validation policy and the validation activities due within a certain period were summarized in the following documents which were discussed during the inspection in January, 2016, no major changes.

Accordingly, the following activities were defined in general:

- Equipment: annual,
- Process validation: every 3 years
- Utility: every 3 years,
- Production equipment: every 3 years
- Cleaning validation: every 5 years.

##### NIR qualification

NIR OQ and PQ protocol and report No XXXX were discussed

##### Tray dryer qualification

Hot air circulation tray dryer re-qualification protocol and report were discussed. Re-qualification was carried out every two years.

##### Coating pan qualification

Coating pan re-qualification protocol and report were discussed.

##### AHU re-qualification

AHU XXXX supplying air to the solid dosage forms workshop re-qualification protocol / report were discussed for the sifting room. Re-qualification was carried out for the following tests in operation:

- T & RH
- Airborne particles
- Pressure differential
- Air changes per hour
- Microbial contamination:
  - Settle plates
  - Active air sampling

##### Cleaning validation

The SOP “Cleaning validation control” was discussed. According to the SOP - rinse, swab and “visual clean” sampling methods were applied in some cases. Validation protocol and report XXXX were discussed. As an example tray dryer and mill were selected for performed study evaluation. Samples were analyzed using HPLC method.

##### Hold time studies

Clean equipment clean hold study was based on the worst case. Clean equipment clean hold study XXXX validation protocol and report were discussed.

#### Process validation

The manufacturing process submitted for the WHO had been validated in 2014 using 3 batches: 1410033, 1410034, and 1410035. Process validation protocols/reports and BMRs were discussed.

#### Analytical method validation

The analytical methods used for the testing of raw materials and finished products had been validated. The method validation documents of the assay test (HPLC) were discussed during the inspection in January 2016, no major changes.

### **5. COMPLAINTS**

The SOP “Customer complaints” and flow chart were discussed. Quality department had overall responsibility for complaints. According to the SOP there was a complaint investigation committee which consisted of the persons from:

- Quality department
- Production department
- Sales department
- Warehouse department
- Purchase department
- R&D department

Complaints register for 2016 was discussed. Till the date of inspection one complaint was registered. Complaint XXXX was discussed.

### **6. PRODUCT RECALLS**

The SOP “Product recall” was discussed. Till the date of inspection there were no recalls. QP and general manager were responsible for execution of recalls. The recalls were classified as:

- Class I; could cause serious effect to the health and should be executed within 24 hours
- Class II; could cause temporary problems to the health and should be executed within 48 hours
- Class III; no effect to the health and should be executed within 72 hours.

According to the SOP effectiveness of the recall (mock recall) should be evaluated every year. The last mock recall was executed in July 2016. The mock recall, Class II report was discussed. Mock recall was executed for the domestic market.

### **7. CONTRACT PRODUCTION AND ANALYSIS**

Not used

### **8. SELF INSPECTION, QUALITY AUDITS AND SUPPLIERS AUDITS AND APPROVAL**

The SOP “GMP self-inspection” was discussed during inspection in January, 2016, no major changes.

#### Items for self-inspection

According to the SOP the following topics should be covered during the self-inspection:

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- Organization and employees
- Facilities and utilities
- Equipment
- Materials and products
- Qualification, validation, calibration
- Documents management
- Record management
- Production and in-process control
- Quality management
- Complaints
- Recalls
- Returns
- Contract manufacture / laboratory controls
- Transportation
- Observations from the last self-inspection

#### Self-inspection team

Self-inspection team consisted of the following team members of the following departments:

- Head of QA
- Head of QC
- Head of production department
- Supply department
- Purchase department
- Warehouse
- Equipment
- Administrative department

#### Frequency of self-inspection

According to the SOP self-inspection should be carried out every 6 months.

#### Self-inspection report

Self-inspection report was written by the group leader and contained observations made during the inspections. CAPAs were proposed by inspected department and approved by the quality manager.

#### Follow-up action

CAPA implementation was followed by the QA and approved by the quality manager.

