

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER: NDA 19777/S6**

**CORRESPONDENCE**



NDA NO. 19-777 REF. NO. S-006  
NDA SUPPL FOR. SCS

HAND DELIVERED

August 24, 1989

Dr. Robert J. Wolters  
Division of Cardio-Renal  
Drug Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
HFD No. 110, Room No. 16B-30  
5600 Fishers Lane  
Rockville, MD 20857

Dear Dr. Wolters:

Re: ZESTRIL® (lisinopril) Tablets 40 mg  
NDA 19-777  
Rework Procedure

The purpose of this submission is to provide a rework procedure for ZESTRIL® (lisinopril) Tablets 40 mg.

The applicant proposes to salvage up to % of milled, recovered ZESTRIL Tablets blended with virgin granulation. Recovered ZESTRIL Tablets 40 mg will be blended with ZESTRIL 40 mg virgin granulation. ZESTRIL 10 mg recovery batches may be manufactured using any combination.

Following reworking, all excipients will be within % of the specified amounts except the lubricant (magnesium stearate NF) which will be within % of the specified amount as set out in the subject New Drug Application.

All tablets to be reworked will be less than one year old with the following exception:

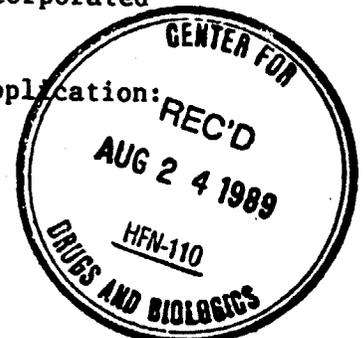
Currently, the applicant has a quantity of material that will qualify for recovery operations. A portion of this material is now over a year old. As a one-time occurrence, the applicant will rework this material.

The expiration date assigned to any batch containing reworked material will be the same as was assigned to the oldest reworked batch incorporated therein.

The following information is submitted in support of this application:

- 1. Recovery or salvage directions (Exhibit 1)

ORIGINAL



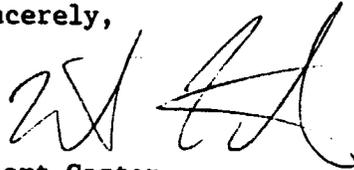
2. Qualitative and Quantitative rework formulations and manufacturing directions for ZESTRIL Tablets 40 mg (Exhibit 2).
3. Comparative dissolution study conducted on 12 tablets from one lot of ZESTRIL Tablets 40 mg containing % reworked material and one lot of regulator production tablets assayed at 10-, 20- and 30-minute intervals indicating that the dissolution characteristics of the reworked batch and the virgin batch are comparable (Exhibit 3).
4. A stability report comparing ZESTRIL Tablets 40 mg made with % virgin material with reworked (up to %) ZESTRIL Tablets 40 mg, showing no significant difference and supporting a 30-month expiry period (Exhibit 4).

The disintegration, hardness and friability specifications referred to in the stability report are the in-process control limits currently in place for Quality Assurance release on nonreworked ZESTRIL (lisinopril) batches. Current in-process control limits are:

Disintegration: less than minutes  
Hardness: 3.6 - 8.6 kg  
Friability: 0.5% max

If you require any further information, please do not hesitate to contact me.

Sincerely,



Robert Castor  
Manager  
Technical Regulatory Affairs and Compliance  
Drug Regulatory Affairs Department  
(302) 886-2594

RC/cmh  
Enclosure