CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

20-386/S-028

Correspondence

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
FOOD AND DRUG ADMINISTRATION

US Mail address:
FDA/CDER/HFD-110
5600 Fishers Lane
Rockville, MD 20857

Woodmont II
1451 Rockville Pike
Rockville, MD 20852

Transmitted to FAX Number:	(484) 344-2516
Attention:	Dr. Jeff Tucker
Company Name:	Merck & Co.
Phone:	(484) 344-7788
Subject:	**Approval Letter w/Labeling for NDA 20-386/S-028 Cozaar (losartan potassium) for Type 2 Diabetic Nephropathy**
Date:	September 17, 2002
Pages including this sheet:	15
From:	**Edward Fromm**
Phone:	**301-594-5332**
Fax:	**301-594-5494**

Please let me know that you received this!!! Thanks

MERCK
Research Laboratories

TELECOPIER MESSAGE

MERCK RESEARCH LABORATORIES
REGULATORY AFFAIRS - DOMESTIC
FIVE SENTRY PARKWAY EAST, BLUE BELL, PA 19422

TO:	Ms. Sandra Birdsong Dr. Douglas Throckmorton	**PHONE:**	301-594-5334
LOCATION:	FDA, WOC2, HFD-110	**FAX:**	301-594-5494
FROM:	Michael C. Elia, PhD, DABT	**PHONE:**	484 344-3180
LOCATION:	BL A-20	**FAX:**	484 344-2516
DATE:	4 / 1 / 2002	**PAGES including cover sheet:**	37 Pages

Special Comments:

NDA 20-386/S-028: COZAAR Tablets (Losartan Potassium)
Amendment to Pending Application

Please see the attached revised labeling for NDA 20-386/S-028: COZAAR Tablets (Losartan Potassium):

- Cover Letter
- Annotated Label
- Table of Revisions

The Official Submission is being sent to the Division today, 4/1/02, via Federal Express.

Michael C. Elia

Michael C. Elia, PhD, DABT
Director, Regulatory Affairs

Michael C Elia, Ph.D., DABT
Director
Regulatory Affairs

Merck & Co., Inc.
BLA-20
P.O. Box 4
West Point PA 19486
Tel 484 344 3180
215 652 5000
Fax 484 344 2516
Email: michael_elia@merck.com

April 1, 2002

Douglas C. Throckmorton, M.D. – Acting Director
Division of Cardio-Renal Drug Products

c/o Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, MD 20852

MERCK Research Laboratories

Dear Dr. Throckmorton:

NDA 20-386/S-028: COZAAR™ Tablets (Losartan Potassium)

Amendment to a Pending Application

Reference is made to the above cited supplemental New Drug Application (sNDA) submitted as an electronic archive on November 9, 2001.

As indicated on the attached Form FDA 356h, this amendment provides for changes in the Labeling Section of the pending supplemental New Drug Application for COZAAR™. The Statement of Organization following this letter describes the sections contained in this application.

This submissions provides for revisions and corrections to our proposed labeling.

Please note that the phrase '_____' has been removed from the proposed Indication. The following is the proposed Indication in the original supplemental NDA:

_____

With this submission, the proposed Indication now reads:

_____

Upon further review, we noted some inconsistencies in both the Executive Summary (ES) and the Clinical Study Report (CSR). For example, some tables had data that did not properly match the table title; in other places, there were inconsistencies with regard to the information contained in a table relative to the corresponding text. Finally, references to the terms "duration of treatment" and "duration of follow-up" have been clarified and/or corrected. Similar revisions have been made to each document. These revisions are outlined in the table located in Item 20 of this submission.

With this submission are the following items:

Labeling
I. Labeling text
   a. Proposed labeling text

Summary
I. Annotated package circular

The Microsoft WORD version of the proposed labeling text is also supplied as PROPOSED.DOC within the labeling folder on the Compact Disk (CD) provided.

This submission is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs*. As an attachment to this letter, Merck Research Laboratories (MRL), a Division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the submission. All documents requiring signatures for certification are included as paper for archival purposes.

All the information is contained on one CD and is not more than ——— We have taken precautions to ensure that the contents of the CD are free of computer viruses (Norton AntiVirus® 4.0, Symantec Corp., 1991-1997) and we authorize the use of anti-virus software, as appropriate.

A list of reviewers from the Division of Cardio-Renal Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Ms. Sandra Birdsong, Regulatory Project Manager, Division of Cardio-Renal Drug Products.

