



WARNING LETTER

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CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Robert Salsmans, Ph.D
President & General Manager
Organon Teknika BV
5281 RM Boxtel.
The Netherlands

Dear Dr. Salsmans,

During the period of September 11 through 14, 2000 Investigator Gerald McGill from the U.S. Food and Drug Administration (FDA's) San Francisco District Office conducted an inspection of your Boxtel, The Netherlands facility to determine whether your firm was in compliance with the Postmarketing Adverse Drug Experience (PADE) reporting requirements of Title 21, Code of Federal Regulations (CFR), Parts 314.80 and Section 505 (k) of the Federal Food, Drug and Cosmetic Act (the Act).

Based on our review of the inspectional report, we conclude that your firm violated 301 (e) of the Act because it failed to comply with 21 CFR 314.80 and Section 505 (k) of the Act.

Deviations from the PADE regulations include the following:

- Failure to submit to the FDA serious and unexpected adverse drug experience reports within 15 calendar days of initial receipt of the information as required by 21 CFR 314.80 (c)(1)(i).

For example:

<u>Drug</u>	<u>MCN</u>	<u>Mfr. Receipt date</u>	<u>Date sent to Organon, Inc. for submission to FDA</u>
Pavulon	Pan9900003	January 13, 1999	March 6, 2000
Pavulon	Pan9900009	May 19, 1999	March 6, 2000
Zemuron	Roc9900024	March 17, 1999	September 16, 1999
Zemuron	Roc9900044	April 12, 1999	September 16, 1999
Zemuron	Roc2000-093	July 7, 2000	August 7, 2000

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These deviations were listed on the FDA-483, "List of Inspectional Observations" which was presented to and discussed with Patrick G.H.L. Boen, M.D., Medical Director and Manager of Medical Affairs at the conclusion of the inspection. We received a response to the FDA-483 dated September 26, 2000, from Dr. Boen and Dr. Peter Denissen, Head, Drug Safety Surveillance Program. While we note your firm's proposed corrective actions with regards to these deviations, we request that you provide us with a specific timetable for their implementation, including your proposed use of the CLINTRACE computer system. Also, please provide specific details of your plan to achieve timely reporting to your West Orange, New Jersey affiliate. Organon's response to the FDA-483 states that some of your delay in submitting ADE reports to the FDA was caused by late reporting from affiliates or representatives. The 15 day reporting timeframe to FDA begins upon your initial receipt of the required report elements for all reports of serious, unlabeled ADEs, from your affiliates and representatives. This reporting responsibility also exists for follow-up reports to the initial ADE report.

Late reporting deviations from PADE regulations were also brought to Organon's attention by Ms. Kowalczyk, Senior Quality Systems Specialist, during and after an inspection of Organon, Inc., West Orange, NJ, conducted in April and May of 1999. That inspection revealed that many of the foreign 15 day reports submitted late by Organon Inc., NJ, to the FDA, had been submitted over 15 calendar days late to them by both your facility, Organon Teknika BV, and by NV Organon, Oss, The Netherlands. In her letter to the FDA dated June 7, 1999, responding to those deficiencies, Ms. Kowalczyk stated that the Organon facility in New Jersey would reiterate to both foreign affiliates the need to report serious and unexpected reports promptly to them so that they could submit ADE reports to FDA within 15 calendar days. Despite promised corrections, the current inspection of your firm revealed that the 5 ADE reports noted above were submitted significantly late to Organon Inc. in New Jersey. One of the 5 reports, involving the death of an infant, was submitted to Organon, NJ, approximately 14 months after receipt by your firm.

The above list of deviations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence to each requirement of the Act and its regulations. FDA expects drug manufacturers to establish reasonable mechanisms to assure that their foreign affiliates and corporate units rapidly transmit information to expedite reporting of serious and unlabeled adverse drug experiences to the FDA.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action without further notice. These actions may include, but are not limited to, seizure and/or injunction. Federal agencies are advised of the issuance of all warning letters about drugs so that they may take this information into account when considering the award of contracts.

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We request that you reply in writing within fifteen (15) working days of receipt of this letter. Please direct your response to the Food and Drug Administration, 7520 Standish Place, Rockville, MD 20855-2737, Attn: Denis Mackey, CSO, Division of Prescription Drug Compliance and Surveillance (HFD-330).

If you have any questions or concerns, please feel free to contact Mr. Mackey at (301) 827-7294.

Sincerely yours,



Lana Ogram
Director
Division of Prescription Drug Compliance
and Surveillance
Center for Drug Evaluation and Research

cc:

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