WARNING LETTER

Sanitor Corporation

MARCS-CMS 616232 — NOVEMBER 29, 2021

Delivery Method:

VIA EMAIL CONFIRMED DELIVERY

Product:

Drugs

Recipient:

Mr. Jon B. Robinson

President

Sanitor Corporation

8400 W. Cerritos Avenue
Stanton, CA 90680
United States

sanilex@hotmail.com (mailto:sanilex@hotmail.com)

Issuing Office:

Division of Pharmaceutical Quality Operations IV

United States

Dear Mr. Robinson:

The U.S. Food and Drug Administration inspected your drug manufacturing facility, Sanitor Corporation, FEI 3005871025, at 8400 W. Cerritos Avenue, Stanton, California, from May 25, 2021, to June 3, 2021.

This warning letter summarizes significant violations of Current Good Manufacturing Practice (CGMP) regulations for finished pharmaceuticals. See Title 21 Code of Federal Regulations (CFR), parts 210 and 211 (21 CFR parts 210 and 211).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug products 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).

Your firm manufactures **(b)(4)** and **(b)(4)** drug products to bleach and/or lighten the skin. These products are unapproved new drugs in violation of section 505(a) of the Federal Food & Cosmetic Act (FD&C Act,) 21 U.S.C. 355(a). Introduction or delivery for introduction of such products into interstate commerce is prohibited under section 301(d) of the FD&C Act, 21 U.S.C. 331(d). In addition, **(b)(4)** is a misbranded drug under section 502(c) of the FD&C Act, 21 U.S.C. 352(c). Introduction or delivery for introduction of such products into interstate commerce is prohibited under section 301(a) of the FD&C Act, 21 U.S.C. 331(a). These violations are described in more detail below.

In addition, **(b)(4)** (Hydroquinone **(b)(4)**), **(b)(4)** (Hydroquinone **(b)(4)**), and **(b)(4)** (Hydroquinone **(b)(4)**) are not listed with FDA as required by section 510(j) of the FD&C Act. Failure to properly list a drug product is prohibited and will render a drug misbranded under 21 U.S.C. 331(p), 352(o). Introduction or delivery for introduction of such products into interstate commerce is prohibited under section 301(a) of the FD&C Act, 21 U.S.C. 331(a). These violations are described in more detail below.

We reviewed your June 24, 2021, response to our Form FDA 483 in detail and acknowledge receipt of your subsequent correspondence. Your response is inadequate because it did not provide sufficient detail or evidence of corrective actions to bring your operations into compliance with CGMP.

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

1. 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).

Inadequate investigations/Lack of process control

You contract manufacture over-the-counter drug products including benzalkonium chloride-based hand sanitizer.[1] Multiple batches of hand sanitizer drug product failed microbial total plate count (TPC) testing with results of Too Numerous to Count (TNTC). Your quality unit (QU) failed to adequately investigate and identify the root cause for the microbial contamination in your hand sanitizer drug product. Instead of conducting a thorough investigation and implementing corrective action to prevent contamination, your QU:

- Approved the addition of an antimicrobial preservative to batches that initially failed microbial TPC testing, and were then released for distribution by your customer; and
- Approved the addition of an antimicrobial preservative to batches not yet tested for microbial TPC so that they would yield a passing result, and were released for distribution by your customer.

Additionally, stability samples of a batch of hand sanitizer drug products (previously released without the addition of the preservative) failed the three-month stability test interval for microbial TPC with a result of TNTC. You stated that you notified the customer and recommended a voluntary recall of the drug product. Your customer declined to do so and informed you that the lot was sold and consumed. No further actions were taken.

In your response, you stated that you have performed a management review with your consultant and determined that your procedures were "inadequately robust and/or detailed." Your response is inadequate in part, because you did not provide a thorough investigation into the microbial failures. You also did not provide adequate details of your consultant's review and remedial actions. Further, your QU did not exercise its duties and oversight to ensure that future investigations are thorough, including root cause determination and appropriate corrective action strategies.

