



HEALTH AND HUMAN SERVICE

DEPARTMENT OF

Public Health Service

94642d

Food and Drug Administration
Kansas City District
Southwest Region
11630 West 80th Street
Lenexa, Kansas 66214-3340

Telephone: (913) 752-2100

March 23, 2004

**CERTIFIED MAIL
RETURN RECEIPT REQUESTED**

WARNING LETTER

Ref. KAN-2004-05

Mr. John C. Brereton, President
Consolidated Chemical, Inc.
dba Care-Tech Laboratories, Inc.
3224 South Kingshighway Blvd.
St. Louis, MO 63139

Dear Mr. Brereton:

During a November 17 - December 2, 2003, inspection of your pharmaceutical manufacturing facility, located at 3224 S. Kingshighway, St. Louis, Missouri, an Investigator from this office documented serious deviations from current Good Manufacturing Practice (cGMP) regulations as delineated in Title 21, Code of Federal Regulations, Parts 210 and 211.

The inspection revealed your firm's Quality, Production, and Laboratory Control systems employed during the manufacture, processing, packing, or holding of your firm's antimicrobial cleansers and over-the-counter topical drug products (used for severe dermal conditions and topical infections), do not conform to cGMP. Therefore, these drug products are adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act). The following are examples of the significant deficiencies regarding your firm's systems. These deficiencies were included on the Form FDA-483, List of Inspectional Observations, presented to you on December 2, 2003.

1. Failure to have a quality control unit that has the responsibility and authority to approve or reject all components, in-process materials, drug products, and all procedures or specifications impacting on the identity, strength, quality, and purity of the drug products [21 CFR 211.22], as demonstrated by:
 - A. The failure to thoroughly investigate batch failures [21 CFR 211.192]. For example, no investigation or an incomplete investigation was conducted/documentated in the following:

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- i. Tech 2000 Dental Rinse, Lots 2414 and 2402, failed initial microbiological testing. Retests with different samples were performed with passing results and no investigations were conducted or documented. The entire Lot 2402 was subsequently distributed. Lot 2414 showed heavy microbiological contamination towards the end of the run. Cases ██████ were rejected and cases ██████ were released and distributed.
- ii. Care-Crème Antimicrobial Transdermal Cream, Lots 2160 and 2164; and Techni-Care Surgical Scrub, Lot 2182, failed active ingredient assay testing. Lots were released and distributed. An investigation was not conducted or documented.
- iii. Tech 2000 Dental Rinse, Lots 2231, 2371, 2374, and 2375 had microbiological contamination. Failure investigations were not conducted or documented for these lots. In addition, the first ██████ cases of Lot 2231 (out of ██████ cases total), were released and the rest of the lot was rejected due to "staph contamination."

B. Drug products failing to meet established specifications were not rejected [21 CFR 211.165(f)]. For example:

- i. Techni-Care Surgical Scrub, Lot 2182 and Care-Crème Antimicrobial Transdermal Cream Lots 2160 and 2164 had out of specification test results for the assay of active ingredient, Chloroxylenol Chloride (PCMX).
- ii. Tech 2000 Dental Rinse, Lots 2248, 2387, 2388, 2391, and 2394 had out of specification test results for pH.
- iii. Techni-Care Surgical Scrub, Lots 2295, 2339, 2358, 2362, and 2364 had out of specification test results for specific gravity.
- iv. Care-Crème Antimicrobial Transdermal Cream, Lots 2284 and 2333, and Techni-Care Surgical Scrub, Lot 2361 had out of specification test results for viscosity.

C. The failure to establish appropriate written procedures designed to prevent objectionable microorganisms in drug products not required to be sterile [21 CFR 211.113(a)].

2. Written procedures are not established for production and process controls designed to assure that the drug products have the identity, strength, quality and purity they purport or are represented to possess [21 CFR 211.100(a)]. For example, process validation has not been conducted for Tech 2000 Dental Rinse and Techni-Care Surgical Scrub.

