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26 June 2007

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

Re: Docket No. 2006N-0454 (June 11, 2007)
Use of Ozone-Depleting Substances; Removal of Essential Use
Designations Proposed Rule

REQUEST FOR EXTENSION OF COMMENT PERIOD

Graceway Pharmaceuticals, LLC (Graceway) hereby submits the following request for an immediate 90 day extension of the comment period for the above-referenced proposed rule, from August 10, 2007, to November 9, 2007. As shown below, Graceway cannot feasibly submit a complete and thorough comment within the 60 days provided. *See* 21 CFR 10.40(b)(3). Moreover, Graceway expects that new information relevant to the governing legal standard will not become available for several more months and that, overall, sound public policy supports an extension of the comment period. *Id.*

Graceway is the sponsor of the new drug application for Maxair® Autohaler® (pirbuterol acetate inhalation aerosol), one of the products directly impacted by the proposed rule. Graceway is a small business, with fewer than 300 employees in the United States and fewer than 100 employees outside of the United States. The rule would have a significant impact on Graceway, both with respect to current revenue and future development plans, making it imperative that Graceway be given sufficient time to prepare a thorough analysis and comment.

I. Additional Time is Needed to Gather the Evidence

After carefully reviewing the proposed rule, Graceway believes it will not be feasible for the company to collect the evidence needed to respond to the proposed rule within a 60 day period. The proposal involves complex issues around whether products with different active ingredients, different formulations, and different delivery systems may be used in place of other products. The patient population at issue in this rulemaking consists primarily of asthma sufferers, many of whom have grown accustomed to their inhaler of choice, and many of whom may have a particular need for a particular product. The process of gathering evidence from Maxair users, and gathering evidence from

2006N-0454

EXT 1

clinicians who rely on Maxair as a key therapeutic option, will take two to three times more than the 60 day period provided by the agency.

Similarly, the process of analyzing the agency's assumptions about the use of four HFA-based products, in place of Maxair, will require far more than 60 days. *See* 72 FR 32030, 32036. This process will require a comprehensive and expert analysis of the agency's economic assessment, which appears to omit the added costs to Maxair users of spacer devices, other healthcare costs associated with materially changing a patient's asthma management program, and the dynamic pricing in the inhaler market, particularly as generic CFC products are withdrawn from the market. This process will also require a detailed analysis of the comparative safety and effectiveness of each of the four HFA products with Maxair, and the possible retention of experts to assist in that analysis. The 60 day period the agency has provided to respond to the specifics of the proposal is simply inadequate to ensure full development of the administrative record.

II. Additional Time is Needed for the Submission of Confidential Information and the Development of Important New Information

The 60 day period is insufficient to address the absence in the proposed rule of a mechanism by which sponsors may submit confidential commercial and trade secret information for consideration as part of the rulemaking proceeding. One of the pivotal factors in this matter is whether there are "substantial technical barriers" to the reformulation of the product without ozone-depleting substances. *See* 21 CFR 2.125(f)(1). The bulk of the evidence relating to this factor is confidential; it is, however, imperative that the administrative record be complete on each factor that bears on the ultimate determination. Thus, additional time is needed to establish a mechanism to allow for the submission to the record of confidential evidence, and then to allow sponsors adequate time to assemble and draft their submissions.

Graceway is also actively working with several outside entities on reformulation plans, and Graceway intends to meet with the Division of Pulmonary and Allergy Products to review its development program, once a suitable outside vendor has been identified. Graceway only recently acquired ownership of Maxair Autohaler and, thus, does not expect to have that information in place until after the August 10, 2007, deadline. In the proposed rule, the agency specifically requested comment on the effective date, including comment on the time needed to reformulate to a non-ODS product. Graceway expects to have that information by or about October 2007, but not before that time.

