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(3)**COPY**

May 13, 1997

Food and Drug Administration
Seattle District
Pacific Region
22201 23rd Drive S.E.
P.O. Box 3012
Bothell WA 98041-3012

VIA FEDERAL EXPRESS

Telephone: 206-486-8788
Fax: 206-483-4996

In reply refer to Warning Letter SEA 97-20

Douglas H. Kazen, President
Aseptico, Inc.
19501 144th Avenue NE
Woodinville, Washington 98072**WARNING LETTER**

Dear Mr. Kazen:

An inspection of your facility conducted on February 19, 24, 25, & 27, 1997, by Investigator V. Teres Speer, Engineer John A. Hall, and Chemist Dan J. Moskowitz documented deviations from the Current Good Manufacturing Practice Regulations (Title 21, Code of Federal Regulations, Parts 210 & 211) regarding your manufacturing of dental retraction cords (aka "gingival retraction agents") containing epinephrine, potassium alum, or epinephrine/potassium alum combination. These products are drugs as defined in Section 201(g) of the Federal Food, Drug, and Cosmetic Act (the Act).

The deviations noted cause drug products distributed by your facility to be adulterated within the meaning of Section 501(a)(2)(B) of the Act.

Among the deviations noted were:

1. Failure to perform specific identity testing or obtain certificates of analysis for raw materials used in the production of epinephrine, potassium alum, or epinephrine/potassium alum combination dental cords. [21 CFR 211.84(a)/(d)]
2. Failure to perform finished product testing to verify the identity, strength, and purity of epinephrine, potassium alum or epinephrine/potassium alum combination dental cords. [21 CFR 211.165(a)]
3. Failure to validate the manufacturing processes for the production of epinephrine, potassium alum, or epinephrine/potassium alum combination dental cords. [21 CFR 211.110(a)]

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4. Failure to have performed sufficient stability testing of finished product to support the assigned three and five year expiration dates for the epinephrine, potassium alum, or epinephrine/potassium alum combination dental cords. [21 CFR 211.166(a)/(b)]

The above identification of violations is not intended to be an all inclusive listing of deficiencies noted during the inspection of your facility. It is your responsibility to assure adherence to the Current Good Manufacturing Practice Regulations (GMPs).

Until the violations are corrected and confirmed by follow up inspection, Federal Agencies will be informed that the Food & Drug Administration recommends against the award of contracts for the affected products.

I am in receipt of your letter dated March 6, 1997 to Investigator V. Teres Speer. In this letter, you offer responses to the listed observations, including comments relevant to the four items identified above.

You acknowledge that item #1 is factually correct. However, you fail to adequately address all facets of the observation, specifically with regard to testing the raw materials epinephrine and zinc chloride. Your comment that these materials are purchased in small quantities and it is not economically feasible to test them is not acceptable. In lieu of actual testing by your firm, the GMP regulations permit you to rely upon the supplier's certificate of analysis accompanying every shipment provided the accuracy of such certificate is initially and periodically verified by subjecting samples to full testing by an independent laboratory. Whether relying upon a qualified vendor and certificate, or conducting full testing on your own, a specific identity test must be performed on a sample representing each shipment upon receipt and prior to release to production.

Your letter states that you disagree with the observation covered by item #2 concerning finished product testing. Your response specifically states that you test "finish solution" which you suggest is tantamount to testing finished product. To clarify, by definition the dry cord is finished product while what you term the "finish solution" is actually by definition an in-process material. While your testing of the in-process material is appropriate, the

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GMP regulations also require testing finished product. We see no reason to exempt your products from finished product testing.

You disagree with the observation covered by item #3 regarding validation of your manufacturing process. You test one sample of an in-process material in support of both finished product quality and validation of the manufacturing process. Your sample size and scheme is insufficient to establish that the process consistently yields product meeting its preestablished quality attributes. Process validation sampling and testing should be designed to ensure a high degree of assurance of product quality from the beginning to the end of the production cycle. Many firms have found that validation is useful in detecting unanticipated and unacceptable variability, and such efforts usually preclude the need for much reprocessing or reworking. Your response to this observation is inadequate.

In your letter, you state that you have performed "more than one" shelf life study (on finished product), which is addressed by item #6. However, your response does not include supporting documentation. Records collected during our recent inspection indicate that original stability testing was begun in 1985 with additional testing performed in 1986. Records for testing in 1987 or 1988 supporting your three year expiration data were reportedly discarded or misplaced. The GMPs state in part that there shall be a written testing program, and that this program shall include specific sample sizes, test intervals, statistical criteria, storage conditions, specific test methods, and be based on finished product testing. Your contention that the testing of in-process solutions is sufficient for stability data and the establishment of expiration dates is incorrect.

Finally, International Organization for Standards (ISO) certification does not preclude the need for the awareness of, and compliance with, FDA regulations.

You should take prompt and immediate action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. These actions may include seizure and/or injunction.

You should notify this office in writing, within fifteen (15) working days of receipt of this letter, of specific steps you have taken to correct the noted violations, including an explanation of

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each step being taken to prevent the recurrence of similar violations. Include copies of any available documentation demonstrating that corrections have been made. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the correction will be completed.

Your reply should be sent to the Food & Drug Administration, Seattle District Office, P.O. Box 3012, Bothell, WA 98041-3012, Attention: H. Tyler Thornburg, Compliance Officer.

Sincerely,



Roger L. Lowell
District Director