

SCHERING CORPORATION

2000 GALLOPING HILL ROAD



KENILWORTH, N.J. 07033

TELEPHONE: (908) 298-4000

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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

**SUBJECT: DOCKET NO. 2003P-0029;
USE OF OZONE-DEPLETING SUBSTANCE;
REMOVAL OF ESSENTIAL-USE DESIGNATIONS**

Dear Sir or Madam,

Schering-Plough firmly supports the Montreal Protocol and the FDA's effort to coordinate removal of ozone-depleting substances (ODSs) in order to protect public health and the environment. In the June 16, 2004, proposed rule the FDA has invited comment on several aspects of the final implementation of the rule to amend its regulations (21 CFR Part 2, Section 2.125, paragraph(e)(2)(i)) to remove the essential-use designation for albuterol used in oral pressurized metered-dose inhalers. This document provides Schering-Plough's comments in response to the proposed rule.

Suitable Alternatives Already Are Available To Patients In The U.S.

In the proposed rule, the FDA has tentatively determined that two non-ODS MDIs are satisfactory alternatives to albuterol MDIs containing ODSs, and has indicated that two such products currently exist on the market. Proventil HFA and Ventolin HFA are the two products reviewed by the FDA and determined to be safe and effective - receiving marketing approval in 1996 and 2001, respectively. Proventil HFA delivers the same amount of drug on the same dosage schedule as Proventil; however, it does not contain CFC propellant. We agree with FDA's conclusion that these HFA products fulfill all of the criteria identified in section IV.A., namely that they have (1) the same active moiety, (2) the same route of administration, (3) the same indication and (4) approximately the same level of convenience of use as the ODS-containing products.

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Adequate Supply of Alternatives

The question identified by the FDA in section IV.B. is not whether suitable alternatives exist but when supplies and production capacity for non-ODS products will exist at levels sufficient to meet patient need. Based upon the expertise it has acquired as the leading developer of albuterol products, Schering-Plough has determined that a 12 month transition period after the final rule has been published until the exemption is ended is optimal to allow for adequate ramp-up of manufacturing supply capabilities. However, in order to facilitate the earliest possible effective date, we will initiate appropriate activities to enable adequate supplies by December 31, 2005 in anticipation of publication of the final rule as previously projected by FDA to occur in March 2005. Should the final rule indicate an effective date that is significantly later than December 2005, we may need to adjust the timing of the ramp-up of manufacturing capabilities. However, Schering-Plough is committed to meeting our expected production levels for the HFA inhalers consistent with the final effective date. For reasons described in the next section, an effective date of December 2005 would also address other key concerns.

Proposed timing of the Effective date

Choosing an effective date of December 2005 is important for several reasons. First, as mentioned in the proposed rule, the parties to the Montreal Protocol may deny continued applications by the U.S. for allocation of CFCs. In light of the fact that the Montreal Technical Group has discussed a target date of 2005 and that other countries (most of the European Union, Canada, Australia, Japan) have achieved the transition to HFA alternatives, it is unclear how much beyond 2005 CFC allocations will be granted to the U.S.

Second, the supply of CFCs from Honeywell's Weert facility must end by the end of 2005. While some CFC inventory is maintained by Schering-Plough and other CFC MDI manufacturers, it is reasonable to expect that all manufacturers will plan their future CFC purchases carefully to coincide with the phase out deadline. Therefore, it is not realistic to expect that the industry will have sufficient supplies from Weert to support CFC MDI manufacture long into the future. Furthermore, qualifying a new source for CFC production involves significant technical work by any MDI manufacturer, and carries technical risk. Should the effort to qualify an alternate source in Schering-Plough's existing CFC-based MDI be unsuccessful, a dramatic disruption in MDI supply is not only possible, but likely, based on the market utilization of Schering-Plough's supply. This disruption can be avoided by planning for an orderly transition coincident with the elimination of this critical raw material source no later than December 2005.

