DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT OFFICE ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
Food and Drug Administration; ORA OPQO HQ 12420 Parklawn Drive, Room 2032 Rockville, MD 20857 email: ORAPHARMInternational483responses@fda.hhs.gov Industry Information: www.fda.gov/oc/industry	11/13-21/2023
	FEI NUMBER 3023765884

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT IS ISSUED

TO: Dr. Caigu (Jack) Huang, CEO

FIRM NAME	STREET ADDRESS
Nanchang Anobri Pharmaceutical CO., LTD	Building B1, No. 888, Jingkai Avenue,
CITY, STATE AND ZIP CODE Nanchang City, Jiangxu CN 330000	TYPE OF ESTABLISHMENT INSPECTED Drug Product Manufacturer

THIS DOCUMENT LISTS OBSERVATIONS MADE BY THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OF YOUR FACILITY. THEY ARE INSPECTIONAL OBSERVATIONS; AND DO NOT REPRESENT A FINAL AGENCY DETERMINATION REGARDING YOUR COMPLIANCE. IF YOU HAVE AN OBJECTION REGARDING AN OBSERVATION, OR HAVE IMPLEMENTED, OR PLAN TO IMPLEMENT CORRECTIVE ACTION IN RESPONSE TO AN OBSERVATION, YOU MAY DISCUSS THE OBJECTION OR ACTION WITH THE FDA REPRESENTATIVE(S) DURING THE INSPECTION OR SUBMIT THIS INFORMATION TO FDA AT THE ADDRESS ABOVE. IF YOU HAVE ANY QUESTIONS, PLEASE CONTACT FDA AT THE PHONE NUMBER AND ADDRESS ABOVE.

The observations noted in this Form FDA 483 are not an exhaustive listing of objectionable conditions. Under the law, your firm is responsible for conducting internal self-audits to identify and correct any and all violations of the quality system requirements.

DURING AN INSPECTION OF YOUR FIRM (I) (WE) OBSERVED:

OBSERVATION 1 (Quality System)

The responsibilities and procedures applicable to the quality control unit are not fully followed.

Specifically, your Quality Unit failed to review the Related Substance Determination by HPLC for the stability studies.

For example; the HPLC chromatograms (deficient peak integrations) and the calculations for the individual impurities (only reported the test results, omitting the raw data calculations in the analytical worksheets) were not reviewed.

Furthermore, the Quality Unit failed to review the executed batch records of the application drug products and Media Fill Simulation batch record.

These failures can impact the accuracy of test results for individual impurities in the application drug products.

Reference: 21 CFR 211.22(d) Procedures not in writing, fully followed

OBSERVATION 2 (Laboratory Control System)

Established test procedures and laboratory control mechanisms are not followed. Specifically,

Your firm failed to follow the SOP # 01/02/02-047-01; titled "Standard Management Procedure of Integration"; R01; Effective Date: 09/15/2023; in that deficient peak integrations were observed in the chromatograms during

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review of the Related Substances determination by HPLC for the Stability Studies (0M, 12M, 18M or 24M for the Long-Term Stability at 25°C/60%RH storage conditions). The following drug products were impacted using deficient integration parameters for the peaks of interest as follow:

(b) (4) Spray; Batch #(b) (4) Time Period: 0M, 12M or 18M; SOP # 01/04/05-002-10; titled "Test Method for(b) (4) Spray"; R10; Effective Date: 11/06/2023. Some peaks are not integrated, and others were not correctly integrated (0M, 12M & 18M; upright & inverted, as applicable). Time periods 0M, 12M & 24M in the peak range from approx.(b) (4) (b) (4)to(b) (4) (after the(b) (4) peak) there are overlapping, and not integrated peaks and the integrated peaks are not well defined or separated. Notably, peaks at(b) (4) (0M) and(b) (4) 12M) are integrated, but the same peak at 18 months (18M) are not integrated, indicating inconsistencies in the peak integration process, leading to possible incorrect test results.

.(b) (4) Spray; Batch #(b) (4) Time Period: 12M & 18M (upright & inverted); SOP # 01/04/05-001-10; titled "Finished Product Test Method for(b) (4) Spray"; R10; Effective Date: 11/06/2023. The impurity(b) (4) Approx(b) (4) nm) is not integrated. In addition, there is an unexplained peak at approx.(b) (4) (12M & 18M upright & inverted).

.(b) (4) Spray; Batch #(b) (4) Time Period: 0M, 12M or 24M; SOP # 01/04/05-002-10; titled "Test Method for(b) (4) Spray"; R10; Effective Date: 11/06/2023. Some peaks are not integrated, and others are not correctly integrated (0M, 12M or 24M; upright & inverted, as applicable). Time period 0M most of the peaks are incorrectly integrated and peak at (b) (4) is not separated in 2 peaks, while the same peaks at 12M and 24M are separated. Time periods 0M, 12M & 24M in the peak range from approx.(b) (4) to(b) (4) (after the(b) (4) peak) there are overlapping peaks where the integrated peaks are not well defined or separated.

