DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
CDER/OPQ/OPMA/ Attn: Christopher Downey, Ph.D., Division Director 10903 New Hampshire Avenue; White Oak Building 51, Room 2269 Silver Spring, MD 20993 E-mail: OPMABLAInspection483Responses@fda.hhs.gov	05/11/2026-05/20/2026
	FEI NUMBER 3016529861
NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED Wei Huang, President	
FIRM NAME Shanghai Henlius Biopharmaceutical Co., Ltd.	STREET ADDRESS No. 1289, Yishan Rd, Xuhui District
CITY, STATE, ZIP CODE, COUNTRY Shanghai, 200233, China	TYPE ESTABLISHMENT INSPECTED Drug Substance and 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.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

OBSERVATION 1

Your firm failed to demonstrate that the manufacturing process remained in a state of control and was capable of consistently producing drug product meeting established quality attributes during process performance qualification (PPQ) for (b)(4) mg (b)(4) mL presentation. Specifically, your firm manufactured three PPQ batches (# (b)(4) of (b)(4) (b)(4) mg (b)(4) mL presentation. These batches exhibited increasingly high overall rejection rates at (b)(4) %, (b)(4) % and (b)(4) % respectively during 100% (b)(4) visual inspection. The rejection rates for major defects were (b)(4) %, (b)(4) % and (b)(4) % for the three batches mainly due to visible particulates. The rejection rates for batches (b)(4) exceeded your pre-defined (b)(4) % acceptance criterion for major visual inspection defects. These results indicate that the PPQ batches did not adequately demonstrate process consistency, reproducibility, and continued control with respect to visible particulate defects.

OBSERVATION 2

Your firm failed to adequately investigate the progressively increasing high visible particulate rejection rates identified during 100% visual inspection of the (b)(4) mg (b)(4) ml PPQ batches. Specifically, to investigate the two (b)(4) mg (b)(4) ml PPQ DP batches (b)(4) that exhibited visible particulate rejection rates exceeding the predefined visual inspection acceptance criterion of (b)(4) %, (b)(4) units from each batch's rejected unit pool of major defect were randomly selected for further identification. This represented (b)(4) % and (b)(4) % sampling from the major defect pools of the two PPQ batches respectively. The sampling of the studies had no documented justification to ensure that the sampled units were representative or scientifically appropriate. The investigation did not provide adequate scientific justification to support that current manufacturing operation is a controlled process. The high and variable visible particulate defects indicate a recurring manufacturing or contamination control issue. The investigation was inconclusive in determining the root cause of the high visible particulate defects in these batches.

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OBSERVATION 3

Your firm failed to maintain adequate quality oversight over changes to the established acceptance criterion for 100% visual inspection. Specifically, your firm retrospectively revised the visual inspection acceptance criterion to (b) (4) % from (b) (4) % as defined in the (b) (4) mg (b) (4) mL PPQ protocol (PV-VP-000027), and the revision of visual inspection acceptance criterion was implemented retrospectively without an approved change control. Your firm did not adequately evaluate the potential impact of the revised criterion on product quality, batch disposition, process control, or the validity of the original acceptance criterion.

OBSERVATION 4

Your firm's cleaning validation programs for manufacturing equipment and components are inadequate in demonstrating that equipment used in drug substance and drug product manufacturing can be consistently cleaned to prevent contamination or carryover. Specifically,

a. Your firm's (b) (4) validations for (b) (4) and (b) (4) used in the manufacture of (b) (4) drug substance did not include swab sampling or visual inspection of the internal product-contact surfaces of the (b) (4) and (b) (4) Your cleaning validation sampling plan did not provide adequate scientific justification demonstrating that rinse samples were representative of the most difficult to clean locations within the (b) (4)

b. Your firm did not perform cleaning validation for indirect product contact equipment used on the filling line. Your cleaning verification studies of indirect product contact filling line equipment did not include testing or scientifically justified acceptance criteria for removal of (b) (4) residues from relevant filling line components, including stopper handling and transferring equipment where (b) (4) carryover may occur.

OBSERVATION 5

During the filling of (b) (4) drug product, (b) (4) mg (b) (4) ml, (b) (4) nl vial on May 13, 2026, an operator failed to set the (b) (4) as indicated in step (b) (4) of SOP-00273 Standard Operating Procedure (version 14, effective date: April 16, 2026). As a result, the (b) (4) settings of

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(b) (4) were observed at (b) (4) respectively, contrary to the (b) (4) settings of corresponding (b) (4) at (b) (4) for (b) (4) ml vials as referenced in section (b) (4) of SOP-00273. The operator confirmed that adjustments of the (b) (4) settings of the (b) (4) were not performed during any time of the operation. No written procedure is established on recording the (b) (4) setting of (b) (4) Additionally, the cover of the (b) (4) (b) (4) was cracked and was held together with transparent tape during operation.

