WARNING LETTER

Harbin Jixianglong Biotech Co., Ltd.

MARCS-CMS 723330 — MAY 01, 2026

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Delivery Method:

Via Electronic Mail - Return Receipt Requested

Reference #:

320-26-73

Product:

Drugs

Recipient:

Mr. Guo Qing Leng

President and General Manager

Harbin Jixianglong Biotech Co., Ltd.

North of Baoan Road, East of Changqing Street

Hulan Qu Harbin Shi Heilongjiang Sheng, 150025

China

Issuing Office:

Center for Drug Evaluation and Research (CDER)

United States

Warning Letter 320-26-73

May 1, 2026

Dear Mr. Leng:

The United States Food and Drug Administration (FDA) inspected your drug manufacturing facility, Harbin Jixianglong Biotech Co., Ltd., FEI 3024038751, at North of Baoan Road, East of Changqing Street, Liminzhen Hulan District, Harbin, Heilongjiang, from November 3 to 7, 2025.

This warning letter summarizes significant deviations from Current Good Manufacturing Practice (CGMP) for active pharmaceutical ingredients (APIs).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your APIs are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

In addition, we reviewed your firm’s drug listing submissions in FDA’s electronic Drug Registration and Listing System (eDRLS) and found that you failed to provide drug listing information for your relabeled semaglutide as required under section 510(j) of the FD&C Act, 21 U.S.C. 360(j), and 21 CFR Part 207. Furthermore, your relabeled semaglutide was

manufactured in an establishment not duly registered with FDA. Failure to provide listing information for a drug in accordance with 510(j) of the FD&C Act is prohibited under section 301(p) of the FD&C Act, 21 U.S.C. 331(p). Under section 502(o) of the FD&C Act, 21 U.S.C. 352(o), a drug is misbranded if, among other things, it was manufactured in an establishment not duly registered under section 510, or if it was not included in a list required by section 510(j). Under section 301(a) of the FD&C Act, 21 U.S.C. 331(a), it is a prohibited act to introduce or deliver for introduction into interstate commerce any drug that is misbranded. These violations are described in more detail below.

Your semaglutide API is also misbranded under sections 502(a) and 502(b)(1) of the FD&C Act, 21 U.S.C. 352(a) and 352(b)(1).

We reviewed your November 26, 2025, response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence.

During our inspection, our investigators observed specific deviations including, but not limited to, the following.

1. Failure of your quality unit to exercise its responsibility to ensure that APIs manufactured at your facility are in compliance with CGMP and failure to maintain complete traceability of APIs in commercial distribution.

Your firm is a manufacturer of peptide APIs, including Glucagon-Like Peptide-1 (GLP-1) Receptor Agonist APIs. FDA investigators observed that your firm lacked adequate quality unit (QU) oversight for the receipt of materials, repackaging, relabeling, and related controls for APIs. Specifically, there is no quality unit approved procedure governing the repackaging and relabeling operations for APIs sourced from external manufacturers prior to distribution to the U.S. market. For example:

- On **(b)(4)**, your firm purchased semaglutide API (batch **(b)(4)**) from **(b)(4)**, a supplier that was not on your approved supplier list. You repackaged and relabeled this batch without documentation and created a new labeled batch number, CP-030-20250711. Furthermore, on the label of the container you identified your firm, “Harbin Jixianglong Biotech Co. Ltd.,” as the manufacturer of API rather than **(b)(4)**, the firm from which you purchased the API. You also changed the manufacturing date of the API from **(b)(4)** to July 25, 2025, and the retest date from to **(b)(4)** to July 24, 2027, without appropriate supporting data. This GLP-1 API was distributed to the U.S. on August 23, 2025.
- On **(b)(4)**, your firm purchased semaglutide API (batch **(b)(4)**) from **(b)(4)**, another supplier that was not on your approved supplier list at time of purchase and release. You repackaged and relabeled this batch without documentation and created a new labeled batch number, CP-030-20250911. You changed the manufacturing date of the API from **(b)(4)** to September 25, 2025, and the retest date from **(b)(4)** to September 24, 2027. This GLP-1 API was distributed to the U.S. on October 3, 2025.

