July 21, 2003

Dockets Management Branch (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

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03P-0029

Re: Docket No. ~~039-0029~~
Citizen Petition Requesting FDA Initiate a Rulemaking to Consider Whether CFC Albuterol MDIs are an Essential Use of Ozone-Depleting Substances

Dear Sir/Madame:

On January 29, 2003, nine organizations representing patients with asthma, chronic obstructive pulmonary disease ("COPD") and other respiratory diseases, physicians specializing in the treatment of these diseases, respiratory therapists, and other healthcare professionals specializing in respiratory care petitioned the Commissioner of Food and Drugs to initiate rulemaking to remove metered-dose inhalers ("MDIs") containing the active moiety albuterol from the list of essential uses of ozone-depleting substances ("ODS") set forth in the Food and Drug Administration's ("FDA") regulation at 21 CFR § 2.125(e)(2).

These nine organizations respectfully submit this supplemental information, in part to respond to comments since entered into the Docket, and also to provide updated information regarding the international supply of a particular ODS, chlorofluorocarbons (CFCs). First, we respond to Document No. 0322 filed on June 3, 2003, the comments of Edward Allera (an attorney who fails to identify the "We" he represents), contending that the Petitioners have failed to provide compelling evidence that each of the specific criteria are met. Second, we respond to Mr. Allera's claim that mere initiation of a rulemaking will harm patients because CFC manufacturers will abruptly exit the market. Lastly, we provide further evidence of why in light of the global commitment to eliminate ODSs, FDA's initiation of a rulemaking is both appropriate and necessary in order to properly protect the millions of U.S. patients who rely on inhaled therapies.

1. THERE IS LEGAL JUSTIFICATION FOR COMMENCING A RULEMKAING

Mr. Allera claims that Petitioners have not satisfied the legal requirements that must be met before the Agency may initiate a rulemaking. Petitioners maintain that we have provided FDA with ample information to trigger the opening of the rulemaking process. Further, we argue that to construe the rule as requiring Petitioners to provide anything additional would be an absurd interpretation of the evidentiary prerequisite. For example, it would be illogical to interpret the rule to suggest that Petitioners need to show an adequate supply of CFC-free products – under no circumstances would Petitioners ever be able to show compelling evidence of such a thing. For the purposes of evidence to justify the initiation of a rulemaking, it should be sufficient to show that there are established, multiple manufacturing sites.[1] The comments submitted into the docket on behalf of GlaxoSmithKline support this interpretation – only individual

[1] Petitioners note that the International Pharmaceutical Aerosols Consortium (IPAC) recently published a statement calling for the elimination of CFC albuterol products ("Metered Dose Inhaler Transition Issues at the Twenty-Third Meeting of the Open Ended Working Group to the Montreal Protocol," IPAC, July 2003.) Petitioners assume this to mean that the manufacturers themselves believe there is now, or can be by the time of a final essentiality determination, adequate production capacity for CFC-free albuterol.

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manufacturers themselves can present to the Agency specific evidence of capacity to ensure adequate supply and to estimate timeframes in which product supply can be made available.

Given the nature of this rulemaking, Petitioners suggest that *the rule must be construed so as to place the burden on the Agency of collecting further ("compelling") information* on many of the criteria. Much of the information that the Agency will need to make an essentiality determination is company proprietary and confidential and will never be in Petitioner's hands. Moreover, the Agency will need to consider information from a variety of sources, making it impossible for all necessary information to ever be held by any one petitioner. Petitioners contend that the evidentiary requirement must be construed so as to require enough evidence be presented such that the Agency believes, through a data collection effort, complete evidence could be gathered to support a final essentiality determination.

2. MERE INTITIATION OF A RULEMAKING WILL NOT HAVE HARMFUL CONSEQUENCES ON PATIENTS

Mr. Allera alleges that mere FDA action to initiate a rulemaking will inexplicably cause CFC suppliers to shut down, leaving patients without CFC-containing MDIs. Petitioners find this claim to be ridiculous. While issues regarding long-term future supply of CFCs remain (as do uncertainties regarding the economics of producing fewer CFC MDIs as the worldwide elimination of ozone-depleting chemicals proceeds), commenters do not explain how mere initiation of a rulemaking by FDA will change these global circumstances or bring about the dire consequences alleged.

