DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

F.O.I

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TRANSMITTED VIA FACSIMILE

Mr. Dan Henry, R.Ph.
Manager, North American Regulatory Affairs
Hoechst Marion Roussel, Inc.
10236 Marion Park Drive
P.O. Box 9707
Kansas City, MO 64134-0707

RE: NDA# 20-911
Qvar (beclomethasone dipropionate) Inhalation Aerosol
MACMIS ID# 7397

Dear Mr. Henry:

As part of its routine monitoring and surveillance program, the Division of Drug Marketing, Advertising, and Communications (DDMAC) has reviewed a press release issued on December 11, 1998, by Hoechst Marion Roussel (HMR) on PRNewswire ("New Studies Indicated That a New Asthma Medication Targets All Airways in the Lungs"), regarding Qvar (beclomethasone dipropionate) (BDP) Inhalation Aerosol, a chlorofluorocarbons (CFC)-free inhaled corticosteroid, that is an unapproved new drug product. Following are selected statements from the press release:

"New data ... showed that a new medication called Qvar (beclomethasone dipropionate), a CFC-free inhaled corticosteroid, targets all airways in the lungs....With the development of Qvar, many improvements have been incorporated into the inhaler. For example, finer aerosol particles are delivered with less impact than the old inhalers, and are able to reach into the smaller airways of the lungs...."

"'To test the clinical relevance of these findings,"..."we undertook a complex dose response study that demonstrated that QVAR was clinically as effective as 2.5 times the dose of CFC-BDP." Improved efficacy was achieved without any increase in side effects. The adverse event profile of QVAR compared favorably with that of CFC-BDP. Study results show that patients treated with QVAR reported significantly fewer adverse events than patients treated with CFC-BDP (cited reference: Thompson et al., Respiratory Medicine 1998: 92 (Suppl A): 33-39."

"Qvar is a CFC-free formulation of beclomethasone dipropionate (BDP) delivered as an extrafine aerosol from an MDI, using an improved press-and-breathe (P&B) inhaler device. Qvar has a unique drug deposition pattern that improved drug delivery to large and small airways. It was effective at doses as low as 40 micrograms (mcg) twice daily, approximately half the dose of current CFC-BDP, and the dose was delivered consistently from the inhaler...."

Based on the above statements, the December 11, 1998, press release is in violation of the Federal Food, Drug, and Cosmetic Act and its implementing regulations (see 21 CFR 312.7) because the labeling promotes an unapproved new drug product by making claims of safety and efficacy, including clinical superiority claims over currently marketed CFC-BDP inhaled corticosteroid products. However, such clinical claims have not been demonstrated by substantial evidence (i.e., adequate and well-controlled studies).

Furthermore, the overall message of various nonclinical claims in the press release misleadingly suggests a clinical benefit for Qvar when no such clinical significance has been demonstrated. Collectively, these statements suggest that Qvar is clinically superior to currently marketed CFC-BDP inhaled corticosteroid products because Qvar's non-CFC BDP smaller particle size traveling as an "extrafine aerosol from the MDI using an improved press and breathe inhaler device" provided "improved drug delivery" with its "unique drug deposition pattern", for more diffuse drug deposition at a dose that is less than half that recommended for CFC-BDP, to "target" and reach large and small lung airways for "improved efficacy" and more favorable safety.

However, the implications of such nonclinical claims are misleading. For instance, notwithstanding an "improved press and breathe inhaler device" and "unique drug deposition pattern" of the more diffusely distributed drug that "targets all airways", there is no known correlation between these nonclinical findings (as identified in radiolabeled drug deposition scintigraphy studies) and increased clinical safety or efficacy. Furthermore, although Qvar may "target all airways", a wider drug distribution does not necessarily correlate with all the airways receiving the drug. In addition, this claim implies that other similar medications do not reach the small airways; however, data exist to show that these other medications also reach the small airways.

Moreover, based on a review of HMR's submitted safety data base, the press release includes a misleading statement that "Qvar reported significantly fewer adverse events." Finally, the press release generally fails to provide fair balance to the various promotional claims, and a citation to a referenced journal article does not remedy this misleading presentation.

DDMAC requests that the distribution and use of materials containing these and similar misleading claims cease immediately, including but not limited to, its removal from the PRNewswire website.

HMR should respond in writing no later than January 12, 1999, to the undersigned at the Food and Drug Administration, Division of Drug Marketing, Advertising and Communications, HFD-40, Rm 17-B-20, 5600 Fishers Lane, Rockville, MD 20857. DDMAC reminds HMR that only written communications are considered official.

In all future correspondence regarding this particular matter, please refer to MACMIS ID# 7397 in addition to the NDA number.

Sincerely,

Joan Hankin, JD
Regulatory Review Officer
Division of Drug Marketing,
Advertising, and Communications