



DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration
Cincinnati District Office
Central Region
6751 Steger Drive
Cincinnati, OH 45237-3097
Telephone: (513) 679-2700
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April 2, 2001

**CERTIFIED MAIL
RETURN RECEIPT REQUESTED**

**WARNING LETTER
CIN-WL-01-4323-0**

Oscar Robertson, CEO and President
ORCHEM Corporation
4293 Mulhauser Road
Fairfield, Ohio 45014

Dear Mr. Robertson:

This letter concerns *E-2 SANITIZING HAND SOAP* manufactured and marketed by your firm for over-the-counter (OTC) topical antimicrobial use. On August 14-15, 2000 and September 18, 2000 the Food and Drug Administration (FDA) inspected your firm at the above address. During that inspection, our Investigator obtained copies of the immediate container label, promotional labeling, production and laboratory records, and information pertaining to the formulation, manufacturing, and testing of this product

Based on the label, which includes such terms as, "sanitizing," and such statements as, "This formulation effectively reduces bacterial flora of the skin," *E-2 SANITIZING HAND SOAP* is intended to kill or reduce the number of microorganisms on the skin and thereby prevent diseases that may be caused by those organisms. According to the information and records obtained during the inspection noted above, this product contains "BTC 2125M" or benzalkonium chloride as the active antimicrobial ingredient. Thus, this product is a "drug" as defined by section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act).

From the information and records obtained during the inspection noted above, *E-2 SANITIZING HAND SOAP* is a "new drug" as defined by section 201(p) of the Act and its marketing violates section 505(a) of the Act because there is no approved new drug application (NDA) for this product. In this regard, your firm's specification for the concentration of "BTC 2125M" or benzalkonium chloride in the finished product is 2.70 ± 0.20 percent. According to the information and records obtained during the inspection, this product actually contains benzalkonium chloride at a concentration of 2.55 to 3.77 percent. When diluted for use as

directed by the label (i.e., 5 cc of product in 15 cc of water) the resulting concentration of this ingredient is 0.638 to 0.943 percent. Since we are not aware of any data establishing general recognition of safety and effectiveness for this product under these labeled conditions for use, *E-2 SANITIZING HAND SOAP* is an unapproved "new drug" as noted above. In the absence of an approved NDA to establish the adequacy of the current directions for use, this product is further misbranded under section 502(f)(1) of the Act.

For your information, *E-2 SANITIZING HAND SOAP* is not being considered under FDA's OTC Drug Review, because we are not aware of a product so formulated and labeled having ever been commercially marketed before the Review began. Benzalkonium chloride-containing antimicrobial cleansers are generally deferred to the Review, but are limited to use-dilutions of 0.13 percent.

We note that the label for *E-2 SANITIZING HAND SOAP* does not disclose the name of the active antimicrobial ingredient. Thus, this product is misbranded under section 502(e) of the Act. This product is further misbranded under section 502(a) of the Act, as described under Title 21 of the Code of Federal Regulations, Part 201.17 (21 CFR 201.17), in that the label does not bear an expiration date. Absent appropriate stability data showing that this product is stable for at least three years, *E-2 SANITIZING HAND SOAP* is not exempt from the requirement to bear an expiration date as described by 21 CFR 211.137(h). Based on information obtained during the inspection noted above, your firm does not have such data.

During the FDA inspection of your drug manufacturing facility our investigators also documented serious deviations from the Current Good Manufacturing Practice Regulations (Title 21 Code of Federal Regulations, Parts 210 and 211). These deviations cause your drug product, *E-2 SANITIZING HAND SOAP* to be adulterated within the meaning of section 501(a)(2)(B) of the Act. The deviations observed include:

Failure to validate the performance of those manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug process. There is no documentation that the manufacturing process for your hand sanitizer will consistently produce product to predetermined specifications. The manufacturing process has not been validated. Of eight lots manufactured one (lot #80952878) exceeded your percent active ingredient (benzalkonium chloride), seven lots exceeded your firm's viscosity specifications, two lots were outside of the specific gravity specification and one lot was outside the limit for pH.

The cleaning process used in non-dedicated manufacturing equipment has not been validated to assure that cross-contamination is minimized. In addition, equipment cleaning and use logs are not maintained for non-dedicated equipment used to process and package your hand sanitizer drug product.

Failure to have any information which would establish stability for the intended period of use of the hand sanitizer. There is no written testing program designed to assess the stability characteristics of the hand sanitizer and no stability tests have been performed to determine an appropriate expiration date for the hand sanitizer to assure that the drug product meets applicable

standards of identity, strength, quality, and purity at the time of use. Your firm has no stability data to justify the 12-month shelf life listed in the Formula Master dated 4/28/99. Management at your firm stated that the 12-month shelf life for the product was arbitrarily chosen.

Failures to assure that components used to manufacture your hand sanitizer are tested to determine conformance with appropriate specifications for purity, strength and quality. Raw material used to manufacture your hand sanitizer are not tested prior to release for use by Quality Control nor are they retested after extended storage. In addition, for components for which a Certificate of Analysis (COA) is received, no identity test is performed and the reliability of COA is not periodically verified.

Failure to assure that in-process and finished drug products are examined and tested to assure that they conform to specifications. For example, no identification or efficacy testing is performed on the finished product. In process testing of bulk drug product from the mixing tank for strength and viscosity are performed using non-validated methodologies.

Failure to establish and maintain adequate batch production and control records for each batch of hand sanitizer including documentation that each significant step in the manufacture, processing, packing, or holding of the batch was accomplished at the time of performance. The mixing/blending records are discarded and only the bill of materials containing hand written quality control tests results are retained. In addition, the bill of materials contain numerous cross-outs which are not initialed and dated and the records are not always initialed and dated as having been reviewed by a second person. Batch yield calculations are not documented in the batch record and batch yields are not always determined.

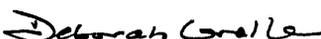
Failure to establish and maintain adequate master production and control records for the drug product in order to assure uniformity from batch to batch. Master production and control records are not independently checked, dated and signed by a second person and there is no written procedure for their preparation. Product specification changes are not controlled. For example, the Quality Assurance Summary record lists the viscosity specification for your hand sanitizer as 600-3000cps while the formula master indicates it is 600-1000cps.

Failure to establish written procedures designed to assure that your drug product has the identity and strength it purports or is represented to possess. There are no written procedures for reprocessing lots of product that do not meet in-process specification. Also, there are no written procedures for investigating out-of-specification results.

The violations described above are not meant to be all-inclusive. It is your responsibility to ensure that all drug products manufactured and distributed by your firm comply with the Act. Federal agencies are advised of the issuance of all Warning Letters pertaining to drugs so that they may take this information into account when considering the award of contracts. We request that you take action immediately to correct these violations. Failure to do so may result in regulatory action without further notice and may include seizure and/or injunction.

Please respond to this office in writing within fifteen (15) working days of receipt of this letter. Your response should describe the specific actions you will take, or have taken, to correct the violations described above. Your response should also include an explanation of each step being taken to prevent recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days state the reason for the delay and the time within which corrections will be completed. Send your response to Evelyn D. Forney, Compliance Officer, Food and Drug Administration, 6751 Steger Drive, Cincinnati, Ohio 45237. If you have any question, you may contact Ms. Forney at (513) 679-2700, ext. 163.

Sincerely,


for Henry L. Fielden
District Director
Cincinnati District

Cc: Shana Robertson-Shaw, COO and Vice President
Barry S. Pokorny, Director of Technology and Regulatory Compliance