Last, FDA must hold one or more public meetings, to hear from patients, healthcare providers and other interested persons, before making a determination on whether a product remains "essential." 21 CFR 2.125(g)(2). This meeting is required by law and integral to the determination of whether a product is essential to patients. As of the date of this letter, only 45 days remain in the comment period and the agency has yet to issue any form of public notice on the scheduling of a meeting. Even if the meeting were to occur before August 10, 2007, the agency would be required to leave open the comment period for post-meeting submissions, and allow for companies such as Graceway to integrate the evidence

gathered during the meeting into their comments. In one recent proceeding, the agency left the docket open for comment for 120 days following a public meeting. *See* 70 FR 48428 (Aug. 17, 2005). The information that arises from the public meeting is integral to the proceeding but likely will not be available to interested persons by the close of the comment period or, at least, in enough time to allow for meaningful comment.

III. Public Policy Also Supports an Extension for Comment

There are sound public policy reasons to extend the comment period. Approximately 400,000 patients in the United States rely on Maxair Autohaler as part of a comprehensive asthma management program. Among other things, Maxair Autohaler provides patients with the convenience and ease of use of a breath actuated delivery system. Under the proposed rule, Maxair patients are being asked to accept a change in active ingredient and formulation, as well as a change to the delivery system on which they have been trained and have come to rely. A number of Maxair Autohaler patients previously failed on albuterol therapy or otherwise selected Maxair, in consultation with their doctor, in place of an albuterol product. It is vitally important to public health and policy that the comment period permit full and complete development of the administrative record on these and other critical points.

When compared with other recent proceedings on specific categories of drug products, including asthma products, a 60 day comment period seems markedly brief. For example, the agency provided a 120 day comment period for its recent proposed rule classifying hydroquinone products, used for skin bleaching, as new drugs. *See* 71 FR 51146 (Aug. 29, 2006). The basis for the hydroquinone rule was new data suggesting that hydroquinone products may cause cancer in humans. Nevertheless, the agency provided a four month comment period. Relative to the hydroquinone proceeding, a 60 day comment period in this instance, where an immediate safety signal is not at issue, seems unwarranted.

Similarly, in the two most recent proposed rules involving bronchodilator and asthma drug products, the agency also allowed a 120 day comment period. *See* 70 FR 40237 (July 13, 2005) (proposing to add "Asthma alert" and revise labeling of over-the-counter bronchodilator products); 70 FR 40232 (July 13, 2005) (proposing to remove certain over-the-counter combination bronchodilator products from monograph consideration). In the current proceeding, the agency has proposed an effective date of December 31, 2009, and specifically asked for comments on whether the date should be extended. A change in the comment period to November 9, 2007, would still be more than two full years before the rule is proposed to go into effect.

There is, thus, little justification for limiting the comment period to 60 days.¹ On the other hand, given the impact the rule would have on hundreds of thousands of asthma patients, and the significant impact on small businesses such as Graceway, there are ample and compelling reasons to extend the comment period by at least 90 days.

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In sum, the issue of removing CFCs from the environment has been a decades long process. Graceway fully supports and recognizes the public interest in reducing the use of CFCs. At the same time, with respect to medical products considered to be essential to public health, the process for doing so is a lengthy one. For example, the agency provided the sponsors of albuterol MDI products four and one-half years – from the date of the proposal to the final effective date – to cease marketing CFC-containing products, and in that situation there were available alternatives with the same active moiety. In this context, allowing several months additional time for development of the record hardly imposes an unreasonable burden on the agency or on public health.

Finally, we urge the agency to reach a decision on this request immediately, rather than defer a decision until the end of the 60 day comment period. Again, as a small business, Graceway has limited resources to devote to this and other projects. The earlier we can be informed of a decision, the more efficiently and effectively we can use our resources.

Respectfully submitted,



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Chairman and Chief Executive Officer

cc: Steven K. Galson, M.D., M.P.H.
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¹ While the agency provided a 60 day comment period for the proposal to remove albuterol from the essential use list, the albuterol rule involved a transition from albuterol chlorofluorocarbon (CFC) products to albuterol hydrofluoroalkane (HFA) products already on the market. The current proceeding involves a more complex showing, in which patients are being asked to move to products with different active ingredients and, in the case of Maxair Autohaler, different delivery systems requiring different physical demands.