In response to this letter, provide the following:

- A comprehensive, independent assessment of your overall system for investigating deviations, discrepancies, complaints, out-of-specification results, and failures. Provide a detailed action plan to remediate this system. Your action plan should include, but not be limited to, significant improvements in investigation competencies, scope determination, root cause evaluation, corrective action and preventive action (CAPA) effectiveness, QU oversight, and written procedures. Address how your firm will ensure all phases of investigations are appropriately conducted.

- Complete investigations into all batches with potential objectionable microbial contamination or an out-of-specification microbiological result (whether or not later invalidated). The investigations should detail your findings regarding the root causes of the contamination.

- An independent assessment and remediation plan for your CAPA program. Provide a report that evaluates whether the program includes effective root cause analysis, ensures CAPA effectiveness, analyzes investigation trends, improves the CAPA program when needed, implements final QU decisions, and is fully supported by executive management.

Approving shipment of drug products before adequate review

Your QU approved drug products for distribution without complete finished product testing. For example, your firm shipped hand sanitizer batch **(b)(4)** to your customer on June 1, 2020. However, the analytical results were only available as of on June 3, 2020, and the microbiological results were received on June 8, 2020. Your QU approved the certificate of analysis on June 3, 2020, before receiving the microbiological test results and after the batch was shipped to your customer.

In your response, you stated that you would "transfer" unreleased finished products to your customers under a verbal agreement that the products would not be distributed into interstate commerce until the batch was approved and released by your QU. This practice is unacceptable and increases the risk that drug products that do not meet their quality attributes are distributed to consumers. Complete testing of each batch of drug product before release is required to determine if the drug products you manufacture meet appropriate specifications.

In response to this letter, provide an independent retrospective review of all hand sanitizer drug products you manufactured to ensure no failing products were distributed. If the review reveals substandard quality drug products were distributed, take rapid corrective actions, such as notifying customers and product recalls.

Inadequate stability program

Your QU lacked adequate quality oversight over your stability program. For example, you failed to follow your *Package Compatibility Test Program* procedure, and place **(b)(4)** of each product on **(b)(4)** stability testing to represent the product and process for your hydroquinone **(b)(4)** drug products.

In your response, you indicated that the formulation for your hydroquinone **(b)(4)** drug products is packaged into **(b)(4)** different products and that all such products were initially placed on stability. Further, you noted that because the formulation, the packaging size, and the material of construction is the same for the **(b)(4)** products, you are using a bracketing design to conduct the **(b)(4)** stability testing. However, your response indicated different container closure system designs. Therefore, the bracketing design does not appear scientifically justified. Additionally, this change to add a bracketing approach to your stability program for these products was implemented without adequate change control.

In response to this letter, provide the following:

- A comprehensive, independent assessment and CAPA plan to ensure the adequacy of your stability program. Your remediated program should include, but not be limited to:
  - Stability studies for each drug product in its marketed container-closure system before distribution is permitted
  - Stability-indicating methods
  - An ongoing program in which representative batches of each product are added each year to the program to determine if the shelf-life claim remains valid
  - Detailed definition of the specific attributes to be tested at each station (timepoint)

- All procedures that describe these and other elements of your remediated stability program.

- A list of expiration dates, with associated justification, for all drug products (e.g., 3 years of real time stability data).

Inadequate quality oversight over documentation

During the review of a batch record for your **(b)(4)** hydroquinone **(b)(4)** drug product, batch **(b)(4)**, our investigators noted that production activities were not recorded contemporaneously. For example, the batch record documented that one employee performed multiple manufacturing steps, such as measuring containers and bulk reconciliation on two separate dates, and a second employee documented the verification of the activities. However, the second employee (verifier) stated to our investigator that they were not at work when these steps were documented as being performed. Your QU oversight does not provide adequate assurance that manufacturing records are accurate, and that production was performed as documented.

