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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 20-757/S-031

Sanofi-Synthelabo  
c/o Bristol-Myers Squibb Company  
Attention: David Ziering, Ph.D.  
P. O. Box 4000  
Princeton, NJ 08543-4000

Dear Dr. Ziering:

Please refer to your supplemental new drug application dated November 26, 2003, received November 28, 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.

This "Changes Being Effected in 30 days" supplemental new drug application provides for Bristol-Myers Squibb Manufacturing Company, Humacao, Puerto Rico, as an alternate manufacturing and release testing site of Avapro tablets.

We have completed our review of this supplemental application and it is 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,

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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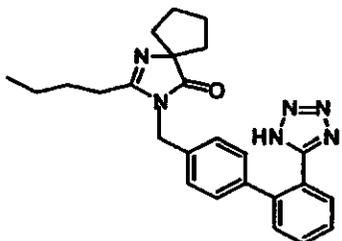
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/s/

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Kasturi Srinivasachar  
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**DIVISION OF CARDIO-RENAL DRUG PRODUCTS**

Review of Chemistry, Manufacturing, and Controls

<b>CHEMIST'S REVIEW</b>	<b>1. ORGANIZATION</b> HFD - 110	<b>2. NDA #</b> 20-757
<b>3. Name and Address of Applicant (City &amp; State)</b> Bristol-Myers Squibb Company P. O. Box 4000 Princeton, NJ 08543-5400		<b>4. Supplement(s) Number(s) Date(s)</b>  SCM-031 11/26/03
<b>5. Drug Name</b>  Avapro	<b>6. Nonproprietary Name</b>  Irbesartan	<b>7. Amendments &amp; Other (reports, etc) - Dates</b>
<b>7. Supplement Provides for:</b> CHANGES BEING EFFECTED IN 30 DAYS the Bristol-Myers Squibb in Humacao, Puerto Rico as an alternate drug product manufacturing and release testing site for Avapro 75 mg, 150 mg, and 300 mg tablets.		
<b>9. Pharmacological Category</b>  Angiotensin II Receptor Antagonist/Hypertension	<b>10. How Dispensed</b>  <input checked="" type="checkbox"/> / RX <input type="checkbox"/> / OTC	<b>11. Related IND(s)/ NDA(s)/DMF(s)</b>  NDA 20-758
<b>12. Dosage Form(s)</b>  Tablets	<b>13. Potency(ies)</b> 75 mg, 150 mg, and 300 mg.	
<b>14. Chemical Name and Structure</b>  2-Butyl-3-[(2'-(1H-tetrazol-5-yl)biphenyl-4-yl)methyl]-1,3-diazaspiro[4.4]non-1-en-4-one.  		<b>15. Records/Reports</b> Current <input checked="" type="checkbox"/> / Yes <input type="checkbox"/> / No  Reviewed <input checked="" type="checkbox"/> / Yes <input type="checkbox"/> / No
<b>16. Comments:</b>  CBE in 30 Days Supplement as per Changes to an Approved NDA or ANDA Guidance, 1999.		
<b>17. Conclusions and Recommendations:</b> The changes reported in the manufacturing of drug product involve addition of alternate drug product manufacturing site. EER status is acceptable. COAs, dissolution profiles, and stability data is satisfactory. Such supplements can be accepted as a CBE-30 and the supplement may be approved.		
<b>18. REVIEWER</b>  Ramsharan D. Mittal		

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

§ 552(b)(5) Deliberative Process

§ 552(b)(5) Draft Labeling

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/s/

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Ramsharan Mittal  
5/19/04 05:59:24 PM  
CHEMIST

Kasturi Srinivasachar  
5/20/04 12:08:21 PM  
CHEMIST



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 20-757/S-031

**CBE-30/CBE-0 SUPPLEMENT**

Sanofi-Synthelabo  
C/o Bristol-Myers Squibb  
Attention: David Ziering, Ph.D.  
P.O. Box 4000  
Princeton, NJ 08543-4000

Dear Dr. Ziering:

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: 031

Date of supplement: November 26, 2003

Date of receipt: November 28, 2003

This supplemental application, submitted as "Supplement - Changes Being Effected in 30 days," proposes to manufacture and release-test the original/current formulation Avapro® (irbesartan) 75, 150, 300 mg Tablets at the Bristol-Myers Squibb site in Humacao, Puerto Rico.

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 27, 2004, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be May 28, 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 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

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/s/

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Zelda McDonald  
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