#### Supplier's audits and approval

The "Vendor evaluation and approval" was discussed. The SOP was applicable for vendors of:

- APIs
- Excipients
- Primary / secondary packaging materials

## **9. PERSONNEL**

### General

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The site organogram was specified in the SOP.

### Job descriptions

The following Job descriptions were spot discussed during the inspection in January 2016, no major changes:

- Job description of qualified person (QP). QP was responsible for the finished products release, investigation of complaints and product recalls. In QP absence deputy quality manager was responsible for the product release
- Job description of Quality Manager (QM)
- Job description of Quality Assurance (QA) supervisor
- Job description of Quality Control (QC) supervisor. QC supervisor was responsible for investigation out of specification (OOS) / out of trends (OOT) results, raw materials, intermediate and packaging materials release/rejection
- Job description of deputy Quality Manager

### Training

The SOP “Training” was discussed during inspection in 2016. The SOP had not been changed. The SOP listed the following training topics.

- Induction training:
  - Chinese drug legislation
  - GMP knowledge
  - Safety and health requirements (EHS)
  - Company history
- On job training:
  - Department documentation & procedures
  - Job description and related SOPs
  - Equipment & instrument operations SOP
  - Related EHS
  - Specific topics
- On-going training – carried out yearly according to the approved training plan.

Training files were kept by the administrative department. Training effectiveness was evaluated by tests (multiple choice questions, open questions and verbal interviews).

The training file for the operator working at the OSD workshop was discussed. The training effectiveness was evaluated by open written questions.

The training file for the analyst was reviewed. The new analyst and experienced analyst had to perform tests on the same samples and results were compared. The discussed training file contained tests of assay (HPLC).

Training records for the topic “Data integrity” were reviewed during follow up inspection in August 2016. Training effectiveness was evaluated by verbal questions and answers to randomly picked trainees from the group.

The SOP “Personnel health control” was discussed during the inspection in January 2016, no major changes. According to the SOP all staff should pass medical examination yearly. Personnel involved in visual control (production and QC) should pass eyesight checks every 6 months.

## **10. PREMISES**

### Production areas

Premises were laid out to allow the production to take place in areas connected in a logical order. In general where starting and primary packaging materials and intermediate or bulk products were exposed to the environment, interior surfaces were acceptable, did not shed particulate matter, and permitted easy and effective cleaning.

### Ancillary areas

Rest and refreshment rooms were separate from manufacturing and control areas.

### Storage areas

Storage facilities were provided for all materials.

### Weighing areas

The weighing (dispensing) of starting materials was carried out in two separate dispensing rooms located in the production department. Solid raw materials were dispensed under vertical Laminar Air Flow. Liquid materials were dispensed in separate room. Balances used for dispensing of materials were calibrated daily using standard weights.

### Quality control areas

The Quality Control laboratories (including physico-chemical and microbiology laboratory, stability chambers, retention sample room and the auxiliary areas) were situated on the 3<sup>rd</sup> floor of building 3.

## **11. EQUIPMENT**

### General

Equipment was located, designed, constructed, adapted and maintained to suit the operations to be carried out. Balances and other measuring equipment were available for production and control operations and were calibrated on a scheduled basis. Calibration due-date labels were attached to the equipment. Current drawings of critical equipment and support systems were maintained.

### Preventive maintenance (PM)

The SOP “Equipment operation and maintenance control” was discussed during inspection in January 2016, no major changes. The SOP was applicable for all equipment and instruments in production and QC laboratory. PM schedule was discussed. Schedule only indicated months for planned PM, but did not indicate date of performed PM. PM SOPs were available for all equipment. PM was carried out according to the relevant equipment check lists. Spot checks showed that schedule was followed.

### Calibration

The SOP “Calibration of instruments and measuring devices” was discussed during inspection in January 2016, no major changes.

The SOP was applicable for instruments and measuring devices in production and QC laboratory. There were two schedules available - one for calibrations carried out by external agencies and one for on-site calibrations.

#### Heating, ventilation and air conditioning system (HVAC)

The environmental conditions in the production areas were controlled by AHU. The clean rooms were classified as “Class D (ISO 8)”.