These discrepancies indicate inconsistencies in peak integration across different time periods, with the most significant issues observed at 0M, potentially affecting the accuracy of test results.

.(b) (4) Spray; Batch #(b) (4) Time Period: 12M & 24 (upright & inverted); SOP # 01/04/05-001-10; titled "Finished Product Test Method for(b) (4) Spray"; R10; Effective

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Date: 11/06/2023. The impurity (b) (4) Approx (b) (4) nm) is not integrated. In addition, there is an unexplained peak at approx. (b) (4) (12M & 18M upright & inverted).

Furthermore, the analytical worksheets for these above batches did not include raw data calculations for individual impurities, reporting only the test results. These failures have the potential to impact the accuracy of test results for individual impurities in the application drug products (release and stability studies).

CFR 211.160(a) Following/documenting laboratory controls.

OBSERVATION 3 (Laboratory Control System)

Laboratory controls do not include the establishment of scientifically sound and appropriate test procedures designed to assure that drug products conform to appropriate standards of identity, strength, quality, and purity. Specifically,

a) The Microbial count SOP # 01/04/10-017-03; Titled "Procedure for Microbiological Limit Test"; R03; Section 4.2 "Applicability test of counting method"; Effective Date: 09/02/2021; is deficient in that it failed to include specific and detailed instructions to ensure complete examination of microbial plates. For example, the procedure fails to include the following details:

- Specific instructions of how bacterial colonies will be evaluated and counted (i.e.: overlapping colonies).
- Specific instructions of how the number of mold and yeast will be counted.
- Guidelines for light usage during plate examination and bacterial counts.
- Instructions for second check analyst to confirm the original analyst bacterial counts reported.
- Analyst re-qualification program for the effectiveness of the bacterial counting technique.

CFR 211.160(b) Scientifically sound laboratory controls

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OBSERVATION 4 (Material System)

There was a failure to handle and store components at all times in a manner to prevent contamination.

Specifically, the following conditions were observed during the inspection of the firm's (b) (4) system:

a) A leakage at the interface of the (b) (4) valve of the industrial (b) (4) pipeline (location: (b) (4) Notably, no work order has been generated for addressing the leakage incident.

21 CFR 211.80(b) Handling and Storage to Prevent Contamination

OBSERVATION 5 (Production System)

Batch production and control records do not include complete information relating to the production and control of each batch.

Specifically,the batch production records of the (b) (4) spray drug products (b) (4) Spray and (b) (4) Spray) fail to include enough documentation to demonstrate the execution of the controls established in the manufacturing procedures of the (b) (4) drug products. This is evidenced in that the batch production records:

a) Do not include documented evidence for the interventions (routine, non-routine, corrective) during the aseptic filling operation process in the filling line. This includes signature records of personnel involved in the interventions.

b) Critical process parameters are not indicated in the batch records.

c) Visual inspection of the filled bottles is not documented in the batch records including the operator that execute the test along with the operator that verify the results reported. In addition, the SOP (04/02/10-019-03; titled "Operating Procedure for (b) (4) Detector"; Effective Date: 05/22/2023) used for the visual inspection is

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not referenced in the batch records.

d) Equipment used during the production of the drug products are not described in the batch records. Example: (b) (4) (FY-1600); (b) (4) (DU006; (b) (4) Compounding System (MMC-C100JL-SS-C001), Aseptic Filling Machine (GR-GZJ-60) and/or (b) (4) (PME-800).

e) Storage conditions and shelf-life (b) (4) of each drug product are not included on the first page of the batch records.

Reference: 21 CFR 211.188 Prepared for each batch, include complete information

OBSERVATION 6 (Facilities and Equipment System)

Procedures for the cleaning and maintenance of equipment are deficient regarding assignment of responsibility for cleaning and maintaining equipment.

