

020757 — S033/

020758 — S.031



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 20-757/S-033  
NDA 20-758/S-031

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 April 30, 2004, received May 3, 2004, 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 August 31, 2004.

These supplemental new drug applications provide for the BMS Cruiserath bulk drug substance facility, located in Dublin, Ireland as a new manufacturing site for the irbesartan drug substance synthesis.

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 Cheryl Ann Borden, Regulatory Health Project Manager, at (301) 594-5315.

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

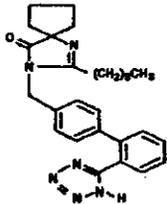
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/s/

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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 Number</b> 20-757
<b>3. Name and Address of Applicant (City &amp; State)</b> Bristol-Myers Squibb Company P. O. Box 5400 Princeton, NJ 08543-5400		<b>4. Supplement(s) Number(s) Date(s)</b>  SCM-033 04/30/04
<b>5. Drug Name</b> Avapro	<b>6. Nonproprietary Name</b> Irbesartan	<b>7. Amendments &amp;</b>
<b>7. Supplement Provides for:</b> PRIOR APPROVAL SUPPLEMENT BMS Cruiserath, bulk drug substance facility, located in Dublin, Ireland as a new manufacturing site : $\left[ \begin{array}{c} \text{ } \\ \text{ } \end{array} \right]$		
<b>9. Pharmacological Category</b>  Angiotensin II Receptor Antagonist/Hypertension	<b>10. How Dispensed</b>  <u>/x</u> / RX / / OTC	<b>11. Related IND(s)/ NDA(s)/DMF(s)</b> NDA 20-758 DMF( $\left[ \begin{array}{c} \text{ } \\ \text{ } \end{array} \right]$ )
<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. Comments:</b> As per Changes to Approved NDA or ANDA Guidance, dated April 2004, the process changes and supporting information described in this supplement are submitted in a Prior Approval Supplement.		
<b>16. Conclusions and Recommendations:</b> The DMF # $\left[ \begin{array}{c} \text{ } \\ \text{ } \end{array} \right]$ has been reviewed for the changes submitted in this supplement. The information provided in DMF is ADEQUATE to support BMS Cruiserath, bulk drug substance facility as a new manufacturing site $\left[ \begin{array}{c} \text{ } \\ \text{ } \end{array} \right]$ . The action date for this supplement is September 3, 2004 and per EER milestone the inspection will be conducted between September 6 - 9, 2004. Except for the inspection of the facility, there is no pending CMC issue. A final action on this supplement can only be taken after the recommendation is received from Office of Compliance regarding the cGMP status of the BMS Cruiserath facility.		
<b>17. REVIEWER</b> Ramsharan D. Mittal		

7 Page(s) Withheld

§ 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  
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CHEMIST

Kasturi Srinivasachar  
9/2/04 06:41:45 PM  
CHEMIST



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 20-757/S-033

**PRIOR APPROVAL 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: 033  
Date of supplement: April 30, 2004  
Date of receipt: May 3, 2004

This supplemental application proposes that the BMS Cruiserath bulk drug substance facility, located in Dublin, Ireland, be included in Bristol-Myers Squibb's Drug Master File (DMF) [redacted] as an additional approved supplier of irbesartan final drug substance ☐

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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 July 2, 2004, in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be September 3, 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 me at (301) 594-5332.

Sincerely,

  
{See appended electronic signature page}

Edward Fromm  
Acting 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/

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Edward Fromm  
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