Forest Laboratories, Inc.

DEVIATION INVESTIGATION

To: CIT-MD-18 File

From: Irene Green

Subject: Investigation of CIT-MD-18 Clinical Study Use of Trade-Dress Pink Citalopram 20mg Tabs

Date: March 8, 2000

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BACKGOUND:

The VP of R&D S. Hariharan brought it to our attention, on February 29, 2000 that some patients enrolled in the study CIT-MD-18 had received pink trade-dress tablets. On 3/7/00 R&D generated the attached deviation report.

INVESTIGATION:

The 20mg trade-dress tablets lot # PO1102 were packaged in bottles of 10 by the Packaging Dept. between 1/15/98 and 9/14/98. It was designated for use in the following clinical studies: CIT-MD-03-97-11-000, CIT-MD-03-97-07-000, CIT-MD-03-97-12-000 and CIT-MD-03-97-17-000.

During packaging the product imprint was verified by both Q.A. and Packaging Supervisory personnel. The instructions from the then PR&D Clinical Assistant Director Ted Miro indicated that the above CIT MD-03 studies would use pink, imprinted 20 mg Celexa tablets.

At the time of release of these bottles of 10 to R&D, a copy of the packaging worksheet was given to R&D, which identified the product as trade-dress with the imprint of FP/20mg. The manufacturers certificate of analysis identifies the product as trade-dress pink with the aforementioned imprint. Another C of A was generated when samples of the lot were submitted to the R&D lab for reassay (8/24/98). The C of A for the reassay failed to include a product description. As of 9/14/98 all bottles of 10 were released to R&D Clinical Group.

A protocol for **CIT-MD-18** was generated 11/24/99 to randomize 160 patients for this multi-center, double-blind placebo controlled, flexible dose and age stratified study. As a blinded study, all products should have been non-trade dress or over-encapsulated.

The material documented in the protocol for use in this study was pulled from the R&D inventory of finished bottled goods. The release of lot # PO1102 along with the other products required for this study were released in accordance with Standard Operating Procedures.

At start-up both R&D and QA personnel verified that the material to be randomized was:

- Consistent with the material identified in the protocol by lot number.
- Consistent with the Certificate of Analysis.
- Properly identified in its labeling.

At the point of pulling material from stock, R&D made no verification as to the status of the lot (trade or non-trade-dress). At the point of the start-up, both R&D and QA failed to detect that the reassay C of A did not include a description of the product.

R&D and QA failed to detect that the inventory record of this lot did not include a description as to whether this was trade-dress or non-trade-dress material.

The study was randomized to completion and released by both R&D and QA on 12/2/99.

CORRECTIVE ACTION TAKEN:

At the time of notification of the deviation some randomized visits were still in-house. This material was quarantined and the visits 2-4 that contained pink trade-dress tablets were removed from the kits.

A 100% verification was made to assure that all the pink trade-dress tablets were removed from these kits.

The kits were replenished with non-trade-dress 20mg tabs, Lot #PO1165. Each bottle of PO1165 was verified by both QA &R&D to contain white non-trade-dress tablets.

The same procedure will be followed to correct kits returned from each site.

NEW PROCEDURES IN PLACE:

To assure that proper material is consistently issued for any clinical study the following procedures are being implemented:

1) At start-up of protocol a sample bottle will be opened to verify description and consistency of each product inclusive of imprint, color, size and shape. This information will be documented in the protocol records.
2) The original C of A and all subsequent C of A's will be reviewed for consistency and correctness against protocol requirements prior to start-up.
3) R&D inventory records of bottled finished goods will include a product description inclusive of imprint, color, size and shape.