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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-757/S-030
NDA 20-758/S-029

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 30, 2003, received July 9, 2003, 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).

These "Changes Being Effected" supplemental new drug applications provide for the Bristol-Myers Squibb Manufacturing Company (Barceloneta) as an additional manufacturing site of irbesartan drug substance () as described in the June 30, 2003 amendment to their DMF # ()

We have completed our review of these supplemental applications 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/

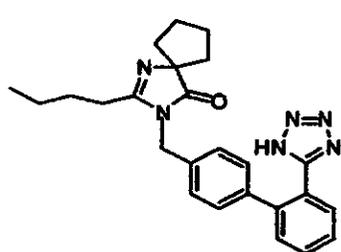
Kasturi Srinivasachar, Ph.D.
Chemistry Team Leader, DNDC I for the
Division of Cardio-Renal Drug Products (HFD-110)
DNDC I, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Kasturi Srinivasachar
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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) SCM-030 06/30/03
5. Drug Name Avapro	6. Nonproprietary Name Irbesartan	7. Amendments & Other (reports, etc) - Dates
7. Supplement Provides for: Bristol-Myers Squibb Manufacturing Company (Barceloneta) as an additional manufacturer of irbesartan drug substance		
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
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 /x / Yes / / / No Reviewed /x / Yes / / / No
		
16. Comments: According to the Guidance For Industry - BACPAC I: Intermediate in Drug Substance Synthesis, February 2001, section IV.A.1 the site change for the synthesis of drug substance should be submitted in a Changes Being Effected Supplement. A request to inspect the BMS, Barceloneta facility was cancelled because the manufacturing site for the does not require inspection. The Office of Compliance did not change the status to acceptable. However, for similar situation, same date (October 6, 2003) and same EES request for NDA 20-758/S-029 the status was changed to ACCEPTABLE.		
17. Conclusions and Recommendations: The DMF # has been reviewed for the alternate site, Bristol-Myers Squibb Manufacturing Company (Barceloneta) to manufacture of the irbesartan synthesis as submitted in this supplement. The information provided in the DMF # is ADEQUATE to support the proposed changes. There are no changes to the synthetic process. This supplement may be approved.		
18. REVIEWER: Ramsharan D. Mittal		

2 Page(s) Withheld

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

 § 552(b)(5) Deliberative Process

 § 552(b)(5) Draft Labeling

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/s/

Ramsharan Mittal
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CHEMIST

Kasturi Srinivasachar
1/2/04 02:26:10 PM
CHEMIST



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-757/S-030

CBE-30/CBE-0 SUPPLEMENT

Sanofi-Synthelabo
c/o Bristol-Myers Squibb Company
Attention: Mr. George Zapf
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: 030

Date of supplement: June 30, 2003

Date of receipt: July 9, 2003

This supplemental application, submitted as "Supplement - Changes Being Effected" proposes to include Bristol-Myers Squibb Manufacturing Company (Barceloneta) as an approved manufacturer of 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 September 7, 2003, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be January 9, 2004.

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

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/s/

Zelda McDonald

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