OBSERVATION 6

Your quality control laboratory procedures and controls for test and sample management are inadequate or not followed. Specifically,

a. Permission assigned to analysts in Empower chromatography software includes the privilege to view quantitation peak fields in review. This allows analysts to view area accounts and results at the time of integration. QC analysts were observed changing the integration parameters without saving interim results. There is no documented justification why the initially applied integration parameters were not suitable before changing the integration parameters.

b. SOP-01655 and test record of size exclusion chromatography (SEC) of aggregates (b) (4) (b) (4) method do not specify how to verify the storage duration for the prepared samples stored in the (b) (4) The (b) (4) aggregates of (b) (4) are sensitive to change of (b) (4) A prolonged (b) (4) of the sample may cause (b) (4) degradation and method variability. SOP-01655 is developed to control (b) (4) (b) (4) of (b) (4) Per SOP-01655, the prepared sample is allowed to be stored in (b) (4) up to (b) (4)

c. Your QC sample management procedure is not adequate for sample reconciliation of the electronic system. Specifically, on May 12, 2026, Laboratory Information Management System (LIMS) showed that a total of (b) (4) samples were historically located in the 2-8 °C refrigerator (QC-C-637) in QC physical chemical lab room (b) (4) Analysts discard QC samples periodically by filling out the "Record for Discarding Remaining Test Samples (Form-00021)". QC samples were not reconciled in LIMS after disposal on April 30, 2026 and May 11, 2026.

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OBSERVATION 7

Your firm failed to establish adequate controls to prevent unauthorized deletion of electronic laboratory data during data archiving process. Specifically, the deletion protection setting for (b) (4) (b) (4) analyzer (b) (4) was removed when IT was archiving electronic data from (b) (4) (b) (4) to (b) (4) During audit on May 12, 2026, an operator demonstrated unauthorized deletion of data files (i.e., (b) (4) from (b) (4) analyzer (b) (4) during data archiving.

OBSERVATION 8

Your firm failed to adequately control non-process equipment located in drug substance manufacturing clean areas. Specifically, a (b) (4) refrigerator is located in Building (b) (4) Room (b) (4) where drug substance formulation, (b) (4) operations are performed. Your firm did not define the intended use or storage controls of the refrigerator, had no written procedure for routine cleaning and disinfection of the refrigerator, and did not perform risk assessment to justify its presence in the clean room or evaluated its potential contamination risk to processing operations.

OBSERVATION 9

Your firm failed to maintain adequate control and traceability of temperature monitoring sensors within the building management system. Specifically, during walkthrough inspection of Building/Equipment Management System (BMS/EMS) located in Building (b) (4) room (b) (4) on May 11, 2026, an alarm record at 13:03:25 on May 8, 2026 associated with sensor TT4038_2 for equipment QC-C-430 refrigerator could not be retrieved when a query was sent to the audit trail system. The firm stated that the sensor TT4038_2 displayed in the audit trail of the (b) (4) product storage Equipment Parameter Monitoring System (ENG-E-140) did not match the actual sensor position. The firm admitted that during the configuration process after equipment location change (Change Control: PR44994), the engineer omitted the "Source" item tag in the audit trail and failed to update the tag from sensor TT4038_2 to sensor TT4039_1.

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OBSERVATION 10

Procedures and practices intended to prevent contamination and maintain appropriate conditions within classified manufacturing areas are inadequate. Specifically,

a. On May 17, 2026, an open biohazardous waste bag containing (b) (4) waste material was observed lying directly on the floor in Grade C manufacturing Room (b) (4) while a (b) (4) (b) (4) operation was in progress. Waste material was observed protruding from the open bag and exposed to the room environment. Room (b) (4) is used for drug substance formulation, (b) (4) (b) (4) No bag rack, holder, or other container was used to secure the biohazardous waste bag and prevent exposure of the waste material to the classified manufacturing environment.

b. On May 17, 2026, while observing (b) (4) operation in Building (b) (4) Grade C Room (b) (4) a (b) (4) waste container containing waste (b) (4) was observed being placed on the lower shelf of a (b) (4) table which is not designated as a waste storage location.

OBSERVATION 11

Your firm failed to investigate a laboratory sample handling error in a timely manner. Specifically, on May 4, 2026, batch record (b) (4) recorded that an operator used a wrong sample to perform (b) (4) testing at Step (b) (4) of the (b) (4) production bioreactor operation for (b) (4) drug substance batch (b) (4) and generated result (b) (4) which was not related to batch (b) (4) but saved with the actual IPC test results (b) (4) (b) (4) No deviation was initiated until May 14, 2026 after inquired by inspector.

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