We note that on September 5, 2025, FDA implemented the Green List of Import Alert 66-80 to help address GLP-1 API drugs offered for import into the United States that appear to be adulterated or misbranded. As part of this Import Alert, GLP-1 API drugs from facilities not on the Green List would be subject to detention without physical examination upon import into the United States. Your firm was added to the Green List on September 5, 2025, based upon previously provided quality information.

However, your firm purchased GLP-1 API (semaglutide) from **(b)(4)**, a facility that is not on the Green List of IA 66-80. You then labeled the GLP-1 API as manufactured by your firm and shipped this batch to the United States, even though it was not manufactured by a facility on the green list. FDA is concerned that identifying your firm and not the actual manufacturers may have been an attempt to circumvent safeguards associated with IA 66-80 and may pose a risk to consumers of receiving substandard GLP-1 APIs.

On February 10, 2026, FDA held a teleconference with you recommending you consider removing the two relabeled batches of semaglutide API drugs currently in distribution from the U.S. market. At the teleconference meeting, you agreed to voluntarily recall the two batches of semaglutide API drugs in current distribution in the United States.

We acknowledge that on February 19, 2026, you initiated a voluntary recall of the two semaglutide API batches distributed in the United States.

Additionally, during the inspection, our investigators discussed with your firm your decision to release and distribute at least **(b)(4)** batches of tirzepatide API to the U.S. market prior to the completion of stability studies to support the **(b)(4)** retest date. Your firm did not have an adequate written scientific justification to support the tentative expiration date applied to these lots before distribution.

In your response, you state that due to high demand of semaglutide API in the U.S., you "occasionally purchased the product externally for resale." You acknowledge lacking appropriate procedures for the release of externally purchased products and lacking batch records for the repackaging and labeling operations.

Your response is inadequate. Although you commit to prohibiting the sale of externally procured products moving forward, you failed to address actions to be taken on the two distributed semaglutide API batches in the U.S market.

In response to this letter, provide:

- A risk assessment of all APIs you repackaged that are missing any required manufacturing documentation for release and distribution., notify your customers and determine if market actions, such as recall, is necessary.
- A summary of your systemic corrective action and preventive action (CAPA) plan to remediate the supplier qualification program and prevent use of unsuitable material suppliers.
- A comprehensive assessment and remediation plan to ensure your QU is given the authority and resources to effectively function. The assessment should also include, but not be limited to:
  o a determination of whether procedures used by your firm are robust and appropriate
  o provisions for QU oversight throughout your operations to evaluate adherence to appropriate practices
  o a complete and final review of each lot and its related information before the QU disposition decision
  o oversight and approval of investigations and discharging of all other QU duties to ensure identity, strength, quality, and purity of all products
- Your stability report and data to support the claimed retest date for all of your APIs intended for U.S. market.

2. Failure to demonstrate that your manufacturing process can reproducibly manufacture an API meeting its predetermined quality attributes and failure to adequately validate written procedures for the cleaning and maintenance of equipment.

Process Validation

You failed to appropriately validate your processes prior to release and distribution of your API. Specifically, you manufactured and distributed two batches of semaglutide API to the U.S. market despite having conducted no process validation.

Without adequate process validation, your firm lacks basic assurance that you can reproducibly deliver products that meet specifications. See FDA's guidance document for general principles and approaches that FDA considers appropriate elements of process validation at https://www.fda.gov/media/71021/download

In your response, you acknowledge that you have not initiated process validation for semaglutide API that you repackage and relabel. You compared the critical process parameters with the planned process validation lots and concluded that releasing these products without process validation was low risk.

Your response is inadequate. Your risk assessment lacks sound scientific testing data to conclude low impact of using non-validated processes on APIs already distributed to the United States. Additionally, you failed to provide a complete process validation protocol for review. Your CAPAs lacked metrics for effectiveness of bringing your operations into compliance with CGMP.

Cleaning Validation

You lacked adequate cleaning validation studies that demonstrate your cleaning procedures for your manufacturing equipment are effective. For example, your cleaning procedure requires calculation of a maximum allowed carry over limit based on API toxicity. However, you did not establish a maximum allowed carryover limit in your cleaning validation study

for the equipment used to manufacture peptide APIs, including semaglutide and tirzepatide. Furthermore, your cleaning validation study did not provide justification for the swab sampling locations, nor did it contain results from the swab sample testing as required by the same cleaning procedure.

