

Subpart B Organization and Personnel

(21 CFR 211.22 – 211.34)

211.22 Responsibilities of quality control unit.

211.25 Personnel qualifications.

211.28 Personnel responsibilities.

211.34 Consultants.

Your firm's quality control unit failed to exercise its responsibility to ensure drug products manufactured are in compliance with CGMP, and meet established specifications for identity, strength, quality, and purity (21 CFR 211.22)

You lacked a QU with appropriate oversight for the manufacture of your drug products. For example, we observed the following deficiencies:

- A. You failed to establish and implement adequate procedures to validate your processes and qualify the equipment used to manufacture your drug products. (21 CFR 211.100(a))
- B. You failed to perform cleaning validation studies for non-dedicated equipment used to manufacture your drug products (21 CFR 211.67(b)).
- C. You failed to establish and maintain an ongoing testing program to support the labeled expiry on your distributed drug products. Therefore, there is no assurance your drug products will remain acceptable throughout their labeled expiry period (21 CFR 211.137).

In your response, you state you will update procedures to clarify responsibilities and authorities of the QU and other departments. You also state you will develop, improve, and implement process and cleaning validation procedures. Furthermore, you state you will develop a stability testing program.

Your response is inadequate. You do not provide a comprehensive review of your QU's authority and ability to carry out its responsibility to ensure compliance with CGMP. You also lack sufficient details of your plans to fully execute process and cleaning validation studies. Furthermore, you do not provide results of reserve sample testing or any additional scientific evidence to support your expiration dates.

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Your firm failed to establish an adequate quality unit (QU) with the responsibilities and authority to oversee the manufacture of drug products. For example, you failed to ensure:

- Adherence to an adequate stability program (21 CFR 211.166(a)).
- Consistent and complete batch records (21 CFR 211.188).
- Appropriate examination of labeling and packaging materials for correctness, including but not limited to sufficiently accounting for all ingredients used in manufacturing, prior to packaging operations (21 CFR 211.130(d)).

There was a fundamental failure of production management to effectively oversee the procedures, practices, and suitability of the manufacturing operations. In addition, even when a QU consists of one or only a few, those persons are still accountable for overseeing ongoing effectiveness of all systems and procedures, and review of the results of manufacture to ensure state of control and adherence to all quality standards.

As noted in the prior charge, your quality unit did not have adequate oversight of documentation, media qualification, and other critical microbiology laboratory programs. In addition, you lacked adequate systems for investigations and ensuring analyst competencies.

Furthermore, your management stated that in the past two years your firm conducted only one product out-of-specification (OOS) investigation and one water out-of-limit (OOL) for total aerobic microbial count (TAMC) investigation. These two investigations were the only ones available for our investigator to review. However, records collected during an FDA inspection of one of your customers (b)(4), indicated that your firm reported several OOL for TAMC and objectionable microorganism results within the past two years. It appears that your firm did not make all requested OOS/OOL test data available during the inspection.

In your response, you commit to implement a multiphase OOS investigation methodology. Your response is inadequate. You did not commit to assessing previous OOS results to ensure the investigations were adequate.

Be reminded that it is your responsibility to ensure all data and information provided are accurate, complete, and readily available for inspection. As a contract laboratory, you must comply with the CGMP regulations that apply to operations you perform, including, but not limited to, those that address the operations of your quality control unit, laboratory, investigation system, and documentation system.

Training Program

Your training program is inadequate. CGMP training is not regularly performed at your firm as required by your established procedure. During the inspection, you could not provide records of CGMP training.

In your response, you state a consultant will assess your training procedure for general CGMP requirements and a suitable CGMP training program shall be developed.

Your response is inadequate. You do not provide any immediate steps to address the training program to ensure all employees are adequately trained to complete CGMP activities. Nor do you commit to stop testing until employees can receive appropriate CGMP training.

Your quality unit (QU) failed to ensure that all CGMP records were retained and available for review. Our investigator discovered two garbage bags containing torn analytical records, including chromatographic results, unidentified number lists, and impurity method validation spreadsheets with handwritten notes. For the method validation study, official records contained only handwritten values, while the original data was discarded in the garbage bags. This practice violated your lab documentation standard operating procedure (SOP) which prohibits destroying records or instrument printouts due to errors and requires filing such documents with original data for traceability with proper justification.

Additionally, laboratory staff used unofficial personal diaries to record procedures, analytical observations, results, method modifications, and deviation descriptions. Your firm lacked procedures to control the use of these personal diaries and to ensure proper retention of all CGMP data.

In your response, you state you opened an investigation and that the validation documents in the garbage bags were not related to drug products destined for the United States. Your response is inadequate. Irrespective of the ultimate use or intended purpose of the validation documents, because your firm operates with a single set of procedures, equipment, and practices for all products tested at your facility, including those destined for the United States, all testing and data must be handled appropriately and in accordance with established procedures. Furthermore, your response fails to describe immediate corrective actions to prevent the destruction of CGMP data or to prevent the use of unofficial diaries to record CGMP data.