The SOP “Air conditioning system; usage and maintenance” was discussed during inspection in January 2016, no major changes. Air was recirculated AHU consisted of the following filter cascade:

- Pre-filter G4
- Secondary filter F6
- HEPA filter H13 (installed in the production rooms).

G4 and F6 filters were replaced when required. HEPA filters integrity checks should be carried out every year.

#### Environmental monitoring (EM)

The SOP “Cleanliness testing of clean area” was discussed during inspection in January 2016, no major changes. EM was carried out every 3 months. Settle plates and active air sampling was used for EM.

#### Purified Water (PW)

PW was used to prepare the binder solution, for cleaning of equipment and washing of garments. PW trends for 2015 were discussed. PW system was sanitized once every two weeks, for 1 hour using hot water (NLT 80 °C).

#### Compressed air (CA)

The SOP “Monitoring Compresses air system” was discussed during inspection in January 2016, no major changes. Compressed air used in production was oil/moisture free. Compressed air was filtered via 1 µ and 0.01 µ filters. Compressed air analyses were carried out every 6 months for the following tests:

- Water content
- Oil content
- Microbial limits (TAMC)
- Airborne particles

## **12. MATERIALS**

### General

The material management records were paper based.

### Starting materials

The SOP “Raw materials receiving and storage control” was discussed during inspection in January, no major changes.

The receipt of the materials was described in material specific SOPs discussed during inspection in January, no major changes.

According to the SOP warehouse staff should check that delivered raw materials were received from the approved suppliers and according to the order. If one delivery of material was made up of different batches, each batch was considered as separate for sampling, testing and release.

The SOP “Packaging damage control” was discussed during inspection in January, no major changes. Damage to containers and any other problem that might adversely affect the quality of a material were recorded and reported to the QA department.

The SOP “Raw materials sampling” was discussed. According to the SOP 100% identity tests were carried out for APIs and excipients using NIR.

#### Packaging materials

The SOP “Packaging materials sampling” was discussed. The SOP was applicable to the sampling of primary and secondary packaging materials printed packaging materials (labels). Sampling of the primary packaging materials was done according to the AQL.

The SOP “Packaging materials distribution control” was discussed.

#### Sampling

Raw materials, excipients and primary packaging materials were sampled in one room under LAF. Solvents were sampled in separate dedicated room. Sampling room’s usage and cleaning log books were discussed.

#### Dispensing

The SOP “Weighing and dosing” and SOP “Dispensing clearance” were discussed.

#### Finished products

The SOP “Products release control” was applicable to intermediates and finished products release.

The SOP was discussed during inspection in January, no major changes.

FPP release was approved by the quality manager. BMR/BPRs were reviewed by head of the workshop, production manager and workshop QA. Quality manager used the Check list for product release.

The SOP “Certificate of analysis (CoA) was discussed during inspection in January, no major changes. Group leader collected information from analysts and drafted CoA. Raw materials, intermediates and packaging materials CoA was signed by analyst who performed the tests, checker and approved by the QC manager. Finished products CoA was signed by analyst, who performed the tests, checker and approved by Quality Manager/QP.

#### Rejected, recovered, reprocessed and reworked materials

According to the company policy reprocessing and reworking of the products was not allowed.

The SOP “Return of customer products” was discussed during inspection in January, no major changes. According to the SOP returned products were stored in the separate returned products room and marked as under quarantine. Afterwards QC will sample and test the products. If the product complied with the specifications, it could be sold again.

The SOP “Rejected products control” was discussed during inspection in January, no major changes. According to the SOP rejected products should be transferred to the rejected products area and after QA approval destroyed.

The returned materials were stored in dedicated area. Returned product can be re-distributed in case the quality of the material is assured by resampling, retesting and release.

#### Packaging material

The SOP “Packaging materials receiving and storage control” was discussed during inspection in January, no major changes. The packaging materials were received, sampled, stored in the primary and packaging material warehouses (see relevant section).