Inadequately cleaned and maintained manufacturing equipment can lead to potential cross-contamination that could compromise your API quality and safety.

In your response you commit to drafting and executing a new cleaning validation protocol during your next production campaign in the original API workshop to include chemical residue testing on both direct and indirect product surfaces. Your response is inadequate because you did not provide a systemic CAPA for the deficiencies related to the misalignment between your cleaning procedure requirements and your cleaning validation study.

In response to this letter, provide:

- Your process validation protocols and reports for all APIs shipped to or intended for the U.S. market.
- An assessment of each API process to ensure that there is a data-driven and scientifically sound program that identifies and controls all sources of variability, such that your production processes, and will consistently meet appropriate specifications and manufacturing standards. This includes, but is not limited to, evaluating suitability of equipment for its intended use, sufficiency of detectability in your monitoring and testing systems, quality of input materials, and reliability of each manufacturing process step and control.
- A comprehensive, independent retrospective assessment of your cleaning effectiveness to evaluate the scope of cross-contamination hazards. Include the identity of residues, other manufacturing equipment that may have been improperly cleaned, and an assessment whether cross-contaminated drugs may have been released for distribution. The assessment should identify any inadequacies of cleaning procedures and practices and encompass each piece of manufacturing equipment used to manufacture more than one product.

3. Failure to ensure that all specifications and test procedures are scientifically sound and appropriate to ensure that your APIs conform to established standards of quality and purity.

You failed to establish that your analytical test methods are appropriately validated and suitable for use in API release testing. For example, in 2024 your firm shipped **(b)(4)** lots of tirzepatide API (about **(b)(4)** total weight) to the U.S. market without completing analytical method validation for assay and related substances by high-performance liquid chromatography, high molecular weight aggregates by size-exclusion chromatography, and amino acid ratio by high-performance liquid chromatography. Furthermore, in 2025, your firm shipped **(b)(4)** lots of tirzepatide API drugs (about **(b)(4)** total weight) without completing method verification for the bacterial endotoxin test.

FDA is also concerned that your analytical method validation for tirzepatide API, specifically for related substance test (R-VTP-TP-11-009-024), is not adequate. The test method validation data you provided indicates poor resolution, overlapping peaks, and absence of structural identification for **(b)(4)** specified impurities. lack of comparative approach using multiple, orthogonal, high-resolution analytical methods for peptide-related impurity characterization. Your microbial limit enumeration test (R-VTP-TP-04-001-2025) validation data includes inconsistencies. For example, your test data for *Pseudomonas aeruginosa* are shown twice, and data for *Bacillus subtilis* is missing.

For FDA's current thinking regarding analytical test method validation and impurity characterization in synthetic peptides, see *Analytical Procedures and Methods Validation for Drugs and Biologics* at https://www.fda.gov/media/87801/download and ANDAs for Certain *Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin* at https://www.fda.gov/media/107622/download

In your response, you acknowledge that your semaglutide and tirzepatide API drugs are in the development stage and full validation of all analytical methods has yet to be completed. You also acknowledge deficiencies in your product release procedure and failure of your quality system processes to identify and correct these non-compliant practices in a timely manner.

Your response is inadequate. Although you intend to implement a new procedure requiring your certificates of analysis to contain a statement of “Only for R&D use purpose” for “developmental drug products,” you did not mention any stipulations on the acceptable quantity to be released for R&D use. Based on your invoice and shipping documents, the quantity of API drugs (as much as **(b)(4)**) shipped into the U.S. is inconsistent with quantities typically used for research and development purposes.

