



DEPARTMENT OF HEALTH AND HUMAN SERVICE

Southwest Region

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Food and Drug Administration
Denver District Office
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P.O. Box 25087
6th Avenue & Kipling Street
Denver, Colorado 80225-0087
Telephone: 303-236-3000
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October 23, 2000

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Mr. Gregory J. Baldwin
President and CEO
Baxa Corporation
13760 East Arapahoe Road
Englewood, Colorado 80112

Ref. #: DEN-01-3

Dear Mr. Baldwin:

On July 31 through August 22, 2000, Investigators Nicholas R. Nance of our office and Madalyn Sheldon of our Center for Devices and Radiological Health conducted an inspection of your establishment in Englewood, Colorado. Our investigators determined that your firm manufactures electro-mechanical infusion pumps and related sterile tubing sets, electro-mechanical pharmacy compounders, mixers and mixing/filling equipment, and other sterile and non-sterile pharmacy accessories. These infusion pumps and pharmacy compounders/mixers are devices as defined by Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The above stated inspection revealed that these devices are adulterated within the meaning of Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Quality System/Good Manufacturing Practice (QS/GMP) for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (21 CFR), Part 820. The deviations are as follows:

1. Failure to conduct planned and periodic audits of the quality assurance program in accordance with written procedures, as required by 21 CFR 820.22. For example, review of your internal audit schedule found that audits scheduled to be performed between January and March 2000 of your quality system for Inspection and Test, Design Control, Process Controls, Corrective Actions, Training, Statistical Techniques and others were not performed. Also, issues identified in prior audits have not been re-audited to insure that corrective actions are completed and adequate.

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2. Failure to assure that all elements of design control are addressed in your design control procedures, as required by 21 CFR 820.30. For example, you do not have procedures for handling design changes, design inputs and outputs, design review and design verification. Also, design modifications have been made to the [XXXXXXXXXX] as a result of complaints of malfunctions, ineffectiveness or reliability problems. There is no evidence that these design modifications were validated or that design controls were addressed.
3. Management reviews of the quality system are not effective in that all quality data is not analyzed, documented and trended, as required by 21 CFR 820.20. For example, in-process failures are not analyzed or trended.
4. Sampling plans are inadequate in that there is no valid statistical rationale to ensure that the sampling plans are adequate for their intended use, as required by 21 CFR 820.250. For example, there is no documented rationale for choosing the levels and AQLs used to sample-specified components and lot quantities. Also, there is evidence of multiple instances of acceptance of incoming components that had been incorrectly sampled. In most cases, less than the number of samples called for by the sampling plan were collected.
5. Failure to establish and maintain procedures for changes to a specification, method, process or procedure, as required by 21 CFR 820.70(b), and failure to verify, or where appropriate, validate such changes as required by 21 CFR 820.75. For example, multiple changes have been made to the [XXXXXX], however, there is no documented evidence that these changes have been fully validated and verified.
6. Failure to establish and maintain procedures for rework, to include re-testing and reevaluation of nonconforming products after rework to ensure the product meets its current approved specifications, as required by 21 CFR 820.90(b)(2). For example, [XXXXXX] that are found to fail during the manufacture of the pump are reworked. There are no approved rework procedures and neither the failure, nor the subsequent rework is documented.
7. Failure to establish and maintain procedures for finished device acceptance to ensure that each production run, lot or batch of finished devices meets acceptance criteria, as required by 21 CFR 820.80(d). For example, review of device history records indicate products were released to finished goods, although in-process failures exceeded the acceptance limit called for by the sampling plan. Also, devices were released to finished goods without required test signatures and data.
8. Failure to establish and maintain procedures for implementing corrective and preventative action (CAPA), to include:

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- not analyzing all significant sources of quality data, and using appropriate statistical methodology where necessary to detect recurring quality problems, as required by 21 CFR 820.100(a)(1). For example, statistical analysis and trending of in-process defect/discrepancy reports (MRR and Scrap Logs) are not performed.
 - not verifying or validating the corrective and preventive action to ensure such action is effective and does not adversely affect the finished device, as required by 21 CFR 820.100(a)(2). For example, complaints regarding occluded administration sets resulted in ECO 101363. There is no evidence that an assessment was performed showing how the corrective action was determined, nor was there justification evident as to why products already distributed were not addressed.
9. Failure to review and evaluate all complaints to determine whether an investigation is necessary, as required by 21 CFR 820.198(b). For example, review of customer service contact reports indicate instances of device malfunctions which were not considered as complaints. There is no written justification for the decision not to handle these as complaints.

