AVAILABLE FOR PUBLIC DISCLOSURE WITHOUT REDACTION

BACKGROUND INFORMATION

ANDA 87-907 was approved on May 23, 1984 for Epinephrine Inhalation Aerosol, USP. The product was contract manufactured by Armstrong Laboratories and its predecessors. Armstrong acquired rights to the ANDA on June 30, 2004, and reintroduced the generic for Primatene® to the market at that time, following approximately three (3) years without a generic presence in the market. The generic epinephrine is sold as a private label product through a number of retail chains. The product is not distributed under the Armstrong brand.

Whether Primatene® or Armstrong's generic, Epinephrine Inhalation Aerosol is the only over-the-counter rescue asthma medication available in the United States. While recognizing that Epinephrine Inhalation Aerosol is not the drug of choice for physicians treating asthma patients, this product serves a vital and irreplaceable role in serving this patient population. The product serves two basic asthma markets that would otherwise be left without any available medication choice.

The first market segment consists of those patients suffering an acute asthmatic episode who failed to carry their prescribed asthma inhaler. For those patients, often traveling away from home, the availability of an over-the-counter asthma inhaler can be and often is a literal lifesaver.

There is also a segment of the asthma population who are economically distressed and without adequate insurance coverage. These patients cannot afford to see a physician or pay for the more expensive prescription asthma inhalation products. As the only over-the-counter asthma inhaler available, Epinephrine Inhalation Aerosol is the only treatment option for these individuals.

CURRENT USAGE

Armstrong's current use of chlorofluorocarbon propellants for its Epinephrine Inhalation Aerosol product is less than 25 metric tons annually. Using IMS Health Data as the basis for calculation, the total use for Epinephrine Inhalation Aerosol is less than 54 tons. The total use of CFC propellants for both Primatene Mist and generic Epinephrine Inhalation Aerosol amounts to only 3.5% of the entire Essential Use Allocation for 2005[1] of 1524.58 metric tons. The amount is miniscule compared to the total authorized for use.

COMMITMENT

Armstrong Pharmaceuticals, Inc. is committed to the development of a non-Ozone Depleting propellant formulation for Epinephrine Inhalation Aerosol, and is in active discussions with the owner of the Primatene® branded product to work in cooperation to produce such a formulation. Although previous attempts have been unsuccessful,

[1] Federal Register Vol. 69, No. 245, December 22, 2004, 76655 at 76657-58

Armstrong has filed patent applications on two different HFA formulations of Epinephrine Inhalation Aerosol. Work to finalize a formulation is ongoing and expected to be completed with clinical trial material available in less than 19 months. Clinical trials are planned, with an eventual filing of an NDA near in the latter portion of this decade. With cooperation from FDA, the completion of this project could be advanced by twelve or more months.

ESSENTIALITY CRITERIA

21 CFR 2.125 sets out the criteria for both determining that a use is an essential use and for determining when the essential use designation no longer applies to a product. A product is considered to fall into the essential use category when:

- Substantial technical barriers exist to formulating the product without ozone depleting substances;
- The product provides an otherwise unavailable important public health benefit;
- Use of the product does not release cumulatively significant amounts of ozone depleting substances into the atmosphere or the release is warranted in view of the otherwise unavailable important public health benefit.

Epinephrine Inhalation Aerosol clearly fits these criteria. As seen by previous unsuccessful attempts to formula a non-CFC Epinephrine Inhalation Aerosol by Wyeth, there are significant and substantial technical barriers to formulating the product without ozone depleting substances. As demonstrated both by Wyeth and Armstrong's presentations, there is no available alternative over-the-counter substitute for the current CFC formulations of Epinephrine Inhalation Aerosol. Finally, the potential amount of CFC emission resulting from the use of the currently approved formulations of Epinephrine Inhalation Aerosol represents only 3.5% of the total allocated CFC propellants for 2005.

NON-ESSENTIALITY CRITERIA

Conversely, 21 CFR 2.125 sets forth the following criteria for determining that a CFC product no longer qualifies for an essential use designation:

- At lease one non-ODS product with the same active moiety is marketed with the same route of administration, for the same indication, and with approximately the same level of convenience of use as the ODS product containing active moiety;
- Supplies and production capacity for the non-ODS product(s) exist or will exist at levels sufficient to meet patient need;
- Adequate U.S. postmarketing use data is available for the non-ODS product(s); and
- Patients who medically required the ODS product are adequately served by the non-ODS product(s) containing that active moiety and other available products.

Epinephrine Inhalation Aerosol clearly falls outside the non-essentiality criteria. There are no other over-the-counter, non-ODS Epinephrine Inhalation Aerosol products available in the U.S. There are no supplies or production of a non-ODS Epinephrine Inhalation Aerosol product in the U.S. There is no postmarketing data available for a non-ODS U.S. Epinephrine Inhalation Aerosol product. Patients who medically require an Epinephrine Inhalation Aerosol product, either as an emergency rescue treatment or for long term use against ongoing asthma incidents have no choice other than use of the CFC Epinephrine Inhalation Aerosol, simply because there are no other over-the-counter substitutes available.
Therefore we urge the Advisory Committee to find that the CFC Epinephrine Inhalation Aerosol products retain their essential use designation until the non-essentiality criteria are fully met by the HFA Epinephrine Inhalation Aerosol currently under development by Wyeth Consumer Products and Armstrong Laboratories, Inc.

HISTORICAL ISSUES

There is a long history of the safe and efficacious use of epinephrine in a number of indications over the last century. Primatene (epinephrine inhalation aerosol) has been in use as an FDA approved treatment for asthma over 38 years, and the generic has been available for over 21 years. The efficacy and side effects profile is well known and well understood.

On September 19, 1994, the Division of Oncology and Pulmonary Drug Products, published a Guidance for Industry titled, "Points to Consider: Clinical Development Programs for MDI and DPI Drug Products." That guidance recommended that a two-phase long-term trial in adult patients be performed. The first phase consists of two 12-week active and placebo controlled safety and efficacy studies, followed by a 200 patient open label safety study following patients for one full year.

This guidance has consistently been applied to conversions of products from CFC formulations to HFA formulations. However, since 1994, both the FDA and industry have accumulated a significant amount of data regarding the changes in delivery between CFC and HFA propellants and the overall safety of HFA propellants. The following HFA propellant products have been approved by the FDA:

NDA NUMBER	PRODUCT	HOLDER	APPROVAL DATE	YEARS EXPERIENCE
020503	Proventil HFA	3M	8/15/96	9+ years
020983	Ventolin HFA	GSK	4/19/01	4+ years
021433	Flovent HFA	GSK	5/14/04	1 ½+ years
021457	Albuterol Sulfate HFA	IVAX	10/29/04	16 months
Cumulative Experience with HFA				16+ years

The cumulative years experience does not include the clinical development time for each of the above products, which in following the above referenced guidance is a minimum of three years for each product or twelve years additional experience.

Based on the extent of the experience with HFA propelled products, and in the interest of expediting further elimination of ozone depleting propellant use, we strongly urge the Division of Pulmonary and Allergy Drug Products revisit the current guidance and consider either eliminating the requirement for a one year, 200 patient safety study, or at a minimum, consider making such a study a post approval Phase IV study. For Epinephrine Inhalation Aerosol HFA, the development timeline could be reduced by at least one full year, speeding the removal of the Essential Use designation for this product type.