



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region *m3304n*

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (973) 526-6009

WARNING LETTER

January 7, 2000

**CERTIFIED MAIL –
RETURN RECEIPT REQUESTED**

Francesca Fazzolari, President
James Alexander Corporation
845 Route 94
Blairstown, New Jersey 07825

File No.: 00-NWJ-19

Dear Ms. Fazzolari:

During an inspection of your manufacturing facility located at 845 Route 94, Blairstown, New Jersey, from November 18 through December 6, 1999, an investigator from this office documented deviations from Current Good Manufacturing Practice Regulations (cGMPs), Title 21, Code of Federal Regulations (CFR), Part 210 & 211. These deviations were noted on the FDA483, List of Inspectional Observations issued to you at the close of the inspection.

The above stated inspection revealed that drug products manufactured at your facility are considered to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the ACT), in that the methods used in, or the facilities and/or controls used in manufacturing and repacking are not in conformance with cGMPs, as follows:

1. The Quality Control Unit failed to identify and evaluate out-of-specification results received for routine stability testing of finished products within expiry. None of the failing results were investigated.

For example: Compound Benzoin Tincture, USP, Lot 8801981, Exp 1/2003, failed USP alcohol content specifications on November 17, 1998 and December 3, 1998. Ammonia Inhalant Solution, Lot 3302961, Exp 2/2001 also failed alcohol content specifications on June 28, 1999. Sting Ease (Pramoxine HCl) Solution failed specific gravity and pH specifications for three different lots.

2. Cleaning validation studies and procedures were found to be inadequate to assure prevention of cross-contamination for products manufactured and filled with non-dedicated equipment.

For example: SOP #4-009010, QA Training Program Maintenance incorporates cleaning procedures which include non-specific instructions, such as "soak parts in acetone for at least a few hours" and "rinse until completely free from soap."

No cleaning validation studies have been conducted for products using non-dedicated equipment to assure the prevention of cross-contamination, such as Zephiran Chloride, Green Soap USP, Insect Sting (Pramoxine HCl) Solution and Iodine Tincture USP.

The cleaning validation studies which were conducted failed to evaluate the removal of all active ingredients and all cleaning agents. Furthermore, the adequacy of analytical methods and sampling methods used to support validation efforts, need to be evaluated and documented.

3. The validation of critical manufacturing processes was found to be incomplete and/or inadequate for several product lines.

For example: The ampoule filling and packaging operations for all products have not been validated. Your firm recently initiated a recall of Ammonia Inhalant, Lot 3398C, Exp 3/2003, due to a packaging mix-up.

Validation data is lacking for all approved batch sizes of Iodine Tincture Solution USP, Medicaine Sting and Bite Relief Solution, Medicaine Topical Antiseptic and Ammonia Inhalant. In addition, critical agitation times were not documented during mixing operations or were non-specific in validation studies. Also, samples taken from the mixing vessels during validation studies, were not conducted in a manner to evaluate uniformity of the mixed solution.

4. The quality of water used as a component has not been demonstrated to be suitable for its intended use.

For example: USP Purified Water is not used in the production of Iodine Tincture Solution. The Reverse Osmosis Water System used to purify the water used in an ingredient has not been validated. Microbial limits have not been established for the water. Conductivity results reviewed from July 6, 1998 through November 15, 1998, revealed nine occasions when established specifications were exceeded. These out-of-specification results were reviewed by the Quality Unit, but not investigated. Water which exceeded specifications for conductivity were used in the production of Medicaine Sting and Bite Relief Solution, Lot C20411981 and Ammonia Inhalation Solution, Lot C3309981.

5. Master Production Batch Records do not contain documentation of critical steps.

For example: The master production records for Medicaine Sting and Bite Relief Solution and Ammonia Inhalant Solution do not require documentation of start and stop times for mixing or identify the type of pump used in processing.

Production procedures allow for the use of CO₂ as needed during the filling of flammable products, however use of this gas is not documented on the production batch records.

6. Analytical test methods used to assure product potency throughout shelf life have not been demonstrated to be stability indicating.
7. Stability sampling was not conducted in accordance with SOP 13-001-02 Drug Product Stability Testing, which specify testing every three months for the first year, every six months the second year and then yearly.

For example: Amyl Nitrate Inhalant, Lot 2203941, Exp 3/97, testing was conducted at fifteen, twenty-eight, thirty-two and forty four months. Lot 2202951, Exp 2/98, testing was conducted at five, sixteen, eighteen and twenty three months. This product has a three-year expiry.

The above list is not intended to be all-inclusive of deficiencies at your facility. It is your responsibility to ensure that the drug products you manufacture are in compliance with the Act and the regulations promulgated under it. Federal agencies are routinely advised of Warning Letters issued so that they may take this information into account when considering the award of contracts. You should take prompt action to correct these deficiencies. Failure to implement corrective measure may result in regulatory action, including seizure and/or injunction, without further notice.

We have received your response, dated December 20, 1999, to the FDA483 Inspectional Observations. Your response to Observation 1 references a calculation error on the retesting of Zephiran Chloride and a unit of error results for Compound Benzoin, thereby concluding that the stability results are within specifications. Be advised that the original results can not be invalidated with retesting done at a later time. This deficiency refers to the failure of your QC Unit to recognize, evaluate and investigate these out-of-specification results. Your proposed corrective actions for handling future out-of-specification results are noted and will be verified during the next inspection.

Concerning your response to Observation 2, we refer you to FDA's Cleaning Validation Guideline booklet for guidance. Regarding Observations 4-7, 9 & 12, please provide timeframes for completion of corrective actions. With regard to Item 12, please demonstrate that stability test methodology used for USP labeled products, are also stability-indicating.

James Alexander Corporation
Blairstown, NJ 07825

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Your corrective actions will be verified during the next inspection.

You should notify this office in writing within 15 working days of receipt of this letter, to specify timeframes for correction of the noted observations. Your further reply should be sent to the New Jersey District Office, FDA, 10 Waterview Blvd., 3rd Floor, Parsippany, New Jersey 07054, Attention: Mercedes Mota, Compliance Officer.

Sincerely,



for Douglas I. Ellsworth
District Director
New Jersey District

James Alexander Corporation
Blairstown, NJ 07825

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Bcc: HFR-CE340 (DCB/MBM/JKT)
HFR-CE350 (DIB/Gp1-SCSO/Cerenzio/PA Mgr-Regina Brown)
HFD-320 (CDER-Division of Manufacturing and Product Quality)
HFA-224
HFC-240 (MPQAS)
HFC-210 (Division of Compliance Policy)
HFI-35 (FOI – stamped & purged copy)
EF (James Alexander Corporation, Blairstown, NJ)

CFN: 2242239
FACTS: Compliance #