



OCT 12 2001

CBER-02-001

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Karl D. Kyle
Chairman of the Board
International Biologicals, Inc.
1619 Bassett Road
Piedmont, Oklahoma 73078

Dear Mr. Kyle:

The Food and Drug Administration (FDA) conducted an inspection of International Biologicals, Inc. (IBI), located at 1619 Bassett Road, Piedmont, Oklahoma, between July 10 and July 13, 2001. During the inspection, the FDA investigator identified violations of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and Title 21, Code of Federal Regulations (21 CFR), Parts 600-680. These documented violations include, but are not limited to, the following:

1. Failure to determine that the method of operation of sterilization equipment ensures the destruction of contaminating microorganisms [21 CFR 600.11(b)] in that the steam autoclave used for the sterilization of [] used in [] production has not been validated for sterilization effectiveness and heat distribution.
2. Failure to ensure that all manufacturing steps are performed so that the product will contain only the [] and other substances intended to be included in the final product, and to provide a ventilation system that will prevent the dissemination of microorganisms from one manufacturing area to another [21 CFR 600.11(a) and 680.2(a)]. For example:
 - a) air pressure differentials are not monitored between the different rooms in the [] production area.
 - b) filter integrity testing has not been performed on [] filters in the [] rooms.
3. Failure to ensure that the [] is free of contaminating materials prior to harvest, and that care is taken during harvesting and subsequent processing to

minimize contamination [21 CFR 680.1(b)(2)(ii)]. For example, there are no data to demonstrate the effectiveness of cleaning agents used to sanitize equipment used in the production of []

4. Failure to maintain standard operating procedures (SOP) that will ensure the identity of the seed cultures, prescribe adequate processing of [] and specify the acceptable limits and kinds of contamination [21 CFR 680.1(b)(2)(iii)]. For example:
 - a) the SOP entitled, “[]” was not followed in that, between the time period of November 1999 and June 2001, eight air quality monitoring samples from the [] lab exceeded the action level and were not investigated. In addition, there is no justification for the use of [] as an action level.
 - b) the SOP entitled, “[]” was not followed in that, between the time period of February 1999 and June 2001, ten water system samples exceeded the action level of [] and the water system was not sanitized after these instances.
 - c) the SOP entitled, “[]” was not followed in that, between the time period February 1999 and July 2001, investigations were not performed on the [] lots that failed due to contamination.
 - d) written procedures have not been established for the maintenance of the [] filters in the [] rooms.

Neither this letter nor the observations noted on the Form FDA 483, which were discussed with you at the conclusion of the inspection, are intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility as a [] supplier to ensure that your operations are in full compliance with all applicable Federal laws and regulations.

You should take prompt action to correct these deviations, including those noted during previous inspections. Failure to promptly correct these deviations may result in further action such as notification of licensed manufacturers, seizure and/or injunction without further notice.

Please notify this office in writing within 15 working days of receipt of this letter of any steps you have taken or will take to correct the noted deviations and to prevent their recurrence. If corrective action cannot be completed within 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 the U.S. Food and Drug Administration, Center for Biologics

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Evaluation and Research, 1401 Rockville Pike, Suite 200 N, Rockville, Maryland 20852-1448, Attention: Division of Case Management, HFM-610. If you have any questions regarding this letter, please contact Ms. Mary Malarkey, Director, Division of Case Management, at (301) 827-6201.

Sincerely,

A handwritten signature in cursive script that reads "Mary Malarkey". Below the signature, the initials "JMT" are written in a smaller, less legible cursive.

John M. Taylor
Director
Office of Enforcement