In response to this letter, provide:

- A comprehensive assessment of your laboratory practices, procedures, methods, equipment, and documentation. Based on this review, provide a detailed plan to remediate and evaluate the effectiveness of your laboratory system.
- Your analytical validation protocols and reports for the release testing of all APIs shipped to or intended for the U.S. market.
- Appropriate microbiological batch release specifications (i.e., total counts, identification of bioburden to detect objectionable microbes) for each of your GLP-1 APIs.
- A detailed risk assessment addressing the hazards posed by distributing APIs with potentially objectionable microbial contamination. Specify actions you will take in response to the risk assessment, such as customer notifications and product recalls.
- A summary of results from testing retain samples of all API drugs distributed to the U.S market and within expiry. You should test all appropriate quality attributes including, but not limited to, identity and strength of active ingredients and microbiological quality (total counts and identification of bioburden to detect any objectionable microbes) of each lot. If testing yields an out-of-specification result, indicate the corrective actions you will take, including notifying customers and initiating recalls.

4. Failure to ensure that water used in the (b)(4) manufacturing steps of a non-sterile API intended for a sterile drug product is monitored and controlled for total microbial counts, objectionable organisms, and endotoxins.

You manufacture GLP-1 APIs that were imported into the United States. These GLP-1 APIs are intended for use in sterile injectable drug products. Your firm failed to ensure that the **(b)(4)** water you used in the **(b)(4)** manufacturing steps of your APIs was suitable for its intended use. For example, your non-sterile semaglutide and tirzepatide API are intended for sterile injectable drug products, and your **(b)(4)** water system has not been evaluated for the absence of objectionable microorganisms. There is no indication that your **(b)(4)** water was tested for endotoxin during manufacturing processing. Furthermore, you failed to conduct sampling and microbial testing of the **(b)(4)** water you manually transported and stored for use in the **(b)(4)** manufacturing process of your APIs.

(b)(4) water must be suitable for its intended use and routinely tested to ensure ongoing conformance with appropriate chemical and microbiological attributes. Routine and representative monitoring of microbial counts and identification of contamination in the system and at the point of use are integral to maintaining a state of control and the suitability of water used in manufacturing operations.

In your response, you acknowledge your failure to perform a risk assessment of objectionable microorganisms and your resulting failure to evaluate the requirements for controlling objectionable microorganisms in your **(b)(4)** water system. You commit to establishing a microbial identification strategy and to adding *E. coli* testing for both the **(b)(4)** water system monitoring and to the API specification. Your response is inadequate. You did not include monitoring of additional objectional organisms as required by the United States Pharmacopeia (USP) monograph for **(b)(4)** water.

In response to this letter, provide:

- Your commitment to routinely monitor and control endotoxins in your **(b)(4)** water to ensure its suitability for API intended for sterile drug products. Include alert/action limits, test methods, water analysis frequency, and diagrams of the water system, and location of all sampling points.
- The identification and assessment of all other aspects of the manufacturing process (e.g., input materials, holding times, equipment quality) that can contribute endotoxin to your APIs that may be used in parenteral manufacturing.

- A procedure for your water system monitoring that specifies routine microbial testing of water to ensure its acceptability for use in each lot of API produced by your firm.
- The current action/alert limits for total counts and objectionable organisms used for your **(b)(4)** water system. Ensure that the total count limits for your **(b)(4)** water are appropriately stringent in view of the intended use of each of the products produced by your firm.
- A procedure governing your program for ongoing control, maintenance, and monitoring that ensures the remediated system consistently produces water that meets **(b)(4)** Water USP monograph specifications, USP monograph tests for specified microorganisms, and appropriate microbial limits.
- Water analysis test results for a period of six months, obtained after implementation of additional testing including, but not limited to, sampling procedures and results for total microbial counts, objectionable organisms, and endotoxins.

Drug Listing Violations

Section 510(j) of the FD&C Act and 21 CFR Part 207 set forth the requirements for the listing of drugs. Under section 510(j)(1) of the FD&C Act and 21 CFR 207.41(a), a registrant must list each drug that it manufactures, repacks, relabels, or salvages for commercial distribution. Upon review of your firm's batch records, it was found that you relabeled semaglutide purchased from **(b)(4)** and **(b)(4)**. You failed to list these relabeled drugs. Additionally, **(b)(4)** and **(b)(4)** are not referenced in any of Harbin's drug listings for semaglutide as establishments where manufacturing is performed as required by 21 CFR 207.49(a)(12). Failure to provide listing information for a drug in accordance with 510(j) of the FD&C Act is prohibited under section 301(p) of the FD&C Act. Further, you relabeled semaglutide that you purchased from **(b)(4)**, a firm whose establishment registration is expired and that has not listed any drugs. 21 CFR 207.29 requires annual review and update of registration information for an establishment involved in the manufacture of drugs. Under section 502(o) of the FD&C Act, a drug is misbranded if, among other things, it was manufactured in an establishment not duly registered under section 510, or if it was not included in a list required by section 510(j). Under section 301(a), it is a prohibited act to introduce or deliver for introduction into interstate commerce any drug that is misbranded.

Complete, accurate, and up-to-date establishment registration and drug listing information is essential to promote and protect patient safety. FDA relies on establishment registration and drug listing information for several key programs, including drug establishment inspections, supply chain security, and post-market surveillance. Establishment registration and drug listing information is also widely used outside FDA for purposes such as electronic prescribing and electronic health records, insurance reimbursement, and patient education.

It is your responsibility to ensure that all drugs manufactured at your establishment comply with all establishment registration and drug listing requirements under section 510 of the FD&C Act, 21 U.S.C. 360, 21 CFR Part 207, and all other applicable FDA regulations. Registration and listing information and instructions on how to properly register an establishment or submit drug listings can be found at *Electronic Drug Registration and Listing Instructions*.

Misbranded Drugs

The semaglutide API labels for batch CP-030-20250711 and CP-030-20250911 bear the statement "Manufacturer: Harbin Jixianglong Biotech Co., Ltd." This statement is misleading because it indicates that the manufacturer of the API in those batches is
Harbin Jixianglong Biotech Co., Ltd. instead of **(b)(4)**. and **(b)(4)**. Therefore, the semaglutide APIs for batch CP-030-20250711 and CP-030-20250911 are misbranded under section 502(a) of the FD&C Act in that the labeling is false or misleading.

In addition, section 502(b)(1) of the FD&C Act requires a drug to contain the name and place of business of the manufacturer, packer, or distributor of the drug. The labels of Harbin's API products referenced above are misbranded under section 502(b)(1) because they misidentify Harbin, which is a distributor or packer, as the manufacturer. As evidenced by Harbin's November 5, 2025 declarations, **(b)(4)**. and **(b)(4)**. are the manufacturers of the semaglutide API in batches CP-030-20250711 and CP-030-20250911, not Harbin Jixianglong Biotech Co., Ltd.

Additional API CGMP Guidance

FDA considers the expectations outlined in ICH Q7 when determining whether APIs are manufactured in conformance with CGMP. See FDA's guidance document *Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients* for guidance regarding CGMP for the manufacture of API at https://www.fda.gov/media/71518/download

CGMP Consultant Recommended

Based upon the nature of the deviations identified at your firm, we strongly recommend engaging a consultant qualified to evaluate your operations to assist your firm in meeting CGMP requirements. We also recommend that the qualified consultant perform a comprehensive audit of your entire operation for CGMP compliance and evaluate the completion and efficacy of your corrective actions and preventive actions before you pursue resolution of your firm's compliance status with FDA.

Your use of a consultant does not relieve your firm's obligations to comply with CGMP. Your firm's executive management remains responsible for resolving all deficiencies and systemic flaws to ensure ongoing CGMP compliance.

Conclusion

The deviations cited in this letter are not intended to be an all-inclusive list of deviations that exist at your facility. You are responsible for investigating and determining the causes of any deviations and for preventing their recurrence or the occurrence of other deviations.

On February 27, 2026, your firm was placed on Import Alert 66-40 *Detention Without Physical Examination of Drugs From Firms Which Have Not Met Drug GMPs* and removed from the Green List of Import Alert 66-80 *Detention Without Physical Examination of Glucagon-Like Peptide-1 (GLP-1) Receptor Agonist Bulk Drug Substances*.

This letter notifies you of our findings and provides you with an opportunity to address them. After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done to address any deviations and to prevent their recurrence. If you believe that your products are not in violation of the FD&C Act, include your reasoning and any supporting information for our consideration. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Send your electronic reply to CDER-OC-OMQ-Communications@fda.hhs.gov. Identify your response with FEI 3024038751 and ATTN: Joan Johnson.

Sincerely,
/S/

Jill P. Furman, JD
Director
Office of Compliance
Center for Drug Evaluation and Research