We acknowledge receipt of your September 1, September 21 and October 6, 2000 responses to the FDA form 483 and also acknowledge that you have contracted the services of a consultant. We previously issued a warning letter to you on March 10, 1999 as a result of our January 25 through February 8, 1999 inspection. Although the current inspection found that you have made improvements in certain areas, several of the deficiencies found during the current inspection continue to be uncorrected from the 1999 inspection. It has been eighteen months since the previous inspection, which is sufficient time to have made full correction and to have your quality systems in place.

We have reviewed your responses and have the following comments:

With regards to Management Responsibility, procedural changes to the audit program are not detailed. The issues involved with this observation concern the kind of data required to be reviewed and how the data is to be presented (i.e. trending, action levels, etc.). Your response does not indicate how these areas will be corrected, only that a new and improved MRR system will be implemented.

Regarding audits, although your response does admit that there have been delays performing them, there is no commitment regarding rescheduling them. In view of the QSR defects identified by your firm, it is important that this delay in scheduling be addressed. You state in your September 1, 2000 response that audits remain open because the work has not been completed. It is crucial that corrective actions identified by audits be completed in a timely fashion as this is the purpose of performing such audits.

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With respect to Sampling Observations as shown in your September 21, 2000 response, it is unclear why you are to train all associates in the use of the ANSI Z 1.4 slide rule if, in fact, you are going to use ~~LXXI~~ as your statistical sampling plan. Your response also states that you will be establishing a statistical rationale for any other sampling plans in use. It would appear that using one sampling plan across all manufacturing operations would decrease the likelihood of errors made in the execution of any sampling operations.

Our inspection also disclosed that you were not adequately tracking your devices as required by 21 CFR 821, but recognize that this is the result of a delay in receiving correspondence from our Agency informing your firm of these requirements. We expect that you will have a fully implemented tracking system in place at the next inspection of your facility.

The above identified deviations are not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure that your establishment is in compliance with all requirements of the Federal regulations. The specific violations noted in this letter and in the Form FDA-483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your establishment's quality system. You are responsible for investigating and determining the causes of the violations identified by the FDA. You also must promptly initiate permanent corrective and preventive action on your Quality System.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for Class III devices to which the QS/GMP deficiencies are reasonably related will be cleared until the violations are corrected. Also, no requests for Certificates to Foreign Governments will be approved until the violations related to the subject devices have been corrected.

In order to facilitate FDA in making the determination that such corrections have been made, thereby enabling FDA to withdraw its advisory to other federal agencies concerning the award of government contracts, to resume marketing clearance for Class III devices for which a 510(k) premarket notification or Premarket Approval application (PMA) have been submitted, and provide Certificates to Foreign Governments for products manufactured at your facility, we are requesting that you submit certification by an outside consultant to this office on the schedule below. Certification by an outside expert consultant should contain assurance that he/she has conducted an audit of your establishment's manufacturing and quality assurance systems relative to the requirements of the device QS/GMP regulation (21 CFR, Part 820). You should also submit a copy of the consultant's report with certification that you have reviewed the report and that your establishment has initiated or completed all corrections called for in the report.

The initial certifications of audit and corrections, and subsequent certifications of updated audits and corrections (if required) should be submitted to this office by the following dates:

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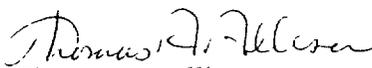
- Initial certifications by consultant and establishment – January 20, 2001.
- Subsequent certifications – bi-monthly thereafter until all corrections have been made.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by us without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

You should notify this office in writing within fifteen (15) working days of receipt of this letter of any other additional steps you have taken to correct the noted violations and to prevent their recurrence. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to Regina A. Barrell, Compliance Officer, Food and Drug Administration, Denver District, P. O. Box 25087, Denver, CO 80225-0087. If you have any further questions, please feel free to contact Ms. Barrell at (303) 236-3043.

Sincerely,


Thomas A. Allison
District Director

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