

020757_5029 + 5028



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-757/S-029
NDA 20-758/S-028

Sanofi-Synthelabo
C/o Bristol-Myers Squibb Company
Attention: George Zapf
P. O. Box 5400
Princeton, NJ 08543-5400

Dear Mr. Zapf:

Please refer to your supplemental new drug applications dated June 5, 2003, received June 11, 2003 (NDA 20-758) and June 16, 2003 (NDA 20-757), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Avapro (irbesartan) Tablets, 75 mg, 150 mg and 300 mg (NDA 20-757) and Avalide (irbesartan/hydrochlorothiazide) Tablets, 75/12.5 mg, 150/12.5 mg and 300/12.5 mg (NDA 20-758).

We acknowledge receipt of your submissions dated October 10, 2003.

These supplemental new drug applications provide for ()irbesartan by () as described in the January 17, 2003 amendment to their DMF # ()

We have completed our review of these supplemental applications as amended, and they are approved. Please note that you should submit () stability data for the drug substance at long-term and accelerated conditions as a correspondence to these supplements as soon as they become available.

We remind you that you must comply with the reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any question, please call Edward Fromm, Regulatory Health Project Manager, at (301) 594-5332.

Sincerely,

ES

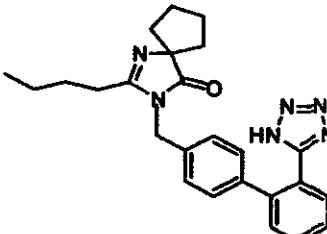
Kasturi Srinivasachar, Ph.D.
Chemistry Team Leader, DNDC I for the
Division of Cardio-Renal Drug Products (HFD-110)
DNDC I, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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

/s/

Kasturi Srinivasachar
10/10/03 04:19:53 PM

DIVISION OF CARDIO-RENAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

CHEMIST'S REVIEW	1. ORGANIZATION HFD - 110	2. NDA Number 20-757
3. Name and Address of Applicant (City & State) Bristol-Myers Squibb Company P. O. Box 5400 Princeton, NJ 08543-5400		4. Supplement(s) Number(s) Date(s) SCS-029 06/05/03
5. Drug Name Avapro	6. Nonproprietary Name Irbesartan	7. Amendments & Other (reports, etc) - Dates SCS-028(BC) 10-10-03
7. Supplement Provides for: changes to manufacturing process of (irbesartan by ())		
9. Pharmacological Category Angiotensin II Receptor Antagonist/Hypertension	10. How Dispensed <input checked="" type="checkbox"/> / RX <input type="checkbox"/> / OTC	11. Related IND(s)/ NDA(s)/DMF(s) NDA 20-758 DMF
12. Dosage Form(s) Tablets	13. Potency(ies) 75 mg, 150mg, and 300 mg.	
14. Chemical Name and structural formula: 2-Butyl-3-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl) methyl]-1,3-diazaspiro[4.4]non-1-en-4-one.		15. Records/Reports Current <input checked="" type="checkbox"/> / Yes <input type="checkbox"/> / No Reviewed <input checked="" type="checkbox"/> / Yes <input type="checkbox"/> / No
		
16. Comments: According to the Changes to an Approved NDA or ANDA guidance, the process changes and supporting information described in this supplement are submitted in a Prior Approval Supplement.		
17. Conclusions and Recommendations: The DMF # has been reviewed for the changes submitted in this supplement. The information provided in DMF is ADEQUATE to support the proposed process changes. Irbesartan drug substance made from (irbesartan manufactured by () by ()) demonstrates equivalency to the batches of irbesartan produced by currently approved process. This supplement may be approved.		
18. REVIEWER: Ramsharan D. Mittal		

5 Page(s) Withheld

§ 552(b)(4) Trade Secret / Confidential

§ 552(b)(5) Deliberative Process

§ 552(b)(5) Draft Labeling

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

/s/

Ramsharan Mittal
10/10/03 03:12:46 PM
CHEMIST

Kasturi Srinivasachar
10/10/03 04:12:24 PM
CHEMIST



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-757/S-029

Sanofi-Synthelabo c/o Bristol-Myers Squibb Company
Attention: Mr. George Zapf
Associate Director
P.O. Box 5400
Princeton, NJ 08543-5400

Dear Mr. Zapf:

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: Avapro (irbesartan) 75, 150, and 300 mg Tablets

NDA Number: 20-757

Supplement number: 029

Date of supplement: June 5, 2003

Date of receipt: June 16, 2003

This supplemental application proposes to _____
_____ for irbesartan drug substance.

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on August 15, 2003, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be October 16, 2003.

All communications concerning this supplement should be addressed as follows:

U.S. Postal Service:
Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products, HFD-110
Attention: Division Document Room, 5002
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, 5002
1451 Rockville Pike
Rockville, Maryland 20852

If you have any questions, please call:

Mr. Edward Fromm
Regulatory Health Project Manager
(301) 594-5332

Sincerely,

{See appended electronic signature page}

Zelda McDonald
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/

Zelda McDonald
6/20/03 11:05:49 AM