Reliability of data is compromised when there is a failure to maintain complete records of the conditions and data associated with all tests. Furthermore, the lack of complete data compromises the QU's ability to exercise its function of ensuring compliance to applicable standards.

Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you test.

We acknowledge that you are using multiple independent third-party consultants to audit your operations and assist in meeting FDA requirements.

You lacked adequate quality unit (QU) oversight for the manufacture of your drug products. For example, your QU failed to ensure the following:

- Establishment of adequate production procedures and process control to assure your drug products have the identity, strength, quality, and purity they purport or are represented to possess (21 CFR 211.100(a)).
- Establishment of adequate batch production and control records that contain the accomplishment of each significant step in the manufacture, processing, packing, or holding of the batch, for each batch of drug product (21 CFR 211.188(b)).
- Validation of test methods to verify their accuracy, sensitivity, specificity, and reproducibility (21 CFR 211.165(e)).

In your response, you commit to drafting and approving procedures and retraining personnel. Additionally, you commit to performing process validation, updating batch records, and validating test methods.

Your response is inadequate because you do not address how you plan to ensure that your quality unit has sufficient resources to carry out its responsibilities and consistently ensure drug quality.

You did not provide details about how you will conduct process validation. Furthermore, you did not provide revised batch production records. Complete and accurate batch production and control records are necessary to ensure that manufacturing processes are consistently followed and reproducible. In addition, you did not provide sufficient evidence to demonstrate in-house methods are equivalent or superior to the USP methods.

Significant findings in this letter demonstrate that your firm does not operate an effective quality system in accordance with CGMP.

Your firm is a contract manufacturer of over-the-counter (OTC) (b)(4) drug products. Your quality unit (QU) did not adequately oversee your drug manufacturing operations. For example, your QU failed to ensure:

- Adequate change control procedures, because after reformulating (b)(4) drug products with a new API, your QU released and distributed batches of these drug products with inaccurate labeling, still showing the previous active pharmaceutical ingredient (API). Specifically, (b)(4) was listed on the product labeling, when the drug product actually contained the reformulated API, (b)(4). Thus, your drug product label to contain (b)(4) actually contained (b)(4) (21 CFR 211.22(d)).

- Appropriate oversight for contract testing laboratories regarding qualification, method validation, and written agreements describing roles and responsibilities (21 CFR 211.22(a) and 211.22(b)).
- Performance of periodic production review at least annually (21 CFR 211.180(e)).

Your quality unit (QU) did not provide adequate oversight for the manufacture of your drug products. For example, your QU failed to ensure the following:

- Appropriate controls were exercised over computer systems to ensure only authorized personnel make changes to master production and control records or other records (21 CFR 211.68(b)).
- Adequate laboratory controls were established with proper specifications, standards, sampling plans, and test procedures to ensure materials and drug products meet required identity, strength, quality, and purity standards (21 CFR 211.160(b)).
- An adequate written stability testing program for drug products (21 CFR 211.166(a)).
- Laboratory records included complete data from all required tests for compliance with specifications and standards (21 CFR 211.194(a)).

Your firm's quality systems are inadequate. See FDA's guidance document Quality Systems Approach to Pharmaceutical CGMP Regulations for help in implementing quality systems and risk management approaches to meet the requirements of CGMP regulations 21 CFR parts 210 and 211 at <https://www.fda.gov/media/71023/download>.

In your response, you provide corrective actions for each deficiency with specific timeframes.

Your response is inadequate because it fails to address the systemic quality deficiencies identified during the inspection. The observed lapses, including but not limited to laboratory controls, documentation practices, and data integrity controls, many of which were also identified during previous inspections, indicate fundamental weaknesses in the QU's oversight function. The proposed corrective actions do not adequately demonstrate how you will strengthen quality oversight to ensure ongoing compliance with CGMP requirements.

Your quality unit (QU) failed to exercise its responsibility to adequately review production records prior to approval (e.g., failed to investigate out-of-specification test results, reprocessing, and errant label reconciliation) and failed to establish and follow written procedures (e.g., annual product reviews, complaints, recalls, CGMP training, process validations, analytical method validation).

Additionally, your QU failed exercise its responsibility to ensure that your component water is suitable for its intended use. Our inspection documented that you used “(b)(4) water” (also referred to as “(b)(4) water” in your batch records) as the main component of manufacturing OTC hand sanitizers. Although your OTC product labels identify purified water as the first inactive ingredient, your QU does not ensure that purified water is used in the product formulation.