Specifically,
a) Your firm failed to have an adequate procedure (SOP #: 04/04/05-049-01; titled "WJ-2400 Cleaning and Maintenance Procedure for Sterile (b) (4) R01; effective date: 09/20/2019) for the cleaning process of the Sterile (b) (4) Equipment ID: QC-527) located in the Grade C room # (b) (4) For example, the cleaning log sheet # 01/02/02-019-02-R4; titled "Cleaning and Maintenance Records of Inspection Instrument and Equipment"; Effective Date: 01/01/2022; does not include the type of cleaning and the time range of the cleaning. In addition, there is no second check operator to verify the cleaning of the (b) (4) in order to prevent cross-contamination between the materials being sampled (APIs & Excipients).

b) For example, the cleaning log sheet is limited to categories such as "Surface", "Desktop" and "Other" with checkboxes, lacking a secondary check operator to verify the cleaning effectiveness in order to prevent potential cross-contamination risks.

c) Additionally, the cleaning procedure does not have enough details to assure that operators consistently clean the sterile (b) (4) in a reproducible and effective manner. Furthermore, the cleaning log sheet (Form #

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01/02/02-019-02-R4) does not establish a clear link with the relevant procedure (SOP # 04/04/05-049-01), impeding traceability and accountability in the cleaning process.

Reference: 21 CFR 211.67(b)(1) Cleaning SOP/responsibility

**********Medical Device Quality System (21 CFR Part 820)**********

OBSERVATION 7 (Design Control)

Design plans that describe or reference the design and development activities and define responsibility for implementation have not been established.

Specifically, the (b) (4) for Project (b) (4) (b) (4) drug-device combination product) does not document the source information such as scientific literature, research papers, product reports used by the design device team during the design and development phase.

Reference: 21 CFR 820.30(b) Design Control Design and Development Planning

OBSERVATION 8 (Design Control)

Procedures for design output have not been adequately established.

Specifically, the (b) (4) Parts (b) (4) for Project (b) (4) that covers (b) (4) was not signed and dated by the project team lead and/or reviewers to document that the phases were reviewed after proceeding to the (b) (4) phase.

Reference: 21 CFR 820.30(d) - Design control output

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OBSERVATION 9 (Quality Audit)

Procedures for quality audit have not be adequately established.

Specifically, the Internal Audit Control Procedure QP-021-04, v04, effective 06.12.2023 states that the management representative is responsible for approving the (b) (4) internal audit plan, appointing the leader audit team and internal auditors, and reviewing and approving the Internal Audit Report. During review of your Internal Audit Plan, the management representative was participating as an auditor for Audit (b) (4)

Reference: 21 CFR 820.22 - Quality Audit

OBSERVATION 10 (Process Validation)

Procedures for monitoring and control of process parameters for a validated process have not been adequately established.

Specifically, the following production equipment validation was not adequately performed:
a) Performance Qualification (PQ) Validation Plan for the (b) (4) Sealing equipment FR-770, Document No. SVP-SC-084-01, Effective 2023/10/23 and the Validation Report for the (b) (4) Sealing equipment FR-770, Document No. SVR-SC-084-01, Effective 2023/10/27 do not identify the sample lot size that was used during the validation process to justify the sample size used in the process to simulate a standard or commercial lot size of the (b) (4) or (b) (4) (drug-device combination product).

b) The validation plans prepared for the (b) (4) Cleaning equipment AK-120, Document No. SVP-SC-059-01, Effective 2022/12/08 and the (b) (4) Document No. SVP-SC-044-01, Effective 2022/12/27 do not document the internal equipment number (SC-144 and SC-146) respectively to correspond with the appropriate validation reports.

c) (b) (4) Wrench Verification Protocol, Document No. SVP-SC-072-01, Effective 2023/03/01 and the (b) (4) Wrench Verification Report, Document No. SVR-SC-072-01, Effective 2023/03/09 were used to validate your firm's (b) (4) wrenches (SC-G-01, SC-G-02, SC-G-03 and SC-G-04) used during the quality check of the (b) (4)

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(b) (4) device assembly. The protocol and report did not document the lot/batch size or number for the (b) (4) samples tested for each of the wrenches used to test the (b) (4) and (b) (4) devices.

Reference: 21 CFR 820.75(b) Process Validation

OBSERVATION 11 (Document Controls)

Document control procedures have not been established and maintained.

Specifically, your Document Control Procedure QP-001-05, v05, Effective 2023/09/28 and Record Control Procedure QP-002-03, v03, Effective 2021/10/09 do not establish steps to:

a) designate the issuance of quality system records that include pre-numbered pages purchased from third party that are used to document templates and forms, such as temperature monitoring logs, retention sample log, management review forms, CAPA forms and internal audit forms.

b) reference the templates that are related to the specific procedure (i.e. complaint records, CAPA records, internal audit forms, management review forms).

Reference: 21 CFR 820.40 - Document control

OBSERVATION 12 (Personnel)

Procedures for training and identifying training needs have not been adequately established.

Specifically, the Head of Device Assembly employee did not receive adequate training to perform the assigned responsibilities in the required quality system requirements such validation, non-conforming product tasks for steps during device assembly that are critical to assess work affecting quality for the DDC (Drug Device Combination) product fo (b) (4) device.

Reference: 21 CFR 820.25(b) - Personnel Training

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