CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

18-998/S-061

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER(S)

NDA 18-998/S-061

Trade Name: Vasotec

Generic Name(s): (enalaprilat)

Sponsor: Merck and Company, Inc.

Agent:

Approval Date: February 4, 2002

Indication: The treatment of hypertension.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 18-998/S-061

Approval Letter(s)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 18-998/S-061
NDA 19-221/S-028
NDA 20-507/S-003

Merck and Company, Inc.
Attention: Virginia G. Snyder
P.O. Box 4, BLA-20
Sumneytown Pike,
West Point, PA 19486

Dear Ms. Snyder:

Please refer to your supplemental new drug applications dated August 23, 2001, received August 24, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vasotec (enalapril maleate) Tablets, 2.5mg, 5mg, 10mg, and 20mg (NDA 18-998), Vaseretic (enalapril maleate/hydrochlorothiazide) Tablets, 5mg/12.5mg and 10mg/25mg (NDA 19-221), and Teczem (enalapril maleate/diltiazem malate) Tablets, 5mg/180mg (NDA 20-507).

These "Changes Being Effected in 30 days" supplemental new drug applications provide for the transfer of enalapril maleate drug substance stability testing to the MMD facility in Wilson, NC.

We have completed the review of these supplemental applications, and they are approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Sandra L. Birdsong, Regulatory Project Manager, at (301) 594-5312.

Sincerely,

{See appended electronic signature page}

Kasturi Srinivasachar, Ph.D.
Chemistry Team Leader, DNDC I for the
Division of Cardio-Renal Drug Products, (HFD-110)
DNDC I, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Kasturi Srinivasachar
2/4/02 09:25:02 AM

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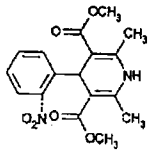
APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 18-998/S-061

Chemistry Review(s)

CHEMIST'S REVIEW	1. ORGANIZATION HFD-110	2. NDA Number 18-998
3. **Name and Address of Applicant (City & State)** Merck & Co., Inc.		4. **Supplement(s)** **Number(s)** **Date(s)** S-061 8/23/01 (CDER Date: 8/24/01)
5. **Drug Name** Vasotec	6. **Nonproprietary Name** Enalapril	8. **Amendments:** None
7. **Supplement Provides for** the transfer of the drug substance stability testing to the MMD facility in Wilson, NC.		
9. **Pharmacological Category** antihypertensive	10. **How Dispensed** [X] Rx [ ] OTC	11. **Related NDA(s):** NDA 19-221/ S-028
12. **Dosage Form(s)** Oral Tablets	**Potency(ies)** 2.5, 5, 10 & 20mg	
14.**Chemical Name and Structure:**  $C_{17}H_{18}N_2O_6$ 346.34 3,5-Pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-, dimethyl ester. Dimethyl 1,4-dihydro-2,6-dimethyl-4-(*o*-nitrophenyl)-3,5-pyridinedicarboxylate [*21829-25-4*].		15. **Records/Reports Current**

16. Comments: This is a PAC ATLS/CBE 30 supplement. The firm provides a summary (i.e., by reference) of the approved test methods and acceptance criteria for stability testing and an environmental impact request for a categorical exclusion which is considered by this reviewer to be acceptable. All post approval commitments relating to the test methods have been fulfilled and the facility was deemed to be in compliance with cGMP as noted by the attached EES report (see scan below – next page)

File: W(11-29-01)S-061(8-23-01)N18-998 (PM is S. Birdsong)

17. **Conclusions and Recommendations:** An approval letter should be written based on the positive evaluative results determined.

Name	Signature	**Date Completed**
Stuart Zimmerman		11/29/01

13-NOV-2001 FDA CDER EES Page 1 of 1

ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application : NDA 18998/061
Org Code : 110
Priority : 1P

Sponsor: MERCK
SUMNEYTOWN PIKE
WEST POINT, PA 19486

Stamp Date : 24-AUG-2001
PDUFA Date : 24-FEB-2002
Action Goal :
District Goal: 20-JAN-2002

Brand Name : VASOTEC
Estab. Name:
Generic Name: ENALAPRIL MALEATE
Dosage Form: (TABLET)
Strength : 2.5MG,5,10 & 20MG

FDA Contacts:			
S. BIRDSONG	Project Manager	(HFD-110)	301-594-5300
S. ZIMMERMAN	Review Chemist	(HFD-110)	301-594-5300
K. SRINIVASACHAR	Team Leader	(HFD-110)	301-594-5376

Overall Recommendation: ACCEPTABLE on 10-SEP-2001by J. D AMBROGIO(HFD-324) 301-827-0062

Establishment : CFN : 1036761 FEI :
MERCK AND CO INC
4633 MERCK RD
WILSON, NC 27893

DMF No: AADA:

Responsibilities: DRUG SUBSTANCE STABILITY TESTER

Profile : CTL OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 10-SEP-01
Decision : ACCEPTABLE
Reason : BASED ON PROFILE

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/s/

Stuart Zimmerman
1/25/02 07:27:05 AM
CHEMIST

Kasturi Srinivasachar
1/31/02 03:35:16 PM
CHEMIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

NDA 18-998/S-061

Administrative/Correspondence

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-998/S-061

Merck & Co., Inc.
Attention: Ms. Virginia G. Snyder
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Ms. Snyder:

We have received your supplemental drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Vasotec (Enalapril Maleate) Tablets

NDA Number: 18-998

Supplement number: S-061

Date of supplement: August 23, 2001

Date of receipt: August 24, 2001

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on October 23, 2001 in accordance with 21 CFR 314.101(a).

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Division Document Room
5600 Fishers Lane
Rockville, Maryland 20857

Courier/Overnight Mail:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Division Document Room
1451 Rockville Pike
Rockville, Maryland 20852

If you have any questions, please call:

Ms. Sandra Birdsong
Regulatory Project Manager
(301) 594-5334

Sincerely yours,

Natalia A. Morgenstern
Chief, Project Management Staff
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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/s/

Natalia Morgenstern
9/14/01 02:46:01 PM