Your quality unit (QU) lacked adequate control over your OTC drug product manufacturing operations and failed to ensure that you had adequate procedures. For example, your quality unit (QU) failed to ensure the following:

- Establishment of adequate procedures describing the roles and responsibilities of the QU, including review of complaints, supplier qualification, change control and periodic product quality review (21 CFR 211.22(a) and 211.22(d)).
- Establishment of appropriate controls over computer or related systems to assure that only authorized personnel institute changes in master production and control records or other records (21 CFR 211.68(b)).
- Establishment of adequate production procedures and process control to assure your drug products have the identity, strength, quality, and purity they purport or are represented to possess (21 CFR 211.100(a)).
- Drug products bear expiration dates that are supported by appropriate stability testing (21 CFR 211.137(a)).
- Establishment of adequate batch production and control records that contain the accomplishment of each significant step in the manufacture, processing, packing, or holding of the batch, for each batch of drug product (21 CFR 211.188(b)).

In your response, you commit to establishing a dedicated QU with associated procedures. Your response is inadequate in that it lacks detail on systemic remediations for your QU and improvements to your quality system. Your response also fails to provide details on how your QU will have the responsibility and authority to perform its functions.

Your quality unit (QU) is inadequate. Your QU did not provide adequate oversight for the manufacture of your OTC drug products. For example, your QU failed to ensure:

- Review of production and control records to ensure completeness and accuracy (21 CFR 211.192).
- Adequate written procedures to document and investigate any unexplained discrepancy or failure of a batch or any of its components to meet any specifications (21 CFR 211.22(d); 21 CFR 211.192).
- Appropriate change control procedures were followed related to drug product manufacturing (21 CFR 211.22(d)).
- Performance of periodic (i.e., at least annual) product review (21 CFR 211.180(e)).

In your response, you state that you will address nonconforming products by quarantining the products and taking action to eliminate detected nonconformity. You also state that you will “follow the annual review of products,” identify nonconforming products, and make any necessary adjustments with supporting documentation.

Your response is inadequate. You do not adequately detail how your quality function plans to improve its oversight of manufacturing quality. You also fail to assess the effects that your insufficient QU oversight had on product quality.

Your QU is responsible for fully exercising its authority and responsibilities. FDA is concerned that your QU may not be conducting appropriate oversight regarding CGMP operations.

Your firm's quality systems are inadequate.

Your firm failed to establish an adequate quality unit (QU) with the responsibilities and authority to oversee the manufacturing of drug products. For example, the QU failed to ensure:

- Establishment of an adequate cleaning and maintenance program for your manufacturing equipment and instruments. (21 CFR 211.67(a))
- Establishment of adequate batch records to include verification checks, appropriately detailed instructions, and labeling. (21 CFR 211.188)
- Adequate investigations with sustainable corrective actions including, but not limited to, unknown residues on equipment and out of specification cleaning rinse samples. (21 CFR 211.192)

Your quality unit does not consistently follow your procedures for the submission of regulatory notification of product quality defects. For example, your procedure for the preparation of "Advisory Notice" documents, including Biological Product Deviation Reports (BPDRs), includes instructions for your quality unit to "[e]scalate and/or report quality and compliance issues that may require Regulatory Body notification to Segment Management and ensure that quality issue management process is followed for decisions regarding issues that have potential to lead to an Advisory Notice."

You received two or more stopper **(b)(4)** complaints for each of **(b)(4)** batches of **(b)(4)**, between November 13, 2023, and November 8, 2024. Responsible officials did not adequately discharge their duties to ensure escalation and sufficient action on these complaints in accordance with your procedure.

Timely submission of BPDRs to regulatory authorities facilitates awareness and evaluation of potentially hazardous product defects. Notably, your comparable procedure for Field Alert Reports (FARs) requires the submission of a FAR upon receipt of "[t]wo or more complaints with the same confirmed defect... with or without a signal." Additionally, your procedure "Advisory Notice US FDA Form 3911 (Drug Notification and Health Authority (HA) Communication-Reportable Events Procedure" requires the submission of a BPDR "... as soon as possible, but no more than **(b)(4)** from the date that information is acquired reasonably suggesting that a reportable incident occurred."

We acknowledge that your firm ultimately submitted a BPDR for the stopper **(b)(4)** complaints, dated December 10, 2024, and your subsequent updates of that BDPR. We also acknowledge your commitment to update procedures associated with the submission of BPDRs.

Your response is inadequate. You identified a root cause for failing to submit a BPDR in accordance with your procedures as "...the recurring complaints were not considered reportable under the current procedure... because the definition of confirmed is related only to cases where the product quality is determined not meeting manufacturing standards or specifications." Although you proposed multiple CAPA to address this root cause and to assess other products in your corporate

portfolio for stopper (b)(4) complaints, you did not propose a retrospective review of complaints implicating marketed product quality to identify additional instances in which a BPDR should have been submitted.

Your quality unit (QU) did not provide adequate oversight for the manufacture and release of your over-the-counter (OTC) drug products. For example, you filled batch (b)(4) of your (b)(4) Spray from vessels (b)(4). Your QU rejected the drug product units filled from vessel (b)(4) because they failed assay test release specification for (b)(4). You attributed insufficient (b)(4) of the corresponding batch in vessel (b)(4) as the root cause. However, you released drug product filled from vessels (b)(4).

