020757_5026+5025
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 in the synthesis of the drug substance, irbesartan, and a rework process for

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,

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
5/21/03 06:12:35 PM
### DIVISION OF CARDIO-RENAL DRUG PRODUCTS
Review of Chemistry, Manufacturing, and Controls

<table>
<thead>
<tr>
<th>CHEMIST’S REVIEW</th>
<th>1. ORGANIZATION</th>
<th>2. NDA Number</th>
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<tbody>
<tr>
<td>HPD - 116</td>
<td></td>
<td>20-757</td>
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<thead>
<tr>
<th>3. Name and Address of Applicant (City &amp; State)</th>
<th>4. Supplement(s)</th>
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<tbody>
<tr>
<td>Bristol-Myers Squibb Company</td>
<td>Number(s) Date(s)</td>
</tr>
<tr>
<td>P. O. Box 5400</td>
<td>SCS-026 11/22/02</td>
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<tr>
<td>Princeton, NJ 08543-5400</td>
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<tr>
<th>5. Drug Name</th>
<th>6. Nonproprietary Name</th>
<th>7. Amendments &amp; Other (reports, etc) - Dates</th>
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<tbody>
<tr>
<td>Avapro</td>
<td>Irbesartan</td>
<td>SCS-026(BC) 5/21/03</td>
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**7. Supplement Provides for:**

- **CHANGES BEING EFFECTED**
  - an alternative manufacturing [ ]
  - [ ] the drug substance, irbesartan
  - [ ] a rework process

<table>
<thead>
<tr>
<th>9. Pharmacological Category</th>
<th>10. How Dispensed</th>
<th>11. Related IND(s)/NDA(s)/DMF(s)</th>
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<tbody>
<tr>
<td>Angiotensin II Receptor</td>
<td>/ RX / OTC</td>
<td>NDA 20-758</td>
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<tr>
<td>Antagonist/Hypertension</td>
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<td>DMF</td>
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<tr>
<th>12. Dosage Form(s)</th>
<th>13. Potency(ies)</th>
<th>15. Records/Reports</th>
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<tbody>
<tr>
<td>Tablets</td>
<td>75 mg, 150 mg, 300 mg.</td>
<td>Current</td>
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<thead>
<tr>
<th>14. Chemical Name</th>
<th>16. Comments:</th>
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<tbody>
<tr>
<td>2-Butyl-3-[2'-(1H-tetrazol-5-yl)biphenyl-4-yl]methyl]-1,1-diazaspiro[4.4]non-1-en-4-one.</td>
<td>As per [ ], the process changes and supporting information described in this supplement are submitted in a CBE Supplement</td>
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<table>
<thead>
<tr>
<th>17. Conclusions and Recommendations:</th>
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</thead>
<tbody>
<tr>
<td>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.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>18. REVIEWER:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ramsharan D. Mittal</td>
</tr>
</tbody>
</table>
___ 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
5/21/03 04:38:25 PM
CHEMIST

Kasturi Srinivasachar
5/21/03 06:00:37 PM
CHEMIST
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 , □ which you are . ▼

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,

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/

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Zelda McDonald
12/18/02 01:57:31 PM