



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

19900 MacArthur Blvd., Ste 300
Irvine, California 92612-2445
Telephone (949) 798-7600

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

April 24, 2001

Mr. Gerald P. Macedo
Executive Officer and Co-Owner
Med-Pharmex, Inc.
2727 Thompson Creek Road
Pomona, CA 91767

W/L Number: 42 - 01
CFN: 20-23,614

Dear Mr. Macedo:

During an inspection of your registered veterinary drug and licensed medicated animal feed manufacturing facility located at the above shown location with the inspection conducted from November 2nd through the 13th of 2000, our Investigators found significant deviations from the Current Good Manufacturing Practice (CGMP) for Finished Pharmaceuticals regulations (Title 21, Code of Federal Regulations, Parts 210 and 211). Such deviations cause veterinary drugs manufactured at this facility to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the "Act" henceforth).

Section 501(a)(2)(B) of the Act states that a drug shall be deemed adulterated if the methods used in, or the facilities or controls used for its manufacture, processing, packing, or holding do not conform to or are not administered in conformity with CGMP, to assure that such drug meets the quality and purity characteristics which it purports or is represented to possess.

Our Investigators documented that there is no assurance that the methods used in and the controls used for the manufacture of your veterinary drug products are in conformity with the CGMPs. These deviations from the regulations were reported to you in the Inspectional Observations form (FDA form 483) which was issued at the conclusion of the inspection and included the following:

1. Your standard operating procedure (SOP) is inadequate in that containers are not sampled and tested for conformance with appropriate specifications for contamination with filth, extraneous adulterants or microbiological contamination before use. Specifically, your firm refills and recycles plastic fifty-five (55) gallon size drums for the shipment of Kao-Pectin, an over-the counter veterinary medication. These empty drug container drums are returned by sales vendors after being previously used.
[21 CFR 211.84]
2. Unexplained discrepancies in production records, including the failure of a batch to meet any of its specifications, were not thoroughly investigated and documented in the form of a written record of the investigation including the conclusions and follow up. Specifically: (a) The laboratory record for the identification of drug ingredient sulfadimethoxine, raw material lot number [REDACTED], was recorded as "[REDACTED]gr". The test was supposed to be performed with [REDACTED]mg of sample material; (b) The raw material disposition record for raw material lot number [REDACTED] of neomycin sulfate identifies a

Page Two of Three
April 24, 2001

re: Warning Letter #42-01
re: Med-Pharmex, Inc.

theoretical weight of █████ kg and a physical weight of █████ kg. This created a shortage of approximately ten kilograms of antibiotic which was unaccounted for; and, (c) The performance qualification (PQ) protocol for the █████ tube filler identifies a target fill weight range of +/- █████%. The █████ (█) PQ batches were filled under the production target fill weight range of +/- █████%. In all these circumstances, the problem was not identified by nor corrective action taken by your quality control unit's supervisor(s) responsible for manufacturing personnel. [21 CFR 211.192]

3. Changes to existing laboratory controls and specifications are not reviewed and approved by the quality control unit. For example: (a) in the SOP on laboratory equipment/instrument maintenance and calibration under incubators (7.13[v](a) and 7.13[v](b)), the procedure lacks the date that the change becomes effective, documenting the need for a change, and the review and approval by the quality control unit for that change to be implemented; and, (b) In document change control Standard Operating Procedure (SOP) 7.24, there is no system in place to identify the SOP's revision level, effective date, or that management has approved such change by signature. [21 CFR 211.160 and 211.22]

The above is not intended to be an all-inclusive list of violations. As a manufacturer of veterinary drugs, you are responsible for assuring that your overall operations and the products you manufacture and distribute are in compliance with the Act.

We acknowledge receipt of your letter, dated November 16, 2000, in which you have made reference to some corrections that your firm has made in response to the FDA form 483 issued to your firm. We understand from your letter that your firm is immediately ceasing to manufacture the Kao-Pectin veterinary drug article in the fifty-five (55) gallon size plastic barrels and, therefore, the use of previously used barrels. We anticipate that this letter will clarify some of the issues raised by your response regarding compliance with CGMPs. These corrections will be verified during the next scheduled inspection of your firm.

For your information, we note that although your firm has an SOP which prohibits the use of expired active drug ingredients in producing finished pharmaceuticals, there was a lack of decision, by management, about the use of expired oxytetracycline and phenylbutazone components which were observed in a quarantine area of the warehouse. You should specifically reinforce this SOP to your employees, or alternately, develop a validated protocol to support such possible intended use of ingredients beyond their expiration date. We also note that SOP 7.24 states that previous out-dated photocopy versions of SOP's can be used if that older version has no effect on its intended use. However, the old out-dated version is not marked or identified as (for example) "OBSOLETE" to rapidly & visually alert management and employees that an older version is being utilized.

We request that you take prompt action to correct the above violations and that you establish procedures whereby such violations do not recur. Failure to do so may result in non-approval of pending New Animal Drug Applications (NADAs) and/or withdrawal of approved NADAs and/or regulatory action such as seizure and/or injunction.

Please advise this office, in writing, within fifteen (15) business days of the receipt of this letter of the additional steps you have taken to bring your firm into compliance with the Act. Please include copies of any available documentation showing that corrections have been made. If you have any questions or clarifications regarding this letter prior to your written response, you can contact Scott Goff, Compliance Officer at telephone number (949) 798-7644.

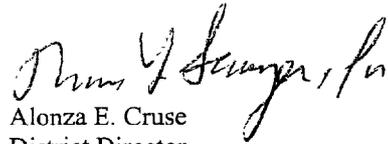
Page Three of Three
April 24, 2001

re: Warning Letter #42-01
re: Med-Pharmex, Inc.

Your written response should be directed to:

Thomas L. Sawyer
Director, Compliance Branch
U. S. Food and Drug Administration
19900 MacArthur Blvd.; Suite #300
Irvine, CA 92612-2445

Sincerely,


Alonza E. Cruse
District Director