CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

20-911

Approval Letter(s)

NDA 20-911

3M Pharmaceuticals
3M Center Building
270-3A-08
St. Paul, MN 55144

Attention: David M. Markoe, Jr.
Regulatory Specialist

Dear Mr. Markoe:

Please refer to your new drug application (NDA) dated May 11, 1998, received May 12, 1998, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Qvar 40 mcg and Qvar 80 mcg (beclomethasone dipropionate HFA 40 mcg and 80 mcg) Inhalation Aerosol.

We acknowledge receipt of your submissions dated September 8, 10, 11 and 23, and October 23, 1998, January 8 and 13, March 22, April 9, August 11 and 17, November 10, and December 2, 1999, and January 10, February 28, April 10, 14, and 20, May 16 and 24, June 23, July 31, August 4, 15, 18 and 29, and September 9, 13 and 14, 2000. The submission of a response to DMF on March 15, 2000, along with your submission of February 28, 2000, constituted a complete response to our February 18, 2000, action letter.

This new drug application provides for the use of Qvar 40 mcg and Qvar 80 mcg (beclomethasone dipropionate HFA 40 mcg and 80 mcg) Inhalation Aerosol for maintenance treatment of asthma as prophylactic therapy and for asthma patients who require systemic corticosteroid administration, where adding Qvar may reduce or eliminate the need for the systemic corticosteroids.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text, with the minor editorial revision listed below. Accordingly, the application is approved effective on the date of this letter.

> Increase the prominence of the words "Inhalation Aerosol" on the product cartons to match the size, font and prominence of the text in the established name.

The final printed labeling (FPL) must be identical and include the minor revision indicated to

the submitted draft labeling (package insert, patient's instructions for use submitted September 14, 2000, immediate container and carton labels submitted September 13, 2000). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug. As requested in your September 9, 2000, submission, for up to 4 months following launch you may utilize actuators that do not contain the strength in the embossed established name.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved NDA 20-911." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitment specified in your submission dated September 14, 2000. This commitment is listed below.

> 3M commits to submitting a supplement for prior approval under 21 CFR 314.70 to obtain an extension of the expiry period for any product configuration. Such a supplement will be supported by standard 3-lot regression analysis as described in the FDA draft guidance "Stability Testing of Drug Substance and Drug Products" (June, 1998), demonstrating that the product has a calculated shelf-life of at least the proposed expiry date.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitment, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

You are reminded of the following agreements.

a. [redacted]

b. An agreement to submit a more reliable method to monitor [redacted] in placebo, by March 31, 2001.

You are also reminded of your agreement to work with [redacted] the actuator/mouthpiece fabricators, to facilitate submission of Type III DMFs for the actuator/mouthpiece.

Be advised that, as of April 1, 1999, all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55 (or 601.27) for children below 12 years of age. We are deferring submission of your pediatric studies until December 1, 2001. However, in the interim, please submit your pediatric drug development plans within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric*

Exclusivity (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Ms. Sandy Barnes, Project Manager, at (301) 827-1055.

Sincerely,

/S/

Robert J. Meyer, M.D.
Director
Division of Pulmonary and Allergy Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

cc:
Archival NDA 20-911
HFD-570/Div. Files
HFD-570/S.Barnes
HFD-570/Nicklas
HFD-570/Chowdhury
HFD-570/Schroeder
HFD-570/Poochikian
HFD-570/Mcgovern
HFD-570/Sun
HFD-570/Wilson
HFD-570/Elashoff
HFD-570/Choi
HF-2/MedWatch (with labeling)
HFD-002/ORM (with labeling)
HFD-102/ADRA (with labeling)
HFD-102/Post-Marketing PM
HFD-104/Peds/T.Crescenzi (with labeling)
HFD-42/DDMAC (with labeling)
HFI-20/Press Office (with labeling)
HFD-400/OPDRA (with labeling)
HFD-613/OGD (with labeling)
HFD-095/DDMS-IMT
HFD-093/DDMS-IST (with labeling)
HFD-820/DNDC Division Director
DISTRICT OFFICE

Drafted by: SB/September 13, 2000
Initialed by:Y. Choi 9/14/00
T. McGovern 9/14/00
Huff 9/14/00
Schroeder 9/14/00
R. Meyer 9/14/00
final:
filename: N20911.AP

APPROVAL (AP) (with Phase 4 Commitments)