020757_5026+5025

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-757/S-026
NDA 20-758/S-025

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 November 22, 2002, received November 25, 2002, 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 May 21, 2003.

These "Changes Being Effected" supplemental new drug applications provide for an alternative manufacturing process [redacted] the [redacted] in the synthesis of the drug substance, irbesartan, and a rework process for [redacted]

We have completed our review of these supplemental applications as amended, and they are approved.

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

/S/

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
5/21/03 06:12:35 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-026 11/22/02
5. **Drug Name** Avapro	6. **Nonproprietary Name** Irbesartan	7. **Amendments &** Other (reports, etc) - Dates SCS-026(BC) 5/21/03
7. **Supplement Provides for:** CHANGES BEING EFFECTED an alternative manufacturing [ ] the drug substance, irbesartan synthesis and a rework process [ ]		
9. **Pharmacological Category** Angiotensin II Receptor Antagonist/Hypertension	10. **How Dispensed** /x/ RX /__/ OTC	11. **Related IND(s)/ NDA(s)/DMF(s)** NDA 20-758 DMF [ ] DMF
12. **Dosage Form(s)** Tablets	13. **Potency(ies)** 75 mg, 150mg, and 300 mg.	
14. **Chemical Name** 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 /x/ Yes /__/ No Reviewed /x/ Yes /__/ No
16. **Comments:** As per [ ] the process changes and supporting information described in this supplement are submitted in a CBE 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 and [ ] for rework. The supplement may be approved.		
18. **REVIEWER:** Ramsharan D. Mittal		

1 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
5/21/03 04:38:25 PM
CHEMIST

Kasturi Srinivasachar
5/21/03 06:00:37 PM
CHEMIST

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-757/S-026

Sanofi-Synthelabo
C/o of Bristol-Myers Squibb Co.
Attention: Mr. George Zapf
Associate Director, Global Regulatory Sciences, CMC
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: 026

Date of supplement: November 22, 2002

Date of receipt: November 25, 2002

This supplemental application, submitted as "Supplement - Changes Being Effected" proposes to provide an [redacted]
which you are [redacted].

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 January 24, 2003 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be May 24, 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: Document Room 5002
1451 Rockville Pike
Rockville, Maryland 20852

If you have any questions, please contact:

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

Sincerely,

/S/

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
12/18/02 01:57:31 PM