The questions about future supply of U.S.-certified, pharmaceutical-grade CFCs are well known to the many parties involved. The sole manufacturer certified to provide CFCs for MDIs to be sold in the U.S., Honeywell, is at the request of the Dutch government closing its production facility in Weert, The Netherlands on or before December 31, 2005.[2] But Honeywell's publicly-stated business plan is to consolidate worldwide CFC manufacture at its Baton Rouge, Louisiana plant prior to the Weert closure. Honeywell is actively seeking FDA approval for its Louisiana facility, and the company repeatedly has stated its commitment to supplying its customers with pharmaceutical-grade CFCs until they are no longer needed. Yet commenters, without any basis in fact, assert that mere initiation of a regulatory action by U.S. FDA could lead Honeywell to abruptly exit the market. To the contrary, Petitioners believe that the statements of Honeywell make obvious that the company, like all other interested actors, is well-aware of the development and adoption of CFC-free MDIs in most of the developing world and expects if not awaits FDA action to effect transition in the U.S.

[2] While it was previously believed that other manufacturers, Atofina for instance, might seek to obtain certification from U.S. FDA to begin providing pharmaceutical-grade CFCs for products to be sold in the U.S., that effort now seems to have been abandoned. Since Honeywell will be the only supplier of pharma-grade CFCs to the U.S., commenters repeated reference to "suppliers" appears to be in error.

3. UNCERTAINTIES REGARDING LONGTERM SUPPLY OF CFCs AND OTHER MDI COMPONENTS, AS WELL AS THE INTERNATIONAL COMMITMENT TO ELIMINATE OZONE-DEPLETING CHEMICALS, MAKES IT INCUMBENT UPON FDA TO PREPARE FOR TRANSITION BY INITIATING A RULEMAKING WITH FULL NOTICE AND COMMENT

Contrary to Mr. Allera's comments alleging that a rulemaking will harm patients, Petitioners argue that *FDA's failure to initiate a rulemaking could have severe consequences to patients.* As mentioned above, there are still uncertainties regarding the long-term supply of CFCs. Costs too are at issue because as developed countries phase out CFC-containing MDIs, the fixed costs of production will need to be spread among fewer MDI units sold in the U.S. There is also concern about long-term supply and costs of the thirty-plus components of the increasingly outdated CFC MDI technology. These uncertainties, in addition to the mounting international pressure on the U.S. to demonstrate true progress on transition, collectively places U.S. patients at risk if there is no preparation whatsoever for transition. The exemption provided for MDIs to continue using ODS was not meant to last indefinitely – that is why most developed countries are on pace to phaseout CFC MDIs by 2005, why MDI manufacturers have spent hundreds of millions of dollars developing and commercializing alternatives, and why patient and medical professional organizations have spent the last nine years engaged in the process, committed to ensuring a safe transition. For FDA to simply sit back and let economic and/or international circumstances dictate how transition will occur in the U.S. is to abdicate its responsibility to protect patients.

At the most recent meeting of the Montreal Protocol Parties, the body that provides technical and economic expertise to signatory nations reiterated that "...for the final transition to be seamlessly and safely implemented, the issue of price needs to be fully explored, understood and dealt with effectively."[3] In requesting FDA initiate a rulemaking, Petitioners are in effect stating the same thing – that the question of how transition will impact patients must be thoroughly considered. As stated on page 11 of our Petition, we believe FDA must undertake a full consideration of these issues in an open and public manner, and we maintain that a rulemaking with full notice and comment is the appropriate forum for doing so. Absent an FDA rulemaking, we fear these issues will not be thoughtfully addressed, and patients in the U.S. will be harmed by being forced to switch to CFC-free treatments in a manner and on a timeline that is determined by politics or market economics, not safety and fairness.

While we believe the Agency has sufficient grounds to proceed with a rulemaking, we suggest that if the Agency believes it needs additional information, it include in the proposed rule a series of questions raised by transition. The Agency also could schedule an Advisory Committee hearing in advance of the notice and comment period to further clarify the issues to be addressed in determining whether the medical needs of patients will be adequately served.

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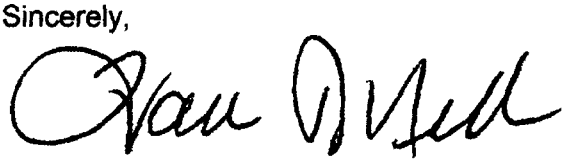
[3] Statement of Dr. Ashley Woodcock at the Twenty-Third Meeting of the Open Ended Working Group, Montreal, Canada, 7 July 2003, citing the May 2003 TEAP Progress Report at p.110.

Petitioners support prompt issuance of a proposed rule and scheduling of any necessary Advisory Committee hearings, and look forward to a complete and meaningful process that ensures patients will be adequately protected as the U.S. complies with its obligations to eliminate ozone-depleting chemicals.

Sincerely,



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