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3. Written procedures are not established for reprocessing batches that do not conform to standards or specifications and the steps to be taken to ensure that the reprocessed batches will conform with all established standards, specification, and characteristics [21 CFR 211.115(a)]. For example, there are no new manufacturing directions or validation studies for the "pasteurization" procedure used to reprocess batches of Tech 2000 Dental Rinse to determine the effects on all quality attributes of the product. This "pasteurization" procedure is used when Tech 2000 Dental Rinse lots fail microbial testing.
4. Cleaning methods and procedures for equipment and utensils are inadequate to prevent objectionable contamination that would alter drug products beyond established requirements [21 CFR 211.67(a)]. Specifically, cleaning procedures have not demonstrated that the cleaning of manufacturing and filling equipment was effective to reduce product residues and objectionable microorganisms to an acceptable level. This observation was also made during the January 2000 establishment inspection.
5. Testing methods are not established to meet proper standards of accuracy and reliability as applied to the product tested, and the suitability of all testing methods used are not verified under actual conditions of use [21 CFR 211.194(a)(2)]. For example, your firm has not evaluated the HPLC method used in assaying Cetylpyridinium Chloride (PCMX) in Tech 2000 Dental Rinse, to assure that it meets proper standards of accuracy and reliability, or that the test method was verified under actual conditions of use. Identification and assay methods for Cetylpyridinium Chloride Topical Solution are contained in the current revision of the United States Pharmacopoeia (USP 27).
6. Stability testing is not consistently performed at the scheduled intervals in accordance with your written stability program [21 CFR 211.166(a)(1)]. For example, the following lots stored at room temperature were not tested at all scheduled intervals:
 - A. Techni-Care Surgical Scrub: Lot 2256 was not tested at 12 months; Lot 2291 was not tested at 9 months; Lot 2326 was not tested at 6 months; and Lot 2362 was not tested at 3 months.
 - B. Tech 2000 Dental Rinse: Lot 2257 was not tested at 12 months; and Lot 2297 was not tested at 9 months.

We also note that you are using municipal water (that passes through a one micron filter and into an XXXXXXXXXX water treatment device) to manufacture pharmaceutical drug products and to clean manufacturing equipment and filling lines. Water used in the manufacture of

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pharmaceutical drug products should be Purified Water, as defined in the United States Pharmacopoeia (USP). 21 CFR 211.84. For additional information, please refer to USP 27 *General Notices and Requirements, Ingredients and Processes, Water*, and USP informational chapter <1231>, *Water for Pharmaceutical Purposes*. The USP requires that Purified Water be monitored for Total Organic Carbon (TOC) and conductivity. Your records (i.e., CCQC39.0, QC Methods for Determination of Water Quality and CCQC40.1, QC Methods for Total Coliform Determination in Batch Processing Water) do not indicate that tests for TOC or conductivity are conducted. Please provide a response on what measures you have or will take to assure that the water used in your facility meets the requirements for Purified Water.

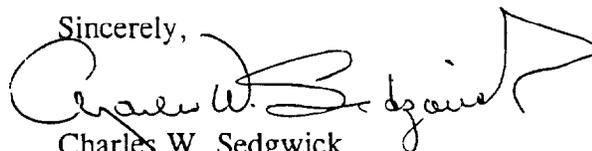
This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure that your firm adheres to all current regulations applicable to your operations. Compliance with cGMPs is dependent on having control systems in place and minimizing, if not eliminating, process variations.

You should know that these serious violations of the law may result in FDA taking regulatory action without further notice to you. These actions include, but are not limited to, seizure and/or obtaining a court ordered injunction against further marketing of your pharmaceutical products.

It is necessary for you to take action on this matter now. Please notify this office in writing within fifteen (15) working days from the date you received this letter. Your response should specifically identify the actions you are taking to correct the violations and provide specific timeframes for achieving compliance.

Your reply should be sent to Nadine Nanko Johnson, Compliance Officer, at the above address.

Sincerely,



Charles W. Sedgwick
District Director
Kansas City District