In your response, you acknowledge that good documentation practices were not followed. You also stated that you performed training of all personnel. Your response is inadequate. Your quality system has not adequately ensured the accuracy and integrity of the data to support the safety, effectiveness, and quality of the drugs you manufacture. Without accurate records, you cannot assure appropriate decisions regarding batch release, product stability, and other matters that are fundamental to the ongoing assurance of quality.

In response to this letter, provide a complete assessment of documentation systems used throughout your manufacturing and laboratory operations to determine where documentation practices are insufficient. Include a detailed CAPA plan that comprehensively remediates your firm's documentation practices to ensure you retain attributable, legible, complete, original, accurate, contemporaneous records throughout your operation.

The examples above demonstrate the fundamental failure of your QU to perform its roles and responsibilities, but not limited to, oversight over process control, investigation handling, batch review and disposition, and appropriate control of data.

In response to this letter, provide the following:

- 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:
  - A determination of whether procedures used by your firm are robust and appropriate
  - Provisions for QU oversight throughout your operations to evaluate adherence to appropriate practices
  - A complete and final review of each batch and its related information before the QU disposition decision

- Oversight and approval of investigations and discharging of all other QU duties to ensure identity, strength, quality, and purity of all products. Also, describe how top management supports quality assurance and reliable operations, including but not limited to, timely provision of resources to proactively address emerging manufacturing/quality issues and to assure a continuing state of control.

On September 20, 2021, FDA held a teleconference with you and your consultant. We recommended that you consider removing all of your firm's hand sanitizer drug products within expiry that were manufactured under the conditions referenced in this letter. On September 21, 2021, you voluntary recalled certain batches of hand sanitizer drug products. On September 22, 2021, FDA notified the public of your lack of adequate controls to prevent microbial contamination at https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-hand-sanitizers-consumers-should-not-use.

See 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.

2. Your firm failed to establish laboratory controls that include scientifically sound and appropriate specifications, standards, sampling plans, and test procedures designed to assure that components, drug product containers, closures, in-process materials, labeling, and drug products conform to appropriate standards of identity, strength, quality, and purity (21 CFR 211.160(b)).

You released and distributed multiple reworked batches and newly reformulated batches of your hand sanitizer drug product, without demonstrating the antimicrobial effectiveness testing of the preservative added to the product formulation. Specifically, a batch of your hand sanitizer drug product failed microbial TPC during bulk stage release testing with a result of TNTC. You reworked this batch by adding an antimicrobial preservative. Your deviation report stated that preservative adds microbial stability while not affecting the benzalkonium assay.

In your response, you stated that you submitted a sample to your contract testing lab to perform antimicrobial effectiveness testing on your hand sanitizer drug product and the results provide evidence of the effectiveness of the addition of the preservative to the formulation.

Your response is inadequate. You did not provide complete laboratory data from your contract laboratory. As per USP <51>, antimicrobial preservatives should not be used as a substitute for good manufacturing practices or solely to reduce the viable microbial population of a nonsterile drug product.

In your response to this letter, provide the following:

- A comprehensive, independent assessment of the design and control of your firm's manufacturing operations, with a detailed and thorough review of all microbiological hazards.

- A detailed risk assessment addressing the hazards posed by distributing drug products with potentially objectionable contamination. Specify actions you will take in response to the risk assessment, such as customer notifications and product recalls.

- Appropriate microbiological batch release specifications (i.e., total counts, identification of bioburden to detect objectionable microbes) for each of your drug products.

- A comprehensive, independent assessment of your laboratory practices, procedures, methods, equipment, documentation, and analyst competencies. Based on this review, provide a detailed plan to remediate and evaluate the effectiveness of your laboratory system.

- An assessment of each drug product 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.