We consider the filing of this amendment to be a confidential matter, and request that the Food and Drug Administration not make its content, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

We apologize for any inconvenience these errors have caused the Agency. Questions concerning this supplement should be directed to Michael C. Elia, Ph.D., DABT (484-344-3180) or, in my absence, to Bonnie J. Goldmann, M.D. (484-344-2383).

Sincerely,

M. C. Elia

Michael C. Elia, Ph.D., DABT
Director, Regulatory Affairs

Enclosure: CD

Federal Express #1

Facsimile (cover letter, annotated label, Table of Revisions)

Desk Copy: Ms. Sandra Birdsong, Regulatory Project Manager, WOC2, HFD-110
(cover letter, annotated label, Table of Revisions)
Federal Express #2

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, Parts 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: March 31, 2003
See OMB Statement on page 2

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT	DATE OF SUBMISSION
Merck & Co., Inc.	01 April 2002
TELEPHONE NO. *(include Area Code)* 484-344-3180	FACSIMILE (FAX) *Number (include Area Code)* 484-344-2516
APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*. Sumneytown Pike, P.O. Box 4, BLA-20 West Point, PA 19486	AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE Michael C. Elia, Ph.D., DABT Director, Regulatory Affairs

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER *(If previously issued)* 20-386

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*	PROPRIETARY NAME *(trade name)* IF ANY
Losartan Potassium	COZAAR®

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(if any)*
2-Butyl-4-chloro-1-[[2'-(1*H*-tetrazol-5-yl)[1,1'-biphenyl]-4-yl]methyl]-1 *H*-imidazole-t-methanol, monopotassium salt

CODE NAME *(if any)*

DOSAGE FORM:	STRENGTHS	ROUTE OF ADMINISTRATION:
Tablets	25 mg, 50 mg	Oral

(PROPOSED) INDICATION(S) FOR USE
Hypertension

APPLICATION INFORMATION

APPLICATION TYPE *(check one)* ☒ NEW DRUG APPLICATION (21 CFR 314.50) ☐ ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☒ 505 (b)(1) ☐ 505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug — Holder of Approved Application

TYPE OF SUBMISSION (check one) ☐ ORIGINAL APPLICATION ☒ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ EFFICACY SUPPLEMENT
☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION:

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY ☐ CBE ☐ CBE-30 ☐ Prior Approval (PA)

REASON FOR SUBMISSION Submit for 5-028: Rev Pages Exec; Rev. Pages CSR; Ann Label; Table of Rev

PROPOSED MARKETING STATUS *(check one)* ☒ PRESCRIPTION PRODUCT (Rx) ☐ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED	THIS APPLICATION IS ☐ PAPER ☒ PAPER AND ELECTRONIC ☐ ELECTRONIC
1	

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary) Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

Created by Media Arts/USDHHS (301) 443-2454 EF

X	2. Labeling (check one) ☒ Draft Labeling ☐ Final Printed Labeling
X	3. Summary (21 CFR 314.50 (c))
	4. Chemistry section
	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))
	15. Establishment description (21 CFR Part 600, if applicable)
	16. Debarment certification (FD&C Act 306 (k)(1))
	17. Field copy certification (21 CFR 314.50 (k)(3))
	18. User Fee Cover Sheet (Form FDA 3397)
	19. Financial Information (21 CFR Part 54)
X	20. OTHER (Specify) Exec. Summ - Rev. Pages; CSR - Rev. pages; Table of Revisions

CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contra i nd icabons, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as req... by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, includir not limited to the following:

1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act Section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE
Michael C Elia	Michael C. Elia, Ph.D., DABT Director, Regulatory Affairs	01 April 2002

ADDRESS (Street, City, State, and ZIP Code)	Telephone Number
Sumneytown Pike, P.O. Box 4, BLA-20 West Point, PA 19486	(484) 344-3180

Proposed Text of Labeling

80 pages redacted from this section of the approval package consisted of draft labeling

Previously Approved Labeling

Not applicable; there are no other drugs approved for the treatment of type 2 diabetic nephropathy.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-386/S-028

Merck & Co., Inc.
Attention: Michael C. Elia, Ph.D., DABT
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, PA 19486

Dear Dr. Elia:

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:	COZAAR (Losartan Potassium) Tablets
NDA Number:	20-386
Review Priority Classification:	Priority (P)
Supplement number:	S-028
Date of supplement:	November 9, 2001
Date of receipt:	November 13, 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 January 12, 2002 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be May 13, 2002.

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:

Mr. Edward Fromm
Regulatory Project Manager
(301) 594-5313

Sincerely yours,

/S/

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Natalia Morgenstern
11/20/01 03:12:54 PM