#### Reagents and culture media

The SOP “Chemical reagent, toxic reagent, precursor reagent, special drugs control” was discussed during inspection in January, no major changes. Expiry dates for solid reagents was set up 5 years, after opening 3 years. Expiry dates for liquid reagents were set up 3 years, after opening 1 year.

Expiry dates for reagents prepared in QC laboratory were set up 3 months. Reagents stability studies were on going; during the inspection 2 M studies were completed.

The SOP “Media’s management” and the “Checking suitability of Media” were discussed. Upon receipt growth promotion tests using different culture strains was carried out for each batch of dry media.

Media were sterilized at 121 °C for 15 minutes.

#### Reference standards (RS) and working standards (WS)

The SOP “Standard substances/reference substances control” was discussed during inspection in January, no major changes. USP RS were used for impurity tests and WS for other tests. WS were qualified against RS. The SOP “Working standards” was discussed. Tests were carried out by two analysts in parallel. Triple tests were carried out for each item listed above. WSs were dispensed in 14 amber vials, each vial for one month used. Dispensing was carried out in QC laboratory.

The reference materials (compendia standards and working standards) were stored in the refrigerator.

The inventory logbook (stock, usage record) of lamivudine compendia standard was available.

#### Waste materials

Not inspected

### **13. DOCUMENTATION**

The SOP “SOP for document control” was discussed. According to the SOP documents should be approved by the Quality manager (QP). Exception was:

- Warehouse
- Purchase

- Production
- Equipment

documents. Above mentioned department's documents were approved by the head of production.

After approval documents were valid for 5 years. There were three levels of the documents:

- Level I – Quality manual
- Level II – Management SOPs
- Level III – Operational SOPs

All documents were distributed by the QA documentation section and distribution was recorded. Expired documents Master copies were kept in QA document archive without time limit.

Warehouse, purchase, production and equipment department's documents were approved by the head of production and signed/reviewed by the QA department.

The list of valid SOPs was available in a list (hard copy).

The SOP "Renewing laws and regulations and standards" was discussed.

#### Specifications and testing procedures

The materials had authorized and dated quality specifications containing the requirements and the corresponding test methods.

#### Specifications for starting and packaging materials, finished products

The quality requirements of the materials were defined in quality specifications with the corresponding SOP of the analytical test methods and the form of "Test Raw Data Sheet".

#### Batch manufacturing records (BMR) / batch packaging records (BPR)

The SOP "BMR/BPR control" was discussed during the inspection in January 2016, no major changes. BMR/BPR were distributed and filed by the QA department. BMR/BPRs were stored 1 year after expiry date of the product. The QA was responsible for the issuance of the BMR master copies to the production. Every page of the copies was authorized by a red QA stamp. The issued BMRs were recorded in a logbook.

The BMR of the batch XXXX was discussed.

#### Batch numbering system

The batch numbering system of the solid dosage forms was based on the item codes as follows according to the SOP. The SOP was discussed during the inspection in January 2016, no major changes.

Product batch number registration log book was discussed.

#### Standard operating procedures (SOP) and records

In general all required SOPs were available.

## **14. GOOD PRACTICES IN PRODUCTION**

### General

In general production operations followed defined procedures. Deviations from procedures were recorded and investigated. Checks on yields and reconciliation of quantities were carried out. Access to production premises was restricted to authorized personnel. To minimizing the risk of cross-contamination and mix-ups, only one product was manufactured in the OSD workshop at the same time.

### Dispensing operations

The SOP “Weighing and dosing” was discussed. All materials including the packaging materials were dispensed in the production workshop in two dispensing rooms, one for solid materials and one for liquids.

### Prevention of cross-contamination and bacterial contamination during production

Production areas were subject to periodic environmental monitoring.

### Processing operations

Before processing operations were started, steps were taken to ensure that the work area and equipment are clean and free from any starting materials, products, product residues, labels or documents not required for the current operation. Time limits for storage of equipment after cleaning and before use were defined 7 days. Significant deviations from the expected yields were recorded and investigated. Intermediates hold time studies were carried out during the process validation.

Measuring, weighing, recording, and control equipment and instruments were serviced and calibrated at specified intervals and records maintained.