- A detailed summary of your validation program for ensuring a state of control throughout the product lifecycle, along with associated procedures. Describe your program for process performance qualification, and ongoing monitoring of both intra-batch and inter-batch variation to ensure a continuing state of control.

- A timeline for performing appropriate process performance qualification for each of your marketed drug products.

- Your process performance protocol(s), and written procedures for qualification of equipment and facilities.

3. Your firm failed to exercise 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)).

Your **(b)(4)** Fourier Transform Infrared (FTIR) Spectroscopy computerized system did not have appropriate controls in place to prevent deletion of raw laboratory data. Specifically, this data is used to create an internal certificate of analysis to release drug components for drug product manufacturing. Further, you did not have appropriate password protection of your software to prevent unauthorized access to data.

In your response, you stated that you have password-protected the software for the FTIR system and only the chemist has access to the data. You also stated that the FTIR data is backed up **(b)(4)** to an external hard drive and a copy is printed and included as part of the raw material test data package.

Your response is inadequate as it did not provide a retrospective review of the integrity of your FTIR, details regarding instrument audit trails and an evaluation of the effectiveness of the computerized system change. It is important to maintain strict controls over CGMP electronic data to ensure all additions, deletions, or modifications of information in your electronic records are authorized and properly documented. Without complete and accurate records, you cannot make appropriate decisions about batch release, stability, and other fundamental factors for ongoing quality assurance.

Your quality system does not adequately ensure the accuracy and integrity of data to support the safety, effectiveness, and quality of the drugs you manufacture. See FDA's guidance document Data Integrity and Compliance With Drug CGMP for guidance on establishing and following CGMP compliant data integrity practices at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/data-integrity-and-compliance-drug-cgmp-questions-and-answers-guidance-industry.

In response to this letter, provide the following:

- Comprehensive investigation into the extent of the inaccuracies in data records and reporting, including results of the data review for drugs distributed to the United States. Include a detailed description of the scope and root causes of your data integrity lapses.

- A current risk assessment of the potential effects of the observed failures on the quality of your drugs. Your assessment should include analyses of the risks to patients caused by the release of drugs affected by a lapse of data integrity and analyses of the risks posed by ongoing operations.

- A management strategy for your firm that includes the details of your global CAPA plan. The detailed corrective action plan should describe how you intend to ensure the reliability and completeness of all data generated by your firm including microbiological and analytical data, manufacturing records, and all data submitted to FDA.

Unapproved New Drug Violations

(b)(4) and **(b)(4)** are drugs as defined by section 201(g)(1)(B) of the FD&C Act, 21 U.S.C. 321(g)(1)(B), because they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease and/or under section 201(g)(1)(C) of the FD&C Act, 21 U.S.C. 321(g)(1)(C), because they are intended to affect the structure or any function of the body. Specifically, these products are intended for use as skin bleaching products.

Examples of the claims observed on your product labels that provide evidence of the intended uses (as defined in 21 CFR 201.128) of your products include, but may not be limited to, the following:

- **(b)(4)**

"Indicated for the depigmentation of dark areas of the skin such as age spots, liver spots, freckles, and other unwanted areas of melanin hyperpigmentation."

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"Indicated for the depigmentation of dark areas of the skin such as age spots, liver spots, freckles, and other unwanted areas of melanin hyperpigmentation."

- **(b)(4)**

"[I]ndicated for the gradual lightening of hyperpigmented skin conditions, such as chloasma, melasma, freckles, senile lentigines, and other unwanted areas of melanin hyperpigmentation."

- **(b)(4)**

"Indications: Skin lightener"

- **(b)(4)**

"Indications Skin lightener"

- **(b)(4)**

"Indications Skin lightener"

All skin bleaching drug products, whether currently labeled as prescription or nonprescription, are considered new drugs as defined in section 201(p)(1) of the FD&C Act.[2] New drugs may not be legally marketed in the United States absent FDA approval of an application filed in accordance with section 505(a) of the FD&C Act, 21 U.S.C. 355(a). Because no FDA-approved applications are in effect these products, the current marketing of these products violate section 505(a) of the FD&C Act, 21 U.S.C. 355(a). Introduction or delivery for introduction of such products into interstate commerce violates section 301(d) of the FD&C Act, 21 U.S.C. 331(d).

