DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-758/S-032

Sanofi-Synthelabo
c/o Bristol-Myers Squibb
Attention: Ms. Grace Heckman, Director
P.O. Box 4000
Princeton, NJ 08543-4000

Dear Ms. Heckman:

Please refer to your supplemental new drug application dated 15 November 2004, received 15 November 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Avalide® (irbesartan/hydrochlorothiazide) 150/12.5, 300/12.5, and 300/25 mg Tablets.

We also acknowledge receipt of your submission dated 4 March 2005.

This supplemental new drug application provides for an additional strength of 300/25 mg tablet of Avalide® (irbesartan/hydrochlorothiazide) with draft labeling revised as follows:

1. **DESCRIPTION**, the last paragraph has been revised to include the new dose strength as follows:

   AVALIDE is available for oral administration in tablets containing either 150 mg or 300 mg of irbesartan combined with 12.5 mg of hydrochlorothiazide or 300 mg of irbesartan combined with 25 mg hydrochlorothiazide. Inactive ingredients include: lactose monohydrate, microcrystalline cellulose, pregelatinized starch, croscarmellose sodium, ferric oxide red, ferric oxide yellow, silicon dioxide, and magnesium stearate. In addition, the 300/25 mg pink film-coated tablet contains ferric oxide black, hypromellose-2910, PEG-3350, titanium dioxide, and carnauba wax.

2. **DOSAGE AND ADMINISTRATION, Dose Titration by Clinical Effect** has been revised as follows:

   - The first paragraph, second sentence stating "Recommended doses of AVALIDE, in order of increasing mean effect, are (irbesartan/hydrochlorothiaze) 150/12.5, 300/12.5, and 300/mg (two 15/12.5 tablets) has been changed to:

     Recommended doses of Avalide®, in order of increasing mean effect, are (irbesartan/hydrochlorothiazide) 150/12.5, 300/12.5, and 300/25 mg.

   - The second paragraph, second sentence stating "More than two tablets once daily is not recommended" has been deleted.

3. Under **HOW SUPPLIED,** the following paragraph and its table was revised to reflect the new dose strength:

    - Avalide® (irbesartan/hydrochorothiazed) Tablets are peach, biconvez, and oval with a heart debossed on one side and 2775 or 2776 on the reverse, supplied as follows (table depicting the two dose strengths) has been changed to:

      AVALIDE® (irbesartan-hydrochlorothiazide) 150/12.5 mg and 300/12.5 mg tablets are peach, biconvex, and oval with a heart debossed on one side and 2775 or 2776 on the reverse side. The 300/25 mg film-coated tablet is pink, biconvex, and oval with a heart debossed on one side and 2788 on the reverse side. Avalide® Tablets are supplied as follows: (table updated to reflect the three dose strengths)

4. Under **STORAGE**, the following sentence was revised:

    - Store at a temperature between 15° C and 30° (59° F and 86° F) [See USP] has been changed to:

      Store at 25° C (77° F); excursions permitted to 15° C - 30° C (59° F - 86° F) [see USP Controlled Room Temperature].

5. Minor administrative changes were noted and appear as follows:

    Distributed by:
    Bristol-Myers Squibb Sanofi-Synthelabo Partnership
    New York, NY 10016

    Bristol-Myers Squibb Company **sanofi~synthelabo**
    [Company Print Codes TBD] Revised TBD
    Bristol-Myers Squibb Company

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling text for the package insert. Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved supplement NDA 20-758/S-032**." Approval of this submission by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to the Division of Cardio-Renal Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions please call:

Cheryl Ann Borden, MSN, RN, CCRN, CCNS
Regulatory Health Project Manager
(301) 594 5312.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Acting Division Director
Division of Cardio-Renal Drug Products
Office of New Drug Evaluation I
Center for Drug Evaluation and Research

cc: Sanofi-Synthelabo
Attention: Ms. Nancy Kribbs
Director, Regulatory Affairs
9 Great Valley Pkwy
Bldg 31 131-L
Malverne, PA 19355

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Norman Stockbridge

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