Third, the December 2005 date provides adequate time for effective implementation of patient education programs. Schering-Plough believes that a critical component of an effective switch from CFC-containing albuterol products to non CFC-containing products is patient education. It is important to communicate to patients and providers that HFA inhalers are as safe and effective as the CFC inhalers to which most patients are accustomed. Proper use of the inhaler must be communicated to patients to address the difference in sensation when using a HFA inhaler and the necessity of proper cleaning of the device. The impact of an expanded successful patient and provider educational campaign will be highly dependent on implementing

the various elements at the right time in relation to a proposed effective date. These programs, to be maximally effective, will need to be timed in coordination with the transition date established by FDA so that the asthma community can be optimally prepared. The December 2005 date would allow appropriate time to prepare patients and healthcare providers for the switch away from ODS products.

In the proposed rule, FDA discussed the possibility of delaying the effective date of the essential use ban to be closer to a time when generic versions of HFA inhalers would be on the market. Such a delay would be problematic because there is no reasonable basis to conclude that generic manufacturers would or could drive the critical communications program required to reach core stakeholders including patients, retail pharmacists and wholesalers, physicians, and managed care.

Innovator pharmaceutical firms have invested in strong infrastructures, inclusive of numerous field forces for specific audiences and patient education and assistance programs, and have established communication channels with these key stakeholders that will be critical to an orderly and smooth transition of patients. The business model for generic firms, however, is predicated on market acceptance of generic products based exclusively on price. This model will not provide a context for any meaningful communication with key stakeholders about the CFC ban and an orderly transition of patients.

This is not a situation – like generic clozapine or generic isotretinoin – in which generic firms could be compelled to offer patient education programs to support these products. Further, we are not aware of any programs offered by generic firms that assist patients who cannot afford the product. In contrast, companies marketing branded pharmaceuticals do provide such assistance programs (see next section). The presence of both education and financial assistance programs is necessary to assure a smooth and orderly transition for patients given the complexities and market dynamics involved.

With regard to timing, Schering-Plough views the transition as an important opportunity to engage the healthcare community to reinforce the appropriate treatment of respiratory conditions. The transition from CFC to HFA products should not be viewed in isolation. Instead, the transition should be seen as being facilitated when it is conducted by organizations with an understanding and long-term commitment to the respiratory community. Through field forces, patient assistance and education programs, public relations efforts and stakeholder education Schering-Plough will commit to these key elements necessary for an orderly transition. These communication channels offer a significant advantage to ensuring the greatest level of patient support during the transition.

Patient Access

Schering-Plough is committed to ensuring that patients who need Proventil HFA have access and are adequately served. Reflecting this strong commitment to meeting patients' needs, Schering-Plough created the SP Cares Program in 1994 to provide primary care products free of charge for patients who qualify. This program is available for Proventil HFA patients. Last year alone, Schering-Plough patient assistance programs provided products free of charge to more than 75,000 low income and uninsured patients. Further, we provided more Proventil brand of products to qualified individuals than any other Schering-Plough drug.

Access to the SP Cares program is broad and easy. Most people learn about the program through their doctors' office. Following publication of the final rule we plan a series of communications to Health Care providers that will include information about the SP Cares program and how it can help their patients who use Proventil HFA. Additionally, information about SP Cares is available on the Schering-Plough corporate web site, on PhRMA's web site, and on the web sites of numerous patient assistance clearinghouses.

Public health benefits of the transition

The increased communication among stakeholders supporting the transition will offer a renewed opportunity for physicians and patients to increase their general dialogue about asthma management. It is well-known that many asthma patients do not regularly visit their healthcare provider. A visit to the healthcare provider prompted by the switch to an HFA inhaler will allow for a re-assessment of the patient's condition and adjustment of treatment, if medically appropriate. This includes addressing over-utilization of albuterol products and careful consideration of moving patients to more suitable medications when deemed appropriate in accordance with established clinical guidelines. Such a medical reevaluation will be especially useful for those patients who may not have seen a physician for some time.

Conclusion

Schering-Plough supports the FDA's proposed rule to amend section 2.125 by removing paragraph (e)(2)(i), i.e., eliminating the essential use designation for albuterol. We are committed to supporting the FDA and the asthma community in effecting a successful transition. The focus throughout the transition from CFC to HFA inhalers must be on education and communication efforts towards patients and providers. We support publication of the final rule in March 2005 with an effective date of December 2005, at which time we would be prepared to meet our production levels to ensure that asthma patients who need Proventil HFA are adequately served.

Sincerely,



Ronald Garutti, M.D.
Group Vice President
Global Regulatory Affairs