Misbranding Violations

In addition, **(b)(4)** is misbranded under section 502(c) of the FD&C Act, 21 U.S.C. 352(c). Introduction or delivery for introduction of such products into interstate commerce is prohibited under section 301(a) of the FD&C Act, 21 U.S.C. 331(a). This violation is described in more detail below.

(b)(4) is a "drug" as defined by section 201(g)(1)(B) of the FD&C Act, 21 U.S.C. 321(g)(1)(B), because it is intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, and/or under section 201(g)(1)(C) of the FD&C Act, 21 U.S.C. 321(g)(1)(C), because it is intended to affect the structure or any function of the body. Specifically, this product is intended for the treatment of acne.

Examples of claims observed on the **(b)(4)** product label and/or labeling that provide evidence of the intended use (as defined in 21 CFR 201.128) of the product include, but may not be limited to, the following:

"Helps to unclog pores with deep cleaning action to prevent future breakouts . . . Drug Facts .... Purpose: Acne Treatment."

(b)(4) is misbranded within the meaning of section 502(c) of the FD&C Act, 21 U.S.C. 352(c), because the label fails to bear a statement of identity as required under 21 CFR 201.61. The label for this product fails to include the established name and general pharmacological category(ies) or principal intended action(s) of the product. For example, the principal display panel should bear "0.5% Salicylic Acid Acne Treatment."

The introduction or delivery for introduction of a misbranded drug into interstate commerce is prohibited under section 301(a) of the FD&C Act, 21 U.S.C. 331(a).

Registration and Listing Misbranding Violations

(b)(4) (Hydroquinone **(b)(4)**), **(b)(4)** (Hydroquinone **(b)(4)**), and **(b)(4)** (Hydroquinone **(b)(4)**) are "drugs" as defined by section 201(g)(1)(B) of the FD&C Act, 21 U.S.C. 321(g)(1)(B), because they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease, and/or under section 201(g)(1)(C) of the FD&C Act, 21 U.S.C. 321(g)(1)(C), because they are intended to affect the structure or any function of the body. Specifically, these products are intended for lightening of skin pigmentation.

Examples of claims observed on the **(b)(4)**, **(b)(4)**, and **(b)(4)** product label and labeling that provide evidence of the intended use (as defined in 21 CFR 201.128) of the products include, but may not be limited to, the following:

“indicated for the gradual bleaching of hyperpigmented skin conditions such as chlosma, melasma, freckles, senile lentigines and other unwanted areas of melanin hyperpigmentation.”

Under section 510 of the FD&C Act, as amended, and 21 CFR Part 207, all drugs manufactured, prepared, propagated, compounded, or processed for U.S. commercial distribution must be listed with FDA (see 21 U.S.C. 360(j)(1) and 21 CFR 207.41). Current drug listing submissions for **(b)(4)** for “Balancer” (NDC **(b)(4)**) and “Skin Lightener (NDC **(b)(4)**) fail to include Sanitor Corporation as the manufacturing establishment for these products. In addition, these two drug listing submissions, and a third drug listing submission for **(b)(4)** (NDC **(b)(4)**) reference private label distributor’s drugs. Each registrant must list each drug it manufactures, repacks, or relabels for commercial distribution under the trade name or label of a private label distributor using an NDC that includes such private label distributor's labeler code (21 CFR 207.41(c)(1)) AND each registrant must list each human drug it manufactures, repacks, or relabels using an NDC that includes the registrant's own labeler code, regardless of whether the drug is commercially distributed under the registrant's own label or trade name or under the label or trade name of a private label distributor (21 CFR 207.41(c)(2)). Your firm’s failure to fulfill its drug listing obligations for **(b)(4)** (Hydroquinone **(b)(4)**), **(b)(4)** (Hydroquinone **(b)(4)**), and **(b)(4)** (Hydroquinone **(b)(4)**) misbrands these products under section 502(o) of the FD&C Act.