Separate bins contained the dispensed material for individual batches.

Punches and dies were stored in locked SS cabinets. Dedicated set of punches and dies was used for lamivudine/zidovudine 150mg/300mg tablet.

### Packaging operations

Before packaging operations begun, steps were taken to ensure that the work area, packaging lines, printing machines and other equipment are clean and free from any products, materials or documents used previously and which are not required for the current operation. The line clearance was performed and recorded.

Roll labels were used for bottles labelling. Batch numbers and expiry dates were printed online. For the cartons batch numbers and expiry dates were printed in separate room using 2 printing machines. Printing machines log books were discussed; line clearance was ensured.

## **15. GOOD PRACTICES IN QUALITY CONTROL**

### General

The QC function was independent from other departments. QC personnel had access to production areas for sampling and investigations if required. The tests performed were recorded in “Test raw data sheets” issued by the QA.

Analyst competency list was available and presented to the inspectors during inspection in January 2016.

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There were 2 analytical balances equipped with on-line printers.

The SOP “Laboratory data management” was discussed.

5 HPLCs and 1 GC were connected to the OpenLabs CDC ChemStation edition software, IR and UV instruments were stand-alone. The list of users of the OpenLabs system was presented to the inspectors.

#### Control of starting materials and intermediate, bulk and finished products

Sufficient samples of starting materials and products were retained to permit future examination of the product.

#### In-process control

In process tests like average weight, tablet weight, disintegration, loss on drying and friability were carried out in OSD production workshop in-process control laboratory.

#### Batch record review

The SOP “BMR/BPR control” was discussed during inspection in January 2016, no major changes. BMR/BPR checked by the workshop QA, workshop vice manager. Deviations were reviewed by the quality manager or authorized QA.

#### Analytical records review

The SOP “Analytical records review” was discussed during inspection in January 2016, no major changes. Analytical records were reviewed using check list. The analytical records and calculations were reviewed / discussed by QC manger, Quality department manager and QP.

#### Certificate of analysis (CoA)

Finished products CoA were drafted by the QC “records” group, reviewed by group leader and approved by the Quality manager (QP).

#### Stability studies

The SOP “Stability study” was discussed during inspection in January 2016, no major changes. Conditions for stability studies were:

- T 40 °C ± 2 °C, RH 75% ± 5%
- T 30 °C ± 2 °C, RH 75% ± 5%
- T 25 °C ± 2 °C, RH 60% ± 5%
- T 30 °C ± 2 °C, RH 65% ± 5%

One stand-by stability chamber was available.

Window periods between withdrawal of samples and analysis were specified.

One batch per year was placed on long term stability monitoring programme. Samples were packed in market simulated conditions.

#### Out of specification results

The SOP “OOS/OOT”, flow chart and register were discussed. The SOP for OOS result investigation was updated and implemented in August 2016. The general principles of the MHRA guideline were included in the SOP. The SOP was applicable for physicochemical and microbial tests. OOS investigation No XXXX was discussed.

#### Retention samples

The SOP “Retain samples control” was discussed during inspection in January 2016, no major changes. The SOP was applicable to the API, excipients and packaging materials. Retained samples were stored in controlled room. Finished products were kept in their final packaging.

#### Microbiological laboratory (MB)

The SOP “Media management” and SOP “Checking suitability of media” were discussed. According to the SOP growth promotion (GP) tests should be carried out for purchased dry medias and ready-made medias as well as medias prepared on site.

### **PART 3**

#### ***Conclusion***

Based on the areas inspected, the people met and the documents reviewed, and considering the findings of the inspection, including the observations listed in the Inspection Report, a Anhui Biochem Bio-pharmaceutical Co., Ltd, located at No. 30 Hongfeng Road, Hi-Tech Development Zone, Hefei, Anhui, People's Republic of China was considered to be operating at an acceptable level of compliance with WHO good manufacturing practices for pharmaceutical products.

All the non-compliances observed during the inspection that were listed in the full report as well as those reflected in the WHOPIR, were addressed by the 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.