In addition, your QU failed to exercise its responsibility by not withholding from distribution all rejected units filled from vessel (b)(4) and instead allowing the distribution of approximately half of the rejected drug product. Your practice of rejecting a partial drug product batch is an indication that your firm does not have well-controlled manufacturing and release procedures.

In your response, you acknowledge that the rejected drug product was not adequately identified and contained due to improper scanning procedure. You took a corrective action that included revising your procedure for non-conforming and rejected materials and retraining your staff.

Your response is inadequate because you do not provide details on how your corrections and corrective actions will prevent recurrences of distributing rejected drug products to customers. You fail to address the fundamental deficiencies in your QU that led to these failures. You do not provide a comprehensive corrective action and preventive action (CAPA) plan with a systematic approach to correct these oversight deficiencies.

Your firm's quality systems are inadequate.

The QU failed to maintain adequate CGMP oversight. For example:

Lack of Written Procedures (211.100)

Numerous written procedures were either missing or lacked sufficient detail to ensure consistent repeatability between operators. For example, the following critical processes were not contained in a written procedure: set-up of the filling line, performing interventions on the filling line, personnel monitoring, and how to perform (b)(4) decontamination of aseptic processing rooms.

In addition, written procedures lacked sufficient detail, including those for cleaning of the filling line and cleaning of the filling room.

Your response is inadequate. You commit to writing procedures for the critical items described above, however you fail to perform a comprehensive review to ensure appropriate procedures are established and followed as part of your quality system. In addition, you did not provide a comprehensive risk assessment of the product impact of the lack of sufficient procedures.

Investigations (211.192)

We noted multiple instances where thorough investigations were not completed. For example, a viable air monitoring plate dated January 22, 2024, had a significant microbial recovery for the ISO 7 area of Line **(b)(4)**, identified as *Cladosporium*, a mold. The available documentation of the *Cladosporium* recovery noted that the same mold was found in multiple areas of the facility. You lacked a meaningful investigation into this trend.

Your response is inadequate as you did not commit to opening an investigation to examine this and other potentially adverse trends.

Complaint Handling (211.198(a))

Your complaint handling and investigation process is inadequate. Retain samples are not always evaluated for sterility unless requested by your distributor, even when the complaint indicates potential contamination. For example, you received a substantial number of complaints for burning or redness but did not perform sterility testing on retain samples until the fourth complaint was received.

Your response is inadequate. You commit to reviewing past complaints and updating your current procedure but fail to provide details for how you will incorporate testing, including but not limited to, sterility, into your complaint handling process in the future.

Raw Material Testing for (b)(4) (211.84(d)(2))

Your incoming raw material sampling and testing plan for **(b)(4)**, which is a component at high-risk of contamination with **(b)(4)**, is inadequate.

Your response is inadequate. While you commit to testing each container of every lot moving forward, you did not commit to testing of finished products that previously used these raw materials to verify that **(b)(4)** are not present above specified levels.

The use of ingredients contaminated with **(b)(4)** has resulted in various lethal poisoning incidents in humans worldwide. See FDA's guidance document Testing of **(b)(4)** to help you meet the CGMP requirements when manufacturing drugs containing ingredients at high-risk for **(b)(4)** contamination at **(b)(4)**.

Your quality unit (QU) did not provide adequate oversight for the manufacture of your drug products. For example, your QU failed to ensure the following:

- Review and approval of written procedures for production and process controls that are designed to assure the quality of your drug products, i.e., process validation (21 CFR 211.100(a)).
- Establishment of an adequate, ongoing stability program (21 CFR 211.166(a)).

- Adequate batch production and control records that include complete documentation of the accomplishment of each significant step in the manufacture, processing, packing, or holding of the batch, for each batch of drug product (21 CFR 211.188).
- Adequate review and approval of production and control records before a batch is released or distributed (21 CFR 211.192)
- Production and process control activities, such as equipment qualification, are documented at the time of performance (21 CFR 211.100(b)). Specifically, investigators observed your quality assurance manager generating and completing equipment qualification documents investigators previously requested. This practice raises concerns about the integrity and reliability of your firm's data and documentation.

Your quality unit (QU) failed to adequately implement the facility's quality function and ensure quality oversight. For example:

You failed to have an adequate procedure to clean (b)(4). Your approved procedure did not include sufficient directions to clean the (b)(4) ducts, including directions on disassembly and visual inspection for cleanliness. Thus, you failed to identify visible residue with the possibility of cross-contaminated drug products being released to the market.

In your response you identify (b)(4), was not designed to facilitate appropriate cleaning. You acknowledge this resulted in residual drug substances inside the (b)(4) duct of your (b)(4). You indicate that you are updating your cleaning procedures to require disassembly and post cleaning inspection.

Your response is inadequate. You do not provide a written approved procedure that would ensure adequate disassembly and cleaning of the (b)(4) duct. And you fail to provide evidence you have implemented CAPA measures ensuring QU oversight of cross-contamination risks from highly potent substances, such as (b)(4), on shared equipment.

You also manufacture (b)(4), a highly potent drug on the same shared equipment. (b)(4) is a hazardous drug that can cause (b)(4) if administered outside of its therapeutic range.

Your firm failed to establish an adequate quality unit (QU) with the responsibilities and authority to oversee the manufacturing of drug products. For example, your QU failed to ensure:

- Establishment of adequate batch production and control records, with complete information relating to the production and control of each batch of drug product produced (21 CFR 211.188).
- Adequate training for employees engaged in the manufacture, processing, packing, or holding of drug products (21 CFR 211.25(a)).
- Establishment of routine calibration and written records of calibration checks according to a written program designed to ensure proper performance of equipment used in the manufacture, processing, packing, and holding of a drug product (21 CFR 211.68(a)).

- Adequate storage and warehousing of drug products, including but not limited to appropriate monitoring of storage conditions for temperature and humidity (21 CFR 211.142).

In your response, you state you have established an independent QU; revised and approved all SOPs; remediated your batch manufacturing records; created training files, including complete GMP training of all personnel; implemented an equipment calibration program; and installed calibrated temperature and humidity data loggers with defined storage ranges to monitor your storage areas.

Your response is inadequate. You do not provide sufficient information and supporting documentation to verify the adequacy and effectiveness of your corrective actions.

Your quality unit (QU) failed to ensure that all CGMP records were retained and available for review. Our investigator discovered two garbage bags containing torn analytical records, including chromatographic results, unidentified number lists, and impurity method validation spreadsheets with handwritten notes. For the method validation study, official records contained only handwritten values, while the original data was discarded in the garbage bags. This practice violated your lab documentation standard operating procedure (SOP) which prohibits destroying records or instrument printouts due to errors and requires filing such documents with original data for traceability with proper justification.

Additionally, laboratory staff used unofficial personal diaries to record procedures, analytical observations, results, method modifications, and deviation descriptions. Your firm lacked procedures to control the use of these personal diaries and to ensure proper retention of all CGMP data.

In your response, you state you opened an investigation and that the validation documents in the garbage bags were not related to drug products destined for the United States. Your response is inadequate. Irrespective of the ultimate use or intended purpose of the validation documents, because your firm operates with a single set of procedures, equipment, and practices for all products tested at your facility, including those destined for the United States, all testing and data must be handled appropriately and in accordance with established procedures. Furthermore, your response fails to describe immediate corrective actions to prevent the destruction of CGMP data or to prevent the use of unofficial diaries to record CGMP data.

Reliability of data is compromised when there is a failure to maintain complete records of the conditions and data associated with all tests. Furthermore, the lack of complete data compromises the QU's ability to exercise its function of ensuring compliance to applicable standards.

Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you test.

Your firm lacks controls to assure the integrity of electronic batch record data. Your quality assurance employee instructed your software vendor to make changes to your electronic batch record which were not captured in the audit trail or managed through your quality system.

During the inspection, you provided written communication from a quality assurance employee to the software vendor that discussed multiple changes and modifications made to the electronic batch record. One of the changes included the replacement of an employee identification number with another employee number for “Dispensed by” in (b)(4) tablets USP (b)(4) mcg batch record (b)(4). The change was not recorded in the audit trail, nor was it noted in the electronic batch record. Additionally, your firm lacked detailed procedural controls to assure the integrity of electronic batch record data when modifications are made after completion of the batch record.

In your response, you indicate that the changes the software vendor made in the electronic batch record corrected inaccuracies only. You state your requests to software vendors to modify data have been terminated. You commit to conducting formal interviews with employees who contacted the vendors to request the data changes and to initiating deviation investigations. You commit to performing a retrospective review of all group and individual email messages sent to the software vendor to determine which email messages contained CGMP instructions. You also commit to conducting a review of the audit trails of all U.S. batches.

Your response is inadequate. You fail to provide documentation of the deviations, interview transcripts, or discussion held with the employees who requested changes to electronic batch record data. You fail to explain why Quality Assurance did not initiate a deviation upon finding discrepancies or why the batch record contained no comments or remarks about the employee identification change. Additionally, your retrospective review of email requests to software vendors for data changes did not include an assessment of communications with other software vendors such as (b)(4).

Your firm failed to establish an adequate quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging materials, labeling, and drug products and the authority to review production records to assure that no errors have occurred or, if errors have occurred, that they have been fully investigated (21 CFR 211.22(a)).

Your ophthalmic drug product, Lubricant PM Ointment, is intended to be sterile. Your firm utilized a CMO to manufacture your ophthalmic drug products. However, your quality unit failed to have adequate supplier qualification procedures to ensure that the drug products received from your CMO were manufactured in compliance with CGMP prior to being distributed in the United States.

For example, our investigators observed that your firm identified several CGMP deficiencies with Brassica in September 2020, such as a failure to maintain raw testing data. Despite identifying these deficiencies, your firm qualified Brassica as an approved CMO. Furthermore, you requalified Brassica in 2023, without evaluating whether subsequent corrective actions and preventive actions adequately addressed the identified deficiencies.

Your firm’s quality unit released Lubricant PM Ointment for distribution without adequate procedures to ensure that the ophthalmic drug products produced for your firm met appropriate quality attributes.

In your response, you state that your procedures have been revised to assess CGMP findings of your CMOs, and that your Quality Assurance must evaluate corrective action and preventive action (CAPA) plans implemented by CMOs.

Your response is inadequate. While you have revised your procedures, you did not provide sufficient details on how you will assess findings that include CGMP deficiencies. Your procedure lacks a process for disqualifying CMOs or maintaining disqualification across product lines. Also, you did not propose evaluating the qualification status of your other CMOs.

In addition, you state that you will be comparing the data reported on the certificate of analysis (COA) against the pre-approved specification before releasing finished product. We note that your quality unit is ultimately responsible for ensuring that your drug products are manufactured in accordance with CGMP. Comparing a COA from a CMO to pre-approved specifications does not overcome your responsibility to evaluate, qualify, audit, and monitor your contract manufacturers. The suitability and competence of potential contractors should be assessed, based on quality risk management principles, before outsourcing operations, and should implement any needed improvements. Your firm should have a robust qualification process of your CMOs, commensurate with risk, ahead of making product disposition determinations based on a COA.

You are responsible for ensuring that the drugs you distribute are not adulterated and are manufactured in accordance with CGMP requirements.

Your firm failed to establish an adequate quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging materials, labeling, and drug products (21 CFR 211.22(a)).

Contract Testing Laboratories

Your quality unit (QU) did not exercise its responsibility to oversee your contract testing laboratory to ensure the appropriate finish product testing was being conducted. For example, you failed to ensure your contract testing laboratory completed the method validation protocol for (b)(4). The Method Validation Report did not identify potential impurities of (b)(4) referenced in the method validation protocol. You did not adequately ensure the executed test method was suitable to monitor all potential impurities.

In your response, you provided an impurity method that did not adequately identify and characterize the potential impurities of your drug products. Your response is inadequate because the method validation protocol should include all potential impurities with the scientific justification for which ones would be included in the test method. You did not commit to performing a retrospective assessment of all the product lots currently on the market within expiry once new method validations are completed.

In addition, your contract testing laboratory was conducting a single dissolution test point for your drug products without scientific justification that a single time point demonstrates a consistent drug absorption over an extended period of time.

Your response states that the **(b)(4)** label claims were removed. Your response is inadequate because you did not provide sufficient scientific justification to support inadequately testing your finished drug product.

Your firm's quality systems are inadequate. See the FDA's guidance document *Quality Systems Approach to Pharmaceutical CGMP Regulations* for help implementing quality systems and risk management approaches to meet the requirements of CGMP regulations 21 CFR, parts 210 and 211 at <https://www.fda.gov/media/71023/download>.

Contract Manufacturing Organizations

Your firm utilizes a contract manufacturing organization (CMO) to manufacture your prescription sterile **(b)(4)** drug product, **(b)(4)**. You stated to our investigators that you received a batch of **(b)(4)** from **(b)(4)**. You received this drug product without performing an evaluation of **(b)(4)**. You do not have adequate procedures to ensure that the sterile **(b)(4)** produced for your firm met appropriate quality attributes.

In your response, you provide documentation indicating that the CMO of **(b)(4)** is **(b)(4)** and provided documentation of an audit performed at this facility. Your response is inadequate because your QU did not ensure the drug product was manufactured in accordance with CGMP requirements.

Drugs must be manufactured in conformance with CGMP. FDA is aware that many drug manufacturers use independent contractors such as production facilities, testing laboratories, packagers, and labelers. FDA regards contractors as extensions of the manufacturer.

FDA sent an electronic request for records and other information pursuant to section 704(a)(4) of the FD&C Act, 21 U.S.C. 374(a)(4) to your CMO of **(b)(4)** Injection USP), **(b)(4)**. After multiple follow-up requests, your CMO failed to respond to these attempted communications or otherwise provide the requested records or other information. It is a prohibited act under section 301(e) of the FD&C Act (21 U.S.C. 331(e)) to refuse to permit access to or copying of any record as required by section 704(a). Because your CMO failed to respond to the section 704(a)(4) records requests and associated communication attempts, FDA placed all drugs and drug products manufactured by your CMO on Import Alert 66-79. Drugs manufactured by facilities on Import Alert 66-79 are subject to refusal of admission pursuant to section 801(a)(3) of the FD&C Act in that all drugs from their facility appear to be adulterated under section 501(j) because they have been manufactured, processed, packed, or held in any factory, warehouse, or establishment and the owner, operator or agent of such factory, warehouse, or establishment delays, denies, or limits an inspection, or refuses to permit entry or inspection.

You are responsible for the quality of your drugs regardless of agreements in place with your contract facilities. You are required to ensure that drugs are made in accordance with section 501(a)(2)(B) of the FD&C Act to ensure safety, identity, strength, quality, and purity.

Your QU did not provide adequate oversight for the manufacture of your products. For example, you stated that you could not provide records to support the CGMP requirements for the manufacture of drugs, including but not limited to the following:

- Finished product original release testing data
- Original stability testing data
- Sample collection and preparation
- Procedures for quality control data review (e.g., raw material, finished product release, and stability testing)
- Batch production and control record

In your response, you state that controls are being implemented to establish requirements for CGMP activities across operations and laboratory staff. Your response is inadequate. You failed to address the potential impacts on all drug product lots distributed to the United States that remain within expiry and were manufactured without documentation of testing performed.

In a previous warning letter (320-23-34), FDA cited similar CGMP violations. You proposed remediation and committed to conducting a full six-system audit with a qualified CGMP consultant in your response. Repeated failures demonstrate that executive management oversight and control over the manufacture of drugs is inadequate.

Your firm failed to establish an adequate quality unit and the responsibilities and procedures applicable to the quality control unit are not in writing and fully followed (21 CFR 211.22(a) and (d)).

The records and information you provided demonstrate that your quality unit (QU) did not effectively exercise its responsibilities to oversee the quality of your drug manufacturing operations. Specifically, your QU failed to:

- Ensure adequate control over laboratory data including deliberate alteration of original data to conceal out-of-specification results (21 CFR 211.194).
- Ensure that batch production and control records are complete (21 CFR 211.188)
- Ensure adequate specifications, sampling plans, and test methods for components and drug products to assure they conform to appropriate standards of identity, strength, quality and purity (21 CFR 211.160(b)).
- Ensure the establishment of a written testing program designed to assess the stability characteristics of drug products and to use the results of stability testing to determine appropriate storage conditions and expiration dates (21 CFR 211.166(a)).

In your response, you state that you will perform certain corrective actions upon resumption of production but acknowledge that you have limited ability to fully implement the proposed systemic changes across the facility. Your response is inadequate because you did not provide documentation in support of any proposed changes or commit to compliance with CGMP before resuming

operations. Furthermore, your response does not address the significant failures in data governance observed during our inspection.

Significant findings in this letter demonstrate that your firm does not operate an effective quality system in accordance with CGMP. In addition to the lack of effective management oversight of your production and laboratory operations, we found that your QU was not enabled to exercise proper authority and insufficiently implemented its responsibilities. Executive management should immediately and comprehensively assess your company's manufacturing operations to ensure that your systems, processes, and products meet CGMP.

You lacked a quality unit (QU) with appropriate oversight for the manufacture of your drug products, and you did not have written quality procedures. Your firm has one SOP that does not adequately govern quality processes for CGMP. For example, you failed to ensure the following:

- Investigation of any unexplained discrepancy or failure of a batch or any of its components to meet any specifications (21 CFR 211.192).
- Written records describing the evaluation of quality standards of each drug product at least annually to determine the need for changes in drug product specifications, manufacturing, or control procedures (21 CFR 211.180(e)).
- Failure to retain and store, under conditions consistent with product labeling, an appropriately identified reserve sample that is representative of each batch of drug product (21 CFR 211.170(b)).
- Establishment of written procedures describing the handling of all written and oral complaints regarding a drug product (21 CFR 211.198(a)).
- Establishment of a system by which the distribution of each lot of drug product can be readily determined to facilitate its recall if necessary (21 CFR 211.150(b)).
- Establishment of adequate batch production and control records that contain the accomplishment of each significant step in the manufacture, processing, packing, or holding of the batch, for each batch of drug product (21 CFR 211.188(b)).
- Establishment of an appropriate program for cleaning and maintenance of equipment (21 CFR 211.67(b)).
- Operators received adequate CGMP training for the production of OTC drug products (21 CFR 211.25(a)).

Your firm failed to establish adequate written responsibilities and procedures applicable to the quality control unit and to follow such written procedures (21 CFR 211.22 (d)).

You lacked adequate quality unit (QU) oversight for the manufacture of your OTC drug products. For example:

- You have not performed an annual product review (APR) of your OTC drug products manufactured since 2022.
- You failed to follow your procedure for raw material sampling, in that multiple different materials were held in the sampling area, which poses the risk of potential contamination and mix-ups.

An adequate QU overseeing all manufacturing operations is necessary to consistently ensure drug quality. Your firm's quality systems are inadequate. See FDA's guidance document Quality Systems Approach to Pharmaceutical CGMP Regulations at <https://www.fda.gov/media/71023/download> for help in implementing quality systems and risk management approaches to meet the requirements of CGMP regulations (21 CFR parts 210 and 211).

In your response, you commit to ensuring that procedures are followed and that programs are up to date and complete going forward.

Your response is inadequate. Although you commit to addressing the observations we identified, your response lacks sufficient details about the systemic remediations needed for your QU and your quality system.

You manufacture over-the-counter (OTC) oral liquid drug products including, but not limited to, analgesics and cough and cold products marketed for infants and children.

You failed to ensure adequate quality unit (QU) oversight for release of your OTC drug products. For example, your QU failed to follow your procedure Batch Record Review and Release for Distribution, SOP No. QA-009, Revision 01, and between April 2024 and May 2025, released numerous batches of drug products for distribution prior to reviewing all test results to ensure they met specifications.

Furthermore, your QU also failed to ensure that:

- each batch of drug products was tested for the strength of active ingredients prior to release (21 CFR 211.165(a))
- laboratory records included complete data derived from all tests necessary to ensure compliance with established specifications and standards (21 CFR 211.194(a))

In your response, you state you anticipated passing results based on historical data and process validation and "only two batches left [y]our facility without receiving passing microbial results." Your response is inadequate because you do not address how you plan to ensure your quality unit has sufficient resources to carry out its responsibilities and consistently ensure drug quality. Your response also lacks sound scientific justification with respect to routine batch manufacturing requirements for finished product testing. You also do not address the potential impact to drug products distributed within the United States that are within expiry.

An adequate QU overseeing all manufacturing operations is necessary to consistently ensure drug quality. Your firm's quality systems are inadequate.

Your quality unit (QU) failed to exercise adequate oversight over your contract testing operations. For example, your QU failed to adequately:

- Establish procedures for critical operations including responsibilities and procedures applicable to a QU, handling of deviations, change control, and cleaning procedures.
- Implement and follow adequate procedures for laboratory investigations.

In your response, you identify the lack of a quality management system as the root cause for this deficiency and commit to creating procedures for items noted above.

Your response is inadequate because you fail to assess the impact of your quality system deficiencies on the test data reported to your customers. You also fail to provide a comprehensive assessment and remediation plan of your quality systems to ensure they function effectively.

Your firm's quality systems are inadequate.

The records and information you provided demonstrate that you failed to implement written procedures to establish a quality unit (QU) with the CGMP responsibilities and authority to oversee the manufacture of your OTC drug products. For example, your response indicated there were no QU procedures for change control, customer complaints, annual product review, batch review, batch release or rejection, reprocessing and reworking, returns and salvaging, specifications, deviations, or corrective action and preventive action.

Based on FDA's review of records and information provided in response to our request, your firm's quality systems are inadequate. Please see FDA's guidance document Quality Systems Approach to Pharmaceutical CGMP Regulations for helpful information regarding implementing quality systems and risk management approaches to meet the requirements of CGMP regulations 21 CFR, parts 210 and 211 at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/quality-systems-approach-pharmaceutical-current-good-manufacturing-practice-regulations>.

Your QU failed to ensure the reliability and integrity of analytical testing data. For example, our investigators observed many torn and discarded original CGMP documents inside your main waste disposal area. These discarded original documents included, but were not limited to, analytical balance weighing printouts, pH meter printouts, and analytical method verification records. The discarded balance printouts were observed containing test weights that were different from those weights documented in testing of raw materials and finished products (including those intended for the U.S. market).

Additionally, during the evaluation of audit trail review for your MassLynx software, our investigator documented that your laboratory analysts performed hundreds of entries related to "Add/Modify/Delete peaks," and "Alter existing file on disk" user privileges between January 16, 2022, and January 23, 2025.

Data integrity is critical throughout the CGMP data lifecycle, including in the creation, modification, processing, maintenance, archival, retrieval, and transmission of data. Customers rely on the integrity of the laboratory data that you generate to make decisions regarding drug quality.

It is important to maintain strict control over electronic data to ensure that any additions, deletions, or modifications of information in your electronic records are authorized and appropriately documented.

In your response, you identify lack of quality oversight and lack of procedures for the proper control of CGMP documents as root causes for these deficiencies. You state that you are performing a protocol-based study to review the sample and system audit trails.

Your response is inadequate. You do not provide a scientific evaluation of whether discarded data may have caused reported test results to fail drug product specifications.

You lacked an adequate quality unit (QU) to provide oversight for the manufacture of your drug products. For example, you did not review, approve, or implement procedures for critical quality operations such as handling non-conformances, change control, training management, and handling out-of-specification events.

In your response, you commit to establishing and implementing quality oversight procedures.

Your response is inadequate. Although you commit to addressing the observations, your response lacks sufficient details about the systemic remediations needed for your QU and your quality system.