The introduction or delivery for introduction of a misbranded drug into interstate commerce is prohibited under section 301(a) of the FD&C Act, 21 U.S.C. 331(a).

Ineffective Quality System

Your executive management oversight and control over the manufacture of drugs is inadequate. Your executive management remains responsible for fully resolving all deficiencies and ensuring ongoing CGMP compliance. You should immediately and comprehensively assess your company’s manufacturing operations to ensure that systems, processes, and the products manufactured conform to FDA requirements.

Responsibilities as a Contractor

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. You are responsible for the quality of drugs you produce as a contract facility regardless of agreements in place with product owners. You are required to ensure that drugs are made in accordance with section 501(a)(2)(B) of the FD&C Act for safety, identity, strength, quality, and purity. See FDA’s guidance document Contract Manufacturing Arrangements for Drugs: Quality Agreements at https://www.fda.gov/media/86193/download.

CGMP Consultant Recommended

We acknowledge the statement in your response dated June 24, 2021, that you have retained a consultant who is knowledgeable and experienced in CGMP compliance issues with pharmaceuticals, medical devices, cosmetics, and dietary supplements. However, based upon the nature of the violations we identified at your firm, we strongly recommend engaging a consultant, as set forth in 21 CFR 211.34, with at minimum, appropriate CGMP expertise in overall quality risk management, data integrity, and investigations to assist your firm in meeting CGMP requirements. Your use of a consultant does not relieve your firm’s obligation to comply with CGMP. Your firm’s executive management remains responsible for resolving all deficiencies and systemic flaws to ensure ongoing CGMP compliance.

Conclusion

Correct any violations promptly. Failure to promptly and adequately address this matter may result in regulatory or legal action without further notice including, without limitation, seizure, and injunction. Unresolved violations may also prevent other Federal agencies from awarding contracts.

Failure to address violations may also cause FDA to withhold issuance of Export Certificates. FDA may withhold approval of new applications or supplements listing your firm as a drug manufacturer until any violations are completely addressed and we confirm your compliance with CGMP. We may re-inspect to verify that you have completed corrective actions to address any violations.

This letter notifies you of our findings and provides you an opportunity to address the above deficiencies. After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done to address any violations and to prevent their recurrence. In response to this letter, you may provide additional information for our consideration as we continue to assess your activities and practices. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Your written response should reference unique identifier CMS 616232 and sent electronically to ORAPharm4_Responses@fda.hhs.gov, or mailed to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV
19701 Fairchild Road
Irvine, CA 92612-2506

If you have any questions regarding this letter, please contact William V. Millar, Compliance Officer, via email at william.millar@fda.hhs.gov or by phone at (503) 671-9711 Ext. 30.

Sincerely,
/s/
CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV

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1. See, e.g., Temporary Policy for Preparation of Certain Alcohol-Based Hand Sanitizer Products During the Public Health Emergency (COVID-19). Because your benzalkonium chloride-based hand sanitizer is not consistent with the formulations in these guidances, it does not fall within any temporary Agency policy not to take action against firms manufacturing hand sanitizer products for violations of section 505 of the FD&C Act.

2. Prior to September 23, 2020, certain drug products intended for skin bleaching, including products that contained 2% or less of hydroquinone, were subject to ongoing over-the-counter (OTC) drug rulemaking. However, beginning on September 23, 2020, all skin-bleaching products that were previously the subject of OTC drug rulemaking are deemed to be a new drug(s) as defined in section 201(p)(1) of the FD&C Act. (See 21 U.S.C. 355G(a)(